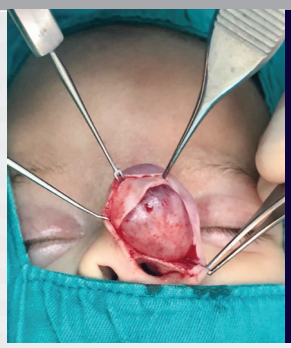
Indexed in PubMed and Web of Science

EISSN 2667-7474

Volume 59 ~ Issue 1 ~ March 2021

Turkish Archives of Otorhinolaryngology

Official Journal of the
Turkish Otorhinolaryngology
Head and Neck Surgery Society



Congenital Mucocele of Nasal Dorsum

Page 84

Original Investigations

turkarchotolaryngol.net

galenos Publishing House

Turkish Archives of Otorhinolaryngology
Türk Otorinolarengoloji Arşivi

Owner and Responsible Manager on behalf of the Turkish Otorhinolaryngology Head and Neck Surgery Society / Türk Kulak Burun Boğaz ve Baş Boyun Cerrahisi Derneği adına Sahibi ve Sorumlu Yazı İşleri Müdürü: Özgür YİĞİT • Publication Type: Yerel süreli / Local periodical • Basım yeri / Printed at: Matsis Matbaa Hizmetleri San. ve Tic.Ltd.Şti, Tevfikbey Mah., Dr. Ali Demir Cad. No: 51, 34290 Sefaköy, Turkey (+90-212-624 21 11) • Basım tarihi / Printing Date: Eylül 2020 / September 2020 • Türk Kulak Burun Boğaz ve Baş Boyun Cerrahisi Derneği tarafından yayımlanmaktadır. Published by Turkish Otorhinolaryngology Head and Neck Surgery Society, Çobançeşme Sanayi Cad. No: 11 Nish İstanbul A Blok D: 8 Yenibosna, İstanbul, Turkey (+90 212 233 11 26)

galenos yayınevi

Galenos Publishing House
Owner and Publisher
Derya Mor
Erkan Mor

Publication Coordinator
Burak Sever

Web Coordinators
Fuat Hocalar
Turgay Akpınar

Graphics Department
Ayda Alaca
Çiğdem Birinci
Gülşah Özgül

Project Coordinators
Aysel Balta
Meltem Acar
Duygu Yıldırm
Hatice Sever
Gamze Aksoy
Gülay Akın
Özlem Çelik Çekil
Pınar Akpınar
Rabia Palazoğlu
Melike Eren

Digital Marketing Specialist
Seher Altundemir

Research & Development
Nihan Karamanlı
Melisa Yiğitoğlu

Finance Coordinator
Sevinç Çakmak

Publisher Contact
Address: Molla Gürani Mah. Kaçamak Sk. No: 21/1
34093 İstanbul, Turkey
Phone: +90 (212) 621 99 25 **Fax:** +90 (212) 621 99 27
E-mail: info@galenos.com.tr/yayin@galenos.com.tr
Web: www.galenos.com.tr **Publisher Certificate Number:** 14521

Publication Date: March 2021
E-ISSN: 2667-7474

International scientific journal published quarterly.

Turkish Archives of Otorhinolaryngology
Türk Otorinolarengoloji Arşivi

International Editorial Board

Turkish Archives of Otorhinolaryngology
Türk Otorinolarengoloji Arşivi

Turkish Archives of Otorhinolaryngology
Türk Otorinolarengoloji Arşivi

Aims and Scope

The Turkish Archives of Otorhinolaryngology (Turk Arch Otorhinolaryngol) is the scientific, peer reviewed, open access journal of the Turkish Otorhinolaryngology Head and Neck Surgery Society. The journal is released at three-month intervals, in March, June, September and December, and one volume of the journal comprises four issues. The journal's publication language is English.

The aim of the journal is to publish qualified original clinical, experimental and basic researches on ear, nose, throat, head and neck diseases and surgery, reviews that contain sufficient amount of source data conveying the experiences of experts in a particular field, case reports and original images of rare clinical pictures which would shed light on the clinical practice and which were not previously published, letters from the readers and experts concerning the published studies, articles about general practice and subject of the journal with historical content, memories of scientific significance, educative and catechetical manuscripts about medical deontology and publication ethics.

Target audience of the journal includes academic members, specialists, residents and other relevant health care professionals in the field of ear, nose, throat, and head and neck disorders and surgery.

The editorial and publication processes of the journal are shaped in accordance with the guidelines of the International Committee of Medical Journal Editors (ICMJE), World Association of Medical Editors (WAME), Council of Science Editors (CSE), Committee on Publication Ethics (COPE), European Association of Science Editors (EASE), and National Information Standards Organization (NISO). The journal is in conformity with the Principles of Transparency and Best Practice in Scholarly Publishing (doaj.org/bestpractice).

Turkish Archives of Otorhinolaryngology is indexed in PubMed Central, Web of Science-Emerging Sources Citation Index, TUBITAK ULAKBIM TR Index, DOAJ, EBSCO, CINAHL and ProQuest.

Processing and publication are free of charge with the journal. No fees are requested from the authors at any point throughout the evaluation and publication process. All manuscripts must be submitted via the online submission system, which is available at www.turkarchotolaryngol.net. The journal guidelines, technical information, and the required forms are available on the journal's web page.

All expenses of the journal are covered by the Turkish Otorhinolaryngology Head and Neck Surgery Society. Potential advertisers should contact the Editorial Office. Advertisement images are published only upon the Editor-in-Chief's approval.

Statements or opinions expressed in the manuscripts published in the journal reflect the views of the author(s) and not the opinions of the Turkish Otorhinolaryngology Head and Neck Surgery Society, editors, editorial board, and/or publisher; the editors, editorial board, and publisher disclaim any responsibility or liability for such materials.

All published content is available online, free of charge at www.turkarchotolaryngol.net. Printed copies of the journal are distributed to the members of the Turkish Otorhinolaryngology Head and Neck Surgery Society, free of charge.

The journal is printed on an acid-free paper.

OPEN ACCESS

Editor in Chief: Taner Kemal Erdağ
Address: Çobançeşme Sanayi Cad. No: 11 Nish İstanbul A Blok D: 8 Yenibosna, İstanbul, Turkey
Phone: +90 (212) 233 11 26
Fax: +90 (212) 233 11 27
E-mail: kbb@kbb.org.tr

Publisher: GALENOS YAYINEVİ
Address: Molla Güranı Mah. Kaçamak Sok. No: 21 /1
34093 Fatih - İstanbul, Turkey
Gsm: +90 (530) 177 30 97
Tel: +90 (212) 621 99 30 / +90 (212) 621 99 25
Fax: +90 (212) 621 99 27
Mail: info@galenos.com.tr
Web: galenos.com.tr

Turkish Archives of Otorhinolaryngology
Türk Otorinolarengoloji Arşivi

Instructions to Authors

CONTEXT

The Turkish Archives of Otorhinolaryngology (Turk Arch Otorhinolaryngol) is an international, scientific, open access periodical published by independent, unbiased, and double-blinded peer-review principles. The journal is the official publication of the Turkish Otorhinolaryngology Head and Neck Surgery Society, and published quarterly in March, June, September and December. The publication language of the journal is English.

The aim of the journal is to publish qualified original clinical, experimental and basic researches on ear, nose, throat, head and neck diseases and surgery, reviews that contain sufficient amount of source data conveying the experiences of experts in a particular field, case reports and original images of rare clinical pictures which would shed light on the clinical practice and which were not previously published, letters from the readers and experts concerning the published studies, articles about general practice and subject of the journal with historical content, memories of scientific significance, educative and catechetical manuscripts about medical deontology and publication ethics.

EDITORIAL AND PUBLICATION PROCESS

The editorial and publication processes of the journal are shaped in accordance with the guidelines of the International Council of Medical Journal Editors (ICMJE), the World Association of Medical Editors (WAME), the Council of Science Editors (CSE), the Committee on Publication Ethics (COPE), the European Association of Science Editors (EASE), and National Information Standards Organization (NISO). The journal conforms to the Principles of Transparency and Best Practice in Scholarly Publishing (doaj.org/bestpractice).

Originality, high scientific quality, and citation potential are the most important criteria for a manuscript to be accepted for publication. Manuscripts submitted for evaluation should not have been previously presented or already published in an electronic or printed medium. The journal should be informed of manuscripts that have been submitted to another journal for evaluation and rejected for publication. The submission of previous reviewer reports will expedite the evaluation process. Manuscripts that have been presented in a meeting should be submitted with detailed information on the organization, including the name, date, and location of the organization.

PEER REVIEW PROCESS

Manuscripts submitted to The Turkish Archives of Otorhinolaryngology will go through a double-blind peer-review process. Each submission will be reviewed by at least two external, independent peer reviewers who are experts in their fields in order to ensure an unbiased evaluation process. The editorial board will invite an external and independent editor to manage the evaluation processes of manuscripts submitted by editors or by the editorial board members of the journal. The Editor in Chief is the final authority in the decision-making process for all submissions.

ETHICAL PROCEDURES

An approval of research protocols by the Ethics Committee in accordance with international agreements (World Medical Association Declaration of Helsinki "Ethical Principles for Medical Research Involving Human Subjects," amended in October 2013, www.wma.net) is required for experimental, clinical, and drug studies and for some case reports. If required, ethics committee reports or an equivalent official document will be requested from the authors. For manuscripts concerning experimental research on humans, a statement should be included that shows that written informed consent of patients and volunteers was obtained following a detailed explanation of the procedures that they may undergo. For studies carried out on animals, the measures taken to prevent pain and suffering of the animals should be stated clearly. Information on patient consent, the name of the ethics committee, and the ethics committee approval number should also be stated in the Materials and Methods section of the manuscript. It is the authors' responsibility to protect the patients' anonymity carefully.

For photographs that may reveal the identity of the patients, signed releases of the patient or their legal representative should be enclosed, and the publication approval must be provided in the Materials and Methods section.

PLAGIARISM

The Turkish Archives of Otorhinolaryngology is extremely sensitive about plagiarism. All submissions are screened by a similarity detection software (iThenticate by CrossCheck) at any point during the peer-review and/or production process. Even if you are the author of the phrases or sentences, the text should not have unacceptable similarity with the previously published data.

When you are discussing others' (or your own) previous work, please make sure that you cite the material correctly in every instance.

In the event of alleged or suspected research misconduct, e.g., plagiarism, citation manipulation, and data falsification/fabrication, the Editorial Board will follow and act following COPE guidelines.

AUTHORSHIP

Each person listed as an author should fulfill the authorship criteria recommended by the International Committee of Medical Journal Editors (ICMJE - www.icmje.org). The ICMJE recommends that authorship is based on the following four criteria:

1. Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND

2. Drafting the work or revising it critically for important intellectual content; AND

3. Final approval of the version to be published; AND

4. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

In addition to being accountable for the parts of the work he/she has done, an author should be able to identify which co-authors are responsible for specific other parts of the work. Also, authors should have confidence in the integrity of the contributions of their co-authors.

All those designated as authors should meet all four criteria for authorship, and all who meet the four criteria should be identified as authors. Those who do not meet all four criteria should be acknowledged in the title page of the manuscript.

The Turkish Archives of Otorhinolaryngology requires corresponding authors to submit a signed and scanned version of the authorship contribution form (available for download through www.turkarchotolaryngol.net) during the initial submission process to act appropriately on authorship rights and to prevent ghost or honorary authorship. If the editorial board suspects a case of "gift authorship," the submission will be rejected without further review. As part of the submission of the manuscript, the corresponding author should also send a short statement declaring that he/she accepts to undertake all the responsibility for authorship during the submission and review stages of the manuscript.

DECLARATION OF INTEREST

The Turkish Archives of Otorhinolaryngology requires and encourages the authors and the individuals involved in the evaluation process of submitted manuscripts to disclose any existing or potential conflicts of interests, including financial, consultant, and institutional, that might lead to potential bias or a conflict of interest. Any financial grants or other support received for a submitted study from individuals or institutions should be disclosed to the Editorial Board. To disclose a potential conflict of interest, the ICMJE Potential Conflict of Interest Disclosure Form should be filled in and submitted by all contributing authors. The journal's Editorial Board resolves cases of a potential conflict of interest of the editors, authors, or reviewers within the scope of COPE and ICMJE guidelines.

The Editorial Board of the journal handles all appeal and complaint cases within the scope of COPE guidelines. In such cases, authors should get in direct contact with the editorial office regarding their appeals and complaints. When needed, an ombudsperson may be assigned to resolve claims that cannot be resolved internally. The Editor in Chief is the final authority in the decision-making process for all appeals and complaints.

COPYRIGHT AND LICENSE

The Turkish Archives of Otorhinolaryngology requires each submission to be accompanied by a Copyright License Agreement (available for download www.turkarchotolaryngol.net). When using previously published content, including figures, tables, or any other material in both print and electronic formats, authors must obtain permission from the copyright holder. Legal, financial and criminal liabilities in this regard belong to the author(s). By signing the Copyright License Agreement, authors retain the copyright of their work and agree that the article, if accepted for publication by the The Turkish Archives of Otorhinolaryngology will be licensed under a Creative Commons Attribution 4.0 International License (CC BY).

DISCLAIMER

Statements or opinions expressed in the manuscripts published in the Turkish Archives of Otorhinolaryngology reflect the views of the author(s) and not the opinions of the editors, the editorial board, or the publisher; the editors, the editorial board, and the publisher disclaim any responsibility or liability for such materials. The final responsibility regarding the published content rests with the authors.

MANUSCRIPT PREPARATION

The manuscripts should be prepared in accordance with ICMJE-Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals (updated in December 2019 - http://www.icmje.org/icmje-recommendations.pdf). Authors are required to prepare manuscripts in accordance with the CONSORT guidelines for randomized research studies, STROBE guidelines for observational original research studies, STARD guidelines for studies on diagnostic accuracy, PRISMA guidelines for systematic reviews and meta-analysis, ARRIVE guidelines for experimental animal studies, and TREND guidelines for non-randomized public behavior.

Manuscripts can only be submitted through the journal's online manuscript submission and evaluation system, available at www.turkarchotolaryngol.net. Manuscripts submitted via any other medium and submissions by anyone other than one of the authors will not be evaluated.

Manuscripts submitted to the journal will first go through a technical evaluation process where the editorial office staff will ensure that the manuscript has been prepared and submitted in accordance with the journal's guidelines. Submissions that do not conform to the journal's guidelines will be returned to the submitting author with technical correction requests.

Authors are required to submit the following:

- Copyright Agreement and Acknowledgement of Authorship Form, and

Instructions to Authors

- ICMJE Potential Conflict of Interest Disclosure Form (should be filled in by all contributing authors) during the initial submission. These forms are available for download at www.turkarchotolaryngol.net.

Preparation of the Manuscript

Title page: A separate title page should be submitted with all submissions and this page should include:

- The full title of the manuscript as well as a short title (running head) of no more than 50 characters,
- Name(s), affiliations, highest academic degree(s), and ORCID IDs of the author(s),
- Grant information and detailed information on the other sources of support,
- Name, address, telephone (including the mobile phone number), and email address of the corresponding author,
- Acknowledgment of the individuals who contributed to the preparation of the manuscript but who do not fulfill the authorship criteria.

Abstract: An abstract should be submitted with all submissions except for Letters to the Editor. The abstract of Original Articles should be structured with subheadings (Objective, Methods, Results, and Conclusion). Please check Table 1 below for word count specifications.

Keywords: Each submission must be accompanied by a minimum of three to a maximum of six keywords for subject indexing at the end of the abstract. The keywords should be listed in full without abbreviations. The keywords should be selected from the National Library of Medicine, Medical Subject Headings database (https://www.nlm.nih.gov/mesh/MBrowser.html).

Main Points: All submissions except letters to the editor and clinical images should be accompanied by 3 to 5 "main points" which should emphasize the most noteworthy results of the study and underline the principle message that is addressed to the reader. This section should be structured as itemized to give a general overview of the article. Since "Main Points" targeting the experts and specialists of the field, each item should be written as plain and straightforward as possible.

Manuscript Types

Original Articles: This is the most important type of article since it provides new information based on original research. The main text of original articles should be structured with Introduction, Methods, Results, Discussion, and Conclusion subheadings. Please check Table 1 for the limitations for Original Articles.

Statistical analysis to support conclusions is usually necessary. Statistical analyses must be conducted in accordance with international statistical reporting standards (Altman DG, Gore SM, Gardner MJ, Pocock SJ. Statistical guidelines for contributors to medical journals. Br Med J 1983: 7; 1489-93). Information on statistical analyses should be provided with a separate subheading under the Materials and Methods section and the statistical software that was used during the process must be specified.

Units should be prepared in accordance with the International System of Units (SI).

Editorial Comments: Editorial comments aim to provide a brief critical commentary by reviewers with expertise or with high reputation in the topic of the research article published in the journal. Authors are selected and invited by the journal to provide such comments. Abstract, Keywords, and Tables, Figures, Images, and other media are not included.

Review Articles: Reviews prepared by authors who have extensive knowledge on a particular field and whose scientific background has been translated into a high volume of publications with a high citation potential are welcomed. These authors may even be invited by the journal. Reviews should describe, discuss, and evaluate the current level of knowledge of a topic in clinical practice and should guide future studies. The main text should contain Introduction,

Table 1. Limitations for each manuscript type

Type of manuscript	Author limit	Word limit	Abstract word limit	Reference limit	Table limit	Figure limit
Original Article	N/A	3500	250 (Structured)	30	6	5 or total of 10 images
Review Article	4	5000	250	50	6	10 or total of 15 images
Case Report	6	1000	200	10	No tables	4 or total of 8 images
Letter to the Editor	3	500	No abstract	5	No tables	No media
Clinical Images	3	500	No abstract	5	No tables	3 or total of 7 images

Clinical and Research Consequences, and Conclusion sections. Please check Table 1 for the limitations for Review Articles.

Case Reports: There is limited space for case reports in the journal and reports on rare cases or conditions that constitute challenges in diagnosis and treatment, those offering new therapies or revealing knowledge not included in the literature, and interesting and educative case reports are accepted for publication. The text should include Introduction, Case Presentation, Discussion, and Conclusion subheadings. Please check Table 1 for the limitations for Case Reports.

Letters to the Editor: This type of manuscript discusses important parts, overlooked aspects, or lacking parts of a previously published article. Articles on subjects within the scope of the journal that might attract the readers' attention, particularly educative cases, may also be submitted in the form of a "Letter to the Editor." Readers can also present their comments on the published manuscripts in the form of a "Letter to the Editor." Abstract, Keywords, and Tables, Figures, Images, and other media should not be included. The text should be unstructured. The manuscript that is being commented on must be properly cited within this manuscript.

Clinical Images: This type of submissions should present a striking image that may challenge and inform readers and contribute to their education. Submissions can include high quality clinical images, radiology results or surgical images. Please check Table 1 for the limitations for Clinical Images.

Tables

Tables should be included in the main document, presented after the reference list, and they should be numbered consecutively in the order they are referred to within the main text. A descriptive title must be placed above the tables. Abbreviations used in the tables should be defined below the tables by footnotes (even if they are defined within the main text). Tables should be created using the "insert table" command of the word processing software and they should be arranged clearly to provide easy reading. Data presented in the tables should not be a repetition of the data presented within the main text but should be supporting the main text.

Figures and Figure Legends

Figures, graphics, and photographs should be submitted as separate files (in TIFF or JPEG format) through the submission system. The files should not be embedded in a Word document or the main document. When there are figure subunits, the subunits should not be merged to form a single image. Each subunit should be submitted separately through the submission system. Images should not be labeled (a, b, c, etc.) to indicate figure subunits. Thick and thin arrows, arrowheads, stars, asterisks, and similar marks can be used on the images to support figure legends. Like the rest of the submission, the figures too should be blind. Any information within the images that may indicate an individual or institution should be blinded. The minimum resolution of each submitted figure should be 300 DPI. To prevent delays in the evaluation process, all submitted figures should be clear in resolution and large in size (minimum dimensions: 100 × 100 mm). Figure legends should be listed at the end of the main document.

All acronyms and abbreviations used in the manuscript should be defined at first use, both in the abstract and in the main text. The abbreviation should be provided in parentheses following the definition.

When a drug, product, hardware, or software program is mentioned within the main text, product information, including the name of the product, the producer of the product, and city and the country of the company (including the state if in USA), should be provided in parentheses in the following format: "Discovery St PET/CT scanner (General Electric, Milwaukee, WI, USA)"

All references, tables, and figures should be referred to within the main text, and they should be numbered consecutively in the order they are referred to within the main text.

Limitations, drawbacks, and the shortcomings of original articles should be mentioned in the Discussion section before the conclusion paragraph.

References

Both in-text citations and the references must be prepared according to the Vancouver style.

While citing publications, preference should be given to the latest, most up-to-date publications. Authors are responsible for the accuracy of references If an ahead-of-print publication is cited, the DOI number should be provided. Journal titles should be abbreviated in accordance with the journal abbreviations in Index Medicus/MEDLINE/PubMed. When there are six or fewer authors, all authors should be listed. If there are seven or more authors, the first six authors should be listed followed by "et al." In the main text of the manuscript, references should be cited using Arabic numbers in parentheses. The reference styles for different types of publications are presented in the following examples.

Journal Article: Erkul E, Cekin İE, Kurt O, Gungor A, Babayigit MA. Evaluation of patients with unilateral endoscopic sinus surgery. Turk Arch Otorhinolaryngol 2012; 50: 41-5.

Book Section: Suh KN, Keystone JS. Malaria and babesiosis. Gorbach SL, Barlett JG, Blacklow NR, editors. Infectious Diseases. Philadelphia: Lippincott Williams; 2004.p.2290-308.

Books with a Single Author: Sweetman SC. Martindale the complete drug reference. 34th ed. London: Pharmaceutical Press; 2005.

Editor(s) as Author: Huizing EH, de Groot JAM, editors. Functional reconstructive nasal surgery. Stuttgart-New York: Thieme; 2003.

Conference Proceedings: Bengisson S. Sothemin BG. Enforcement of data protection, privacy and security in medical informatics. In: Lun KC, Degoulet P, Piemme TE, Rienhoff O, editors. MEDINFO 92.

Proceedings of the 7th World Congress on Medical Informatics; 1992 Sept 6-10; Geneva, Switzerland. Amsterdam: North-Holland; 1992. pp.1561-5.

Scientific or Technical Report: Cusick M, Chew EY, Hoogwerf B, Agrón E, Wu L, Lindley A, et al. Early Treatment Diabetic Retinopathy Study Research Group. Risk factors for renal replacement therapy in the Early Treatment Diabetic Retinopathy Study (ETDRS), Early Treatment Diabetic Retinopathy Study Kidney Int: 2004. Report No: 26.

Thesis: Yılmaz B. Ankara Üniversitesindeki öğrencilerin beslenme durumları, fiziksel aktiviteleri ve beden kitle indeksleri kan lipidleri arasındaki ilişkiler. H.Ü. Sağlık Bilimleri Enstitüsü, Doktora Tezi. 2007.

Manuscripts Accepted for Publication, Not Published Yet: Slots J. The microflora of black stain on human primary teeth. Scand J Dent Res. 1974.

Epub Ahead of Print Articles: Cai L, Yeh BM, Westphalen AC, Roberts JP, Wang ZJ. Adult living donor liver imaging. Diagn Interv Radiol. 2016 Feb 24. doi: 10.5152/dir.2016.15323. [Epub ahead of print].

Manuscripts Published in Electronic Format: Morse SS. Factors in the emergence of infectious diseases. Emerg Infect Dis (serial online) 1995 Jan-Mar (cited 1996 June 5): 1(1): (24 screens). Available from: URL: http:/ www.cdc.gov/ncidodlElD/cid.htm.

REVISIONS

When submitting a revised version of a paper, the author must submit a detailed "Response to the reviewers" that states point by point how each issue raised by the reviewers has been covered and where it can be found (each reviewer's comment, followed by the author's reply and line numbers where the changes have been made) as well as an annotated copy of the main document. Revised manuscripts must be submitted within 30 days from the date of the decision letter. If the revised version of the manuscript is not submitted within the allocated time, the revision option may be canceled. If the submitting author(s) believe that additional time is required, they should request this extension before the initial 30-day period is over.

Accepted manuscripts are copy-edited for grammar, punctuation, and format. Once the publication process of a manuscript is completed, it is published online on the journal's webpage as an ahead-of-print publication before it is included in its scheduled issue. A PDF proof of the accepted manuscript is sent to the corresponding author and their publication approval is requested within 2 days of their receipt of the proof.

WITHDRAWAL POLICY

Out of respect to the reviewers, journal staff and the Editorial Board, authors are asked to submit a withdrawal request only if the reasons are compelling and unavoidable.

Withdrawal requests should be submitted in written form, signed by all contributing authors of the manuscript. Reasons for withdrawal should be stated clearly. Each request will be subject to the Editorial Board's review and manuscripts will only be assumed withdrawn upon Editorial Board's approval.

PEER-REVIEW AND ETHICS

Peer-review

Editorial policies of the journal are conducted according to the rules advised by Council of Science Editors and reflected in the Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication (http://www.icmje.org/).

Submitted manuscripts are subjected to single-blind peer-review. The scientific board guiding the papers' selection to be published in the Journal consists of elected experts of the Journal and if necessary, selected from national and international experts in the relevant field of research. All manuscripts are reviewed by the editor, section associate editors and at least three internal and external expert referees. All research articles undergo review by a statistical editor as well.

The authors of the accepted manuscripts should be in consent that the editor and associate editors could make corrections without changing the main text of the paper. Manuscript format should be in accordance with Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication (http://www.icmje.org/).

Turkish Archives of Otorhinolaryngology
Türk Otorinolarengoloji Arşivi

Instructions to Authors

Ethics

For the experimental, clinical and drug human studies, approval by ethical committee and statement on the adherence of the study protocol to the international agreements (Helsinki Declaration revised 2008 (www.wma.net/e/policy/b3.html) are required. In experimental animal studies, the authors should indicate that the procedures followed were in accordance with animal rights (Guide for the care and use of laboratory animals, www.nap.edu.catalog/5140.html) and they should obtain animal ethics committee approval. The Ethics Committee approval document should be submitted to the Turkish Archives of Otorhinolaryngology together with the manuscript.

The approval of the ethics committee, statement on the adherence to international guidelines mentioned above and that the patients` informed consent is obtained should be indicated in the `Material and Method` section and is required for case reports whenever data/media used could reveal the identity of the patient. The declaration of the conflict of interest between authors, institutions, acknowledgement of any financial or material support, aid is mandatory for authors submitting a manuscript and the statement should appear at the end of the manuscript. Reviewers are required to report if any potential conflict of interest exists between reviewer and authors, institutions.

Plagiarism: To re-publish whole or in part the contents of another author's publication as one's own without providing a reference.

Fabrication: To publish data and findings/results that do not exist. Duplication: Use of data from another publication, which includes re-publishing a manuscript in different languages.

Salamisation: To create more than one publication by dividing the results of a study preternaturally. We disapproval upon such unethical practices as plagiarism, fabrication, duplication, and salamisation, as well as efforts to influence the review process with such practices as gifting authorship, inappropriate acknowledgements, and references. Additionally, authors must respect participant right to privacy. On the other hand, short abstracts published in congress books that do not exceed 400 words and present data of preliminary research, and those that are presented in an electronic environment are not accepted pre-published work. Authors in such a situation must declare this status on the first page of the manuscript and in the cover letter. (The COPE flowchart is available at http://publicationethics.org) All responsibility of the articles published belongs to the authors.

Submitted manuscripts are also subjected for the evaluation of plagiarism, duplicate publication by automatic software. Authors are obliged to acknowledge if they published study results in full or in part in form of abstracts.

We use "iThenticate" to screen all submissions for plagiarism before publication.

Cases of plagiarism, authorship disputes or fraudulent use of data will be handled in accordance with COPE guidelines.

Editor in Chief: Taner Kemal Erdağ
Address: Çobançeşme Sanayi Cad. No: 11 Nish İstanbul A
Blok D: 8 Yenibosna, İstanbul, Turkey
Phone: +90 (212) 233 11 26
Fax: +90 (212) 233 11 27
E-mail: kbb@kbb.org.tr

Publisher: GALENOS YAYINEVİ
Address: Molla Güranı Mah. Kaçamak Sok. No: 21 /1
34093 Fatih - İstanbul, Turkey
Gsm: +90 (530) 177 30 97
Tel: +90 (212) 621 99 30 / +90 (212) 621 99 25
Fax: +90 (212) 621 99 27
Mail: info@galenos.com.tr
We page: galenos.com.tr

Turkish Archives of Otorhinolaryngology
Türk Otorinolarengoloji Arşivi

Contents

Turkish Archives of Otorhinolaryngology
Türk Otorinolarengoloji Arşivi

Editorial

Dear colleagues,

We are here with the first issue of 2021. This year there have been some changes in our journal. First of all, our publisher has changed. We would like to thank "AVES" which we have worked together successfully and in harmony for many years. We aim to achieve new successes with our new publisher "Galenos".

We hope you enjoy our new web page, which has been changed with the new year. Another important novelty is the article uploading and processing system. We think that with the new system, authors and reviewers will work more easily and efficiently. This system will also facilitate the work of the editorial board.

As the official journal of Turkish Otorhinolaryngology, Head and Neck Surgery Society, we will have some innovations in our 59th year. We hope that a comprehensive supplement on allergic rhinitis, which will be published in a few weeks, will be of great benefit to the ENT physicians. Another good news is about an online course, "Peer Review in Academic Journals" which will be held between April 7th-8th 2021. We invite all our colleagues to this course that will be organized with the support of the Turkish Otorhinolaryngology, Head and Neck Surgery Society and our publisher Galenos.

We would like to thank our authors, readers, and reviewers for their support and wish this year to be very successful for Turkish Archives of Otorhinolaryngology.

Taner Kemal Erdağ, MD
Editor in Chief

Effect of Suture Type and Suture Distance on Holding Strength in Nasal Septal Laceration Model

Original Investigation

Alper Köycü, Evren Hızal, Ozan Erol, Adnan Fuat Büyüklü

Department of Otolaryngology, Head and Neck Surgery, Başkent University, Ankara, Turkey

Abstract

Objective: Septal mucosal-perichondrial flaps can be lacerated during the elevation of the flaps. Appropriate repair of the lacerations is essential to prevent the development of septal perforation during the healing process. We aimed to determine the superior suture type and suture distance to use in repairing the lacerations of nasal septal mucosal-perichondrial flaps.

Methods: The study used 128 nasal septal mucosal-perichondrial flaps prepared from sheep heads. Experimentally induced lacerations on the mucosal-perichondrial flaps were sutured with two interrupted sutures using one of four suture materials (4-0/5-0 Polyglactin 910, 4-0/5-0 Polydioxanone) and leaving either 5 mm or 10 mm distance between the sutures. Maximum tissue holding strength (HS_{max}) was measured for each suture material and suture distance used.

Results: Mean HS_{max} values were higher for Polyglactin 910 sutures ($p<0.001$) and 10 mm suture distance ($p=0.008$) when the groups were compared in terms of suture material and suture distance, respectively. There was no statistically significant difference between the mean HS_{max} values of sutures with 4-0 and 5-0 diameters ($p=0.057$).

Conclusion: Polyglactin 910 suture material with 10 mm space between two adjacent sutures may be more durable than the other suture materials when repairing nasal septal mucosal lacerations.

Keywords: Holding strength, nasal septum, septal perforation, suture distance, suture material, cadaveric animal study

This manuscript has been presented in 40th Turkish National Congress of Otorhinolaryngology Head and Neck Surgery.

ORCID ID of the authors:

A.K. 0000-0003-1290-3509;
E.H. 0000-0002-9699-6783;
O.E. 0000-0002-4209-9403;
A.F.B. 0000-0003-1528-0036.

Cite this article as: *Köycü A, Hızal E, Erol O, Büyüklü AF. Effect of Suture Type and Suture Distance on Holding Strength in Nasal Septal Laceration Model. Turk Arch Otorhinolaryngol 2021; 59(1): 1-7.*

Corresponding Author:
Alper Köycü; alperkoycu@gmail.com

Received Date: 27.10.2020
Accepted Date: 15.02.2021

DOI: 10.4274/tao.2021.6100

Introduction

Nasal septal perforation is one of the complications of septorhinoplasty that can lead to uncomfortable symptoms such as crusting, a feeling of nasal obstruction and epistaxis (1). Closure of the nasal septal perforation generally requires additional surgery that is technically difficult, and even if surgical closure is successful, nasal symptoms may persist even in the long-term follow-up (2, 3). Therefore, all necessary measures should be taken to prevent the development of septal perforation.

During septorhinoplasty, unwanted tears of the septal mucosal perichondrium and/or periosteum may occur. Especially in revision septorhinoplasty cases, septal

mucosal-perichondrial flaps can be lacerated during the elevation of the flaps. Appropriate repair of the lacerations is essential to prevent the development of septal perforation during the healing process. For a successful repair, the wound edges should be approximated end-to-end with minimal tissue tension. However, it can be hard to achieve tension-free closure, especially in revision cases. As the intranasal area is narrow and the surgeon has limited space for maneuvers, the repair of nasal septal mucosal-perichondrial lacerations can be quite challenging, especially when the gap between the wound edges is large. In addition, the sutures must be able to remain in the correct position until mucosal healing is completed, without opening, breaking, or causing secondary mucosal tears. In attempt to overcome technical difficulties in septal mucosal-perichondrial suturation, various suture materials and techniques have been developed (4-6). However, the effect of different suture materials and/or techniques on wound closure and prevention of septal perforation remains controversial.

Tensile strength is the maximum power of the suture resisting breakage. Holding strength, on the other hand, is defined as the amount of force that results in violation of the tissue or slippage of the suture (7). Together with the tensile strength of the suture, the holding strength of the tissue is also important to achieve stable wound closure. Approximation of the wound edges in nasal septal lacerations may result in tension in the flaps, making the holding strength of the flaps critical for the successful repair of the defect. There are studies in the literature that have measured the holding strength in various tissues such as the kidney (7, 8). To the best of our knowledge, the holding strength of nasal septal mucosa is unknown. In addition, the effects of the suture material and the distance between the sutures on the holding strength in nasal septum mucosa are yet to be established.

The aim of this study was to measure the holding strength of nasal septal mucosal-perichondrial flaps that have been experimentally lacerated and repaired with various suture materials applied at different spatial intervals.

Methods

This experimental study was conducted between March and May 2018, at Başkent University Hospital, Department of Otolaryngology, Head and Neck Surgery. This study was approved by Başkent University's Institutional Review Board (project no: DA18/09, date: 18.09.2018). Seventy heads of slaughtered young adult merino sheep (6–12 months of age) were obtained from a butcher. Sheep nasal septums that were unintentionally torn during submucosal-perichondrial elevation were excluded from the study. A total of 128 nasal septal mucosal-perichondrial flaps prepared from the 64 heads of sheep were used. The flaps were lacerated and repaired with various suture materials applied at different spatial intervals. The maximum holding strength (HS_{max}) of the sutured flaps were then measured and compared with each other.

The sheep heads were stored at a temperature of 2–4 °C for conservation until the procedures were performed and frozen specimens were not used. All test procedures were performed at room temperature within 24 hours of each animal's death.

Preparation of Nasal Septal Mucosal-Perichondrial Flaps

The nasal septum was completely removed from the sheep head. The thickness of the mucosal-perichondrial layer varies throughout the craniocaudal axis of the sheep's nasal septum. The most caudal part of the nasal septum is covered with the thickest layer of mucosa-perichondrium and the thickness of the mucosal-perichondrial wall decreases as it advances cranially. To enable standardized measurements, the middle third section of the septum, i.e., the region between the 4th and 8th cm from the most caudal part of the septum, was used (Figure 1). Bilateral mucosal-perichondrial flaps were elevated from the cartilage septum, except for the most dorsal and ventral 1 cm-height parts. The flaps were not raised along the dorsal and ventral borders of the septum, keeping the 1 cm-height mucosal-perichondrial attachments to the underlying cartilage intact. Septal cartilage between those superior and inferior 1 cm-height edges was removed. The upper cartilage strip that was left intact was then longitudinally cut into two equal parts, resulting in two mucosal-perichondrial leaves on either side of the septal base. A horizontal incision was made through the mid-height of the mucosal-perichondrial leaf to simulate a tear. The incision was then sutured with two interrupted sutures using one of the four suture materials described below and leaving either 5 mm or 10 mm distance between the sutures (Figure 2). Non-identical four-throw sliding knots were applied for each suture since these are widely used in septum surgery. A 3 mm suture tail was left on each side of the knot. The same surgeon tied all knots for each suture type, size, and distance.

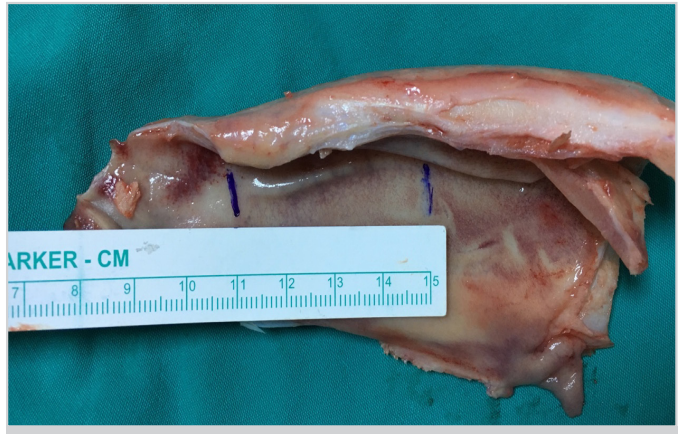


Figure 1. Sheep nasal septum. The region that was prepared for the experiment is marked with vertical blue lines

Suture Groups

To assess the effect of the type and diameter of different suture materials to the HS_{max}, 4-0 Polyglactin 910 (Vicryl Rapide, Ethicon, Johnson & Johnson Medical N.V., Belgium), 5-0 Polyglactin 910 (Vicryl Rapide, Ethicon, Johnson & Johnson Medical N.V., Belgium), 4-0 Polydioxanone (PDS II, Ethicon, Johnson & Johnson Medical N.V., Belgium) and 5-0 Polydioxanone (PDS II, Ethicon, Johnson & Johnson Medical N.V., Belgium) were used. A 16-mm curved cutting needle was used in all suture materials. To determine the effect of the distance between two adjacent sutures on HS_{max}, spaces of 5 mm and 10 mm were left between the adjacent sutures for each suture material. Consequently, HS_{max} measurements were taken from eight groups, i.e., 4-0 PDSII (5mm), 4-0 PDSII (10 mm), 5-0 PDSII (5 mm), 5-0 PDSII (10 mm), 4-0 Vicryl Rapide (5 mm), 4-0 Vicryl Rapide (10 mm), 5-0 Vicryl Rapide (5 mm), and 5-0 Vicryl Rapide (10 mm). At least 16 measurements were made for each suture group of mucosal-perichondrial flaps. We excluded mucosal-perichondrial flaps with undesired tears, excessive elevation, and broken cartilage strip during the preparation.

HS_{max} Measurements

The HS_{max} were measured and quantified in Newton units using a commercially available portable digital Newton-meter (SF50, Geratech, China) (Figure 3). Two towel forceps were fixed into one of the cartilage strips. The hook of the Newton-meter was placed into the middle of the other cartilage strip. Holding the tissue sample with the aid of a Cottle elevator and pulling the Newton-meter downwards, tensile force was applied to the sutures (Figure 2). This measurement method is similar to that used in a recent study on tissue holding strength of porcine kidney (7).

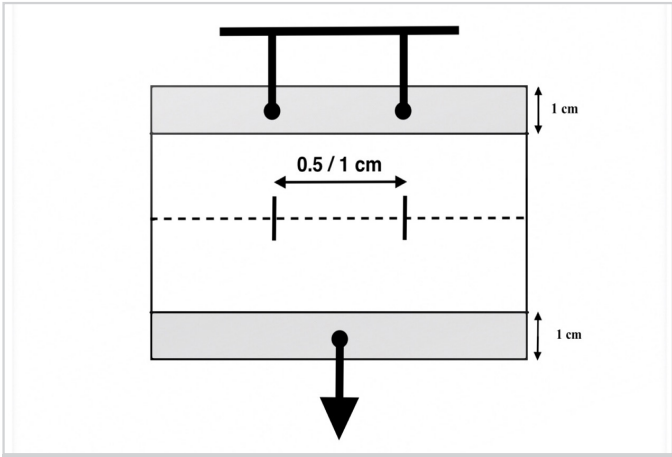


Figure 2. Schematic representation of the HS_{max} measurements. Horizontal dashed line symbolizes the laceration. Vertical thin solid lines crossing the dashed line symbolize the sutures. Arrow stands for the Newton-meter and shows the direction of the tensile force applied
HS_{max}: Maximum tissue holding strength, cm: Centimeter

All measurement procedures were recorded on video using the digital camera of a cellphone (iPhone®7 Plus, Apple Inc, Cupertino, California, USA) by one of the authors (A.K). The video records were then analyzed in the computer environment (iMovie, Apple Inc.) by another author (O.E) who did not participate in the video recording process. The values that had been read on the screen of the Newton-meter at the time points when the force caused opening of the knot or tearing of the mucosal-perichondrial leaflet were noted.

Statistical Analysis

Statistical analyses were performed using IBM SPSS for Windows software (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY, USA). The number of nasal septum specimens was determined by performing power analysis and it was found that at least 16 sheep nasal septal flaps should be included for each suture group in the study when 90% significance and α=0.05 level was calculated. Continuous variables were presented as mean ± standard deviation values. The Independent Samples t-test was used to compare the means of two independent groups. Comparisons of the mean holding strength of the same suture material at different distances were analyzed with Mann-Whitney U test. A value of $p<0.05$ was considered statistically significant. Linear regression analyses were performed to determine the strength of predictors, and p values <0.05 were considered statistically significant.

Figure 3. Digital Newton-meter that was used for measurements

Results

The mean HS_{max} values for each suture group are given in Table 1. The highest (12.74±2.40 N), and lowest (6.74±3.03 N) mean HS_{max} values were detected in the 5-0 Vicryl Rapide (5 mm), and 4-0 PDS II (5 mm) groups, respectively.

The Independent Samples t-test was applied to assess the effect of suture material, suture diameter and suture distance on HS_{max}. The mean HS_{max} value for polyglactin 910 and polydioxanone sutures was 11.44±3.41 N and 8.26±3.34 N, respectively (p<0.001). The mean HS_{max} value for 5 mm and 10 mm suture distance was 8.98±3.81, and 10.71±3.45, respectively (p=0.04). Linear regression analysis also showed that the HS_{max} was greater for polyglactin 910 sutures and at 10 mm suture distance (Table 2). There was no statistically significant difference between the mean HS_{max} values of sutures with 4-0 (9.22±3.67 N) and 5-0 (10.47±3.69 N) diameters (p=0.057). Additionally, comparisons of the mean holding strengths of the same suture material for 5 mm and 10 mm suture distance are given in Table 3.

Tensile force resulted in the opening of the knots or tearing of the mucosal-perichondrial flaps. PDS II and Vicryl Rapide sutures were compared in terms of sliding of the knots. Tensile force resulted in the opening of the knots in

Table 1. Mean holding strength according to suture variants and suture distance

Suture variants and distance of the sutures	Holding strength (N) (mean ± SD)	Holding strength (N) (minimum-maximum)
4-0 PDS II (5 mm)	6.74±3.03	2.76–13.63
4-0 Vicryl Rapide (5 mm)	8.89±4.10	4.02–18.69
5-0 PDS II (5 mm)	7.55±2.55	3.38–11.64
5-0 Vicryl Rapide (5 mm)	12.74±2.40	9.59–18.37
4-0 PDS II (10 mm)	9.23±3.02	4.55–14.53
4-0 Vicryl Rapide (10 mm)	12±2.53	9.06–16.66
5-0 PDS II (10 mm)	9.49±4.02	3.74–17.54
5-0 Vicryl Rapide (10mm)	12.08±3.21	6.01–16.60

N: Newton, SD: Standard deviation, PDS II: Polydioxanone, Vicryl Rapide: Polyglactin 910, mm: Millimeter

Table 2. Comparison of suture types, diameters, and distances in terms of mean HS_{max}

	n	Holding Strength (Newton) (mean ± SD)	p*
Suture type			
Vicryl Rapide	64	11.44±3.41	<0.001
PDS II	64	8.26±3.34	
Suture diameter			
4-0	64	9.22±3.67	0.057
5-0	64	10.47±3.69	
Suture distance			
5 mm	64	8.98±3.81	0.04
10 mm	64	10.71±3.45	

Significant p-values are shown in bold.

n: Sample size, PDS II: Polydioxanone, Vicryl Rapide: Polyglactin 910, *Independent samples t-test, SD: Standard deviation, HS_{max}: Maximum tissue holding strength

Table 3. Comparisons of the mean holding strength of the same suture material at different distances

	4-0 PDS II (5 mm) vs 4-0 PDS II (10 mm)	5-0 PDS II (5 mm) vs 5-0 PDS II (10 mm)	4-0 Vicryl R. (5mm) vs 4-0 Vicryl R. (10 mm)	5-0 Vicryl R. (5 mm) vs 5-0 Vicryl R. (10 mm)
*p-values	0.029	0.214	0.005	0.451

PDS II: Polydioxanone, Vicryl R. (Vicryl Rapide): Polyglactin 910, vs: Versus, mm: Millimeter, *: Mann-Whitney U test

35.9% (n=23) of the polydioxanone and 6.2% (n=4) of the polyglactin 910 sutures, respectively ($p<0.05$).

Discussion

Different tissues show varying resistance to stress. Several studies have measured the maximum resistance strength before tears in some tissues and organs (6-8). Rodrigues et al. (8) measured HS_{max} values in 10 pigs using 3-0 vicryl in eight intra-abdominal organs (fascia, aorta, vena cava, peritoneum, small and large bowel, uterus, and fallopian tube). The most resistant tissue was the fascia at 11.43 N, and the weakest was the fallopian tubes at 1.25 N. Thus, it was determined what force surgeons could apply to which tissues during suturation in laparoscopic surgery. Tarin et al (9) made HS_{max} measurements of various sutures in the renal capsule. Hem-o-lok clips were found to be more resistant and their use was recommended. In our study, HS_{max} measurements were made in the sheep nasal septum for two different suture materials, two different suture diameters and two different suture spacings. It was determined that the use of polyglactin 910 as the suture material and 10 mm as the suture spacing resulted in higher HS_{max} values. In other words, polyglactin 910 should be preferred as the suture material and 10 mm space should be left between adjacent sutures when repairing nasal septal mucosal lacerations. Although the mean HS_{max} value of 5-0 sutures (10.47 N) was higher than that of the 4-0 sutures (9.22 N), there was no statistically significant difference between the two sutures in terms of suture diameter ($p=0.057$).

The PDS II monofilament suture group was observed to have a greater tendency to slippage and opening, compared to the Vicryl Rapide suture group. This showed that even if PDS II sutures used in septal mucosal-perichondrial laceration repair remain for a long time without hydrolysis, they are less reliable in the short-term. PDS II sutures are more slippery as they are monofilament, and because of their structural properties, if monofilament sutures are to be used, it can be considered more appropriate to apply more than 4 knots. Trimbos et al. (10) evaluated the performance of opening knots in multifilament and monofilament suture materials. Non-identical and parallel sliding knots were reported to differ little in respect of knot reliability. In addition, five-throw knots were significantly stronger than three-throw knots if monofilament suture material was used (11, 12). In our study, non-identical sliding knots with four throws were used to prevent the knots opening.

Apart from Vicryl Rapide and PDS II, there are many types of absorbable monofilament and multifilament sutures that can be used inside the nose, such as Caprosyn (Polygytone 6211), Monocryl (Poliglecaprone 25), Maxon (Polyglyconate), and PGA (Polyglycolic acid). Each of these suture types has advantages and disadvantages in respect of the inflammatory reaction created in the tissue, the time to absorption, tensile strength, and suture reliability. Retrieving sutures used in septal mucosal-perichondrial laceration repair from the nose is an extremely challenging procedure and so absorbable sutures are preferred in the majority of cases, as they do not require long-term care. A good suture must be biocompatible, be able to be effectively absorbed, resistant and appropriate to the organ or area where it is to be used (13). Two types of suture that are often used in septal mucosal-perichondrial laceration and septal perforation repairs are Vicryl Rapide (polyglactin 910) and PDS II (Polydioxanone). In our study, Vicryl Rapide and PDS II suture types were evaluated at the two different diameters of 4-0 and 5-0. As the absorption time of PDS II is longer than that of Vicryl Rapide and the study results showed a lower HS_{max} value for PDS II, it can be said that the use of Vicryl Rapide is more advantageous in the repair of septal mucosal-perichondrial lacerations. In our clinical practice, we prefer 4-0 Vicryl Rapide or 5-0 Vicryl Rapide suture types and we place the stitches at 10 mm distance in the repair of nasal septal mucosal-perichondrial tears.

In the literature, there is no objective information about which material should be applied at which distance in the repair of nasal septal mucosal-perichondrial lacerations. In our study, two different suture distance groups were formed as 5 mm and 10 mm to examine whether the suture spacing had any effect on the HS_{max} value. The HS_{max} values measured at 10 mm spacing were seen to be higher than those measured at 5 mm spacing. This might be an inherent result of using closer sutures, which in turn caused more tissue violation. Using the proper suture material, size, and the proper distance between two adjacent sutures, will potentially, to a great extent, reduce septal perforation rates and increase quality of life for patients. Furthermore, extensive studies would be useful to examine the HS_{max} value of different types of sutures in the repair of tears in nasal septal mucosal-perichondrial flaps.

There were some limitations to this study. In a postmortem study by Rosen et al. (14), tissue resistance was shown to be significantly weaker than the results of *in vivo* studies. Although the use of postmortem tissue could be seen as a limitation of the current study, the aim of the study was not to measure the exact tissue resistance of the sheep septum, but to compare the effect of different types of sutures on holding strength. Therefore, the use of postmortem tissue can be considered not to have affected the results. Sheep septum was selected as a model for the practical reasons of ease of availability and because sheep nasal septal flaps are comparable to human nasal septal flaps in terms of resistance, ease of mucosal-perichondrial elevation, size, and thickness. Additionally, tissue resistance of this study was measured at room temperature and not measured at "living" tissue temperature, and physiological events such as airflow, crusting, inflammatory reactions will not occur in postmortem tissue. Since the results of this study represent the outcomes obtained from a postmortem animal experiment at best and should be confirmed by further *in vivo* and/ or fresh human cadaver studies.

Conclusion

The type of suture material and the distance between sutures should be taken into consideration when repairing nasal septal mucosal-perichondrial lacerations. Polyglactin 910 suture material with 10 mm spacing between two adjacent sutures may be more durable than the other suture materials when repairing nasal septal mucosal lacerations.

Ethics Committee Approval: This study was approved by Başkent University's Institutional Review Board (project no: DA18/09, date: 18.09.2018).

Informed Consent: Experimental study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Conception: A.K., A.F.B., E.H., O.E., Design: A.K., A.F.B., E.H., O.E., Supervision: A.K., A.F.B., E.H., Materials: A.K., A.F.B., E.H., O.E., Data Collection and/or Processing: A.K., A.F.B., E.H., O.E., Analysis and/or Interpretation: A.K., A.F.B., E.H., O.E., Literature Review: A.K., E.H., Writing: A.K., A.F.B., E.H., O.E., Critical Review: A.K., A.F.B., E.H., O.E.

Conflict of Interest: The authors have no conflicts of interest to declare.

Financial Disclosure: This manuscript supported by the Başkent University Research Fund (project no: DA18/09).

Main Points

- Appropriate repair of nasal mucosal lacerations is essential to prevent the development of septal perforation during the healing process.
- The PDS II (polydioxanone) monofilament suture group was observed to have a greater tendency to slippage and opening, compared to the Vicryl Rapide (polyglactin 910) suture group.
- Using Vicryl Rapide (polyglactin 910) with a distance of 10 mm in repair of mucosal-perichondrial flaps may be more appropriate than other suture materials and suture distances.

References

1. Brain DJ. Septo-rhinoplasty: the closure of septal perforations. J Laryngol Otol 1980; 94: 495-505. [Crossref]
2. Dosen LK, Haye R. Surgical closure of nasal septal perforation. Early and long term observations. Rhinology 2011; 49: 486-91. [Crossref]
3. Flavill E, Gilmore JE. Septal perforation repair without intraoperative mucosal closure. Laryngoscope 2014; 124: 1112-7. [Crossref]
4. Yildirim G, Cingi C, Kaya E. Septal stapler use during septum surgery. Eur Arch Otorhinolaryngol 2013; 270: 939-43. [Crossref]
5. Nawrocki JG, Nonnenmann H, Mooney M, Sutton N, Schmitz ND. A high-strength, absorbable, antibacterial knotless tissue control device for fascial closure. Curr Obstet Gynecol Rep 2017; 6: 175-81. [Crossref]
6. Kazkayasi M, Yalcinozan ET. Uncinate process in the repair of nasoseptal perforation. Aesthetic Plast Surg 2011; 35: 878-81. [Crossref]
7. Özkuvanci Ü, Akpinar H, Karadag MA, Dönmez Mİ, Altunrende F. Holding strength of suture: an experimental study using porcine kidney. JSLS 2017; 21: e2017.00029. [Crossref]
8. Rodrigues SP, Horeman T, Dankelman J, van den Dobbelsteen JJ, Jansen FW. Suturing intraabdominal organs: when do we cause tissue damage? Surg Endosc 2012; 26: 1005-9. [Crossref]
9. Tarin T, Kimm S, Chung B, Shinghal R, Reese J. Comparison of holding strength of suture anchors on human renal capsule. J Endourol 2010; 24: 293-7. [Crossref]
10. Trimbos JB, Van Rijssel EJ, Klopper PJ. Performance of sliding knots in monofilament and multifilament suture material. Obstet Gynecol 1986; 68: 425-30. [Crossref]
11. Van Leeuwen N, Trimbos JB. Strength of sliding knots in multifilament resorbable suture materials. Gynecol Surg 2012;9: 433-7. [Crossref]
12. Silver E, Wu R, Grady J, Song L. Knot security-how is it affected by suture technique, material, size, and number of throws? J Oral Maxillofac Surg 2016; 74: 1304-12. [Crossref]

13. Karabulut R, Sonmez K, Turkyilmaz Z, Bagbanci B, Basaklar AC, Kale N. An in vitro and in vivo evaluation of tensile strength and durability of seven suture materials in various pH and different conditions: an experimental study in rats. Indian J Surg 2010; 72: 386-90. [Crossref]

14. Rosen J, Brown JD, De S, Sinanan M, Hannaford B. Biomechanical properties of abdominal organs in vivo and postmortem under compression loads. J Biomech Eng 2008; 130: 021020. [Crossref]

Characteristics of Otorhinolaryngological Emergencies in the Elderly

Original Investigation

Sibel Yıldırım, Zahide Çiler Büyükatalay, Ahmed Majid Naji Agha Oghali, Rıdvan Kılıç, Gürsel Dursun

Department of Otorhinolaryngology Head and Neck Surgery, Ankara University School of Medicine, Ankara, Turkey

Abstract

Objective: This study was designed to characterize the distribution of otorhinolaryngological emergencies seen in the geriatric population in one year. In this article we present our results and discuss the differences between our results and those reported in the current literature.

Methods: The study was carried out in a tertiary care university hospital. All patients aged 65 years or over that were referred by the general emergency department (ED) to the otorhinolaryngology emergency room in a one-year period were retrospectively reviewed. Demographic characteristics (age, gender), findings of physical examination, accompanying systemic diseases, diagnosis, and treatment methods were documented. Hospitalization and referral needs were also analyzed.

Results: In the one-year period from April 2017 to April 2018, a total of 12,780 patients aged 65 or older presented to the ED and the otorhinolaryngology physician was consulted for 195 (1.5%) of these patients. The age range of the patients was 65–96 years, with a mean age of 75 years. The most common cause for presenting to the ED was maxillofacial trauma (31.7%), followed by epistaxis (18.7%). Dyspnea (9.7%) and peripheral facial paralysis (9.7%) were the third most frequent causes. The outcome analysis revealed that 9.7% of the patients were hospitalized.

Conclusion: Identifying the characteristics of the geriatric patients presenting to EDs is important for developing proper management algorithms. Maxillofacial traumas were the most frequently seen ORL emergencies in our cohort of geriatric patients, followed by epistaxis. The distribution and the prevalence of the cases could differ according to the institutional protocols.

Keywords: Emergency, geriatrics, maxillofacial injury, epistaxis, hospitalization, otorhinolaryngology

ORCID ID of the authors:

S.Y. 0000-0002-5494-6198;
Z.Ç.B. 0000-0002-0992-0079;
A.M.N.A.O. 0000-0001-5282-7200;
R.K. 0000-0003-0976-8107;
G.D. 0000-0003-2542-8268.

Cite this article as: *Yıldırım S, Büyükatalay ZÇ, Agha Oghali AMN, Kılıç R, Dursun G. Characteristics of Otorhinolaryngological Emergencies in the Elderly. Turk Arch Otorhinolaryngol 2021; 59(1): 8-13.*

Corresponding Author:
Sibel Yıldırım; yldrmsib@gmail.com

Received Date: 17.12.2020
Accepted Date: 26.01.2021

DOI: 10.4274/tao.2021.6193

Introduction

The geriatric population has become the fastest growing segment of the society as life expectancy increases worldwide. Compared to all other age groups, this population uses the most medical resources, has the longest hospital stays, as well as the highest rates of emergency department (ED) admissions (1). Overall, the elderly account for 15%–25% of ED visits (2).

These developments have inevitably increased the number of elderly patients seeking otorhinolaryngologic care.

Otorhinolaryngology (ORL), as a specialty, deals with a wide range of health conditions, including communication disorders, allergies, and a variety of infections involving head and neck, as well as complex head and neck malignancies. Given this spectrum, one-third of the patients seen by the average otolaryngologist are over 65 years old (3). However, the principles of geriatric medicine and the issues specific to geriatric patients have not been sufficiently defined in relation to otorhinolaryngological emergencies.

Moreover, there are very few studies that have projected the epidemiological profile of geriatric otorhinolaryngological emergencies (1, 4). Therefore, this study was designed to determine the characteristics of the otorhinolaryngological emergencies seen in the geriatric population in one year in a single institution.

Methods

The study was approved by the institutional ethics committee (number: 06-298-17) and conducted in accordance with the relevant privacy guidelines and applicable regulatory requirements. The data collected on the patients did not involve personal information or data that might affect patient privacy, and the study is exempt from the informed consent requirement due to its retrospective nature.

In this study, which was carried out at a tertiary care university hospital, we retrospectively reviewed the one-year data (2017-2018) involving all patients aged 65 years or over that were referred to the ORL emergency room from the general ED for consultation. Our hospital protocol for referrals states that patients do not have direct access to the ORL emergency room; instead, they need to be triaged by the ED physician to establish the severity of the emergency and the need for ORL evaluation.

Demographic characteristics (age, gender), findings of physical examination, accompanying systemic diseases, diagnosis, and treatment methods were documented, and the need for hospitalization and referral were analyzed. Descriptive statistical analysis was performed using Microsoft Excel (Microsoft Corp., Redmond, WA).

Results

A total of 12,780 geriatric patients (aged 65 years or over) presented to the ED in the one-year period from April 2017 to April 2018. Of these patients, 195 (1.5%) were referred to the ORL physician for consultation. The age range of the patients was 65–96 years, with a mean of 75 years. Of these 195 patients 52.3% were in the youngest age group (65 to 74 years), 34.3% in the intermediate age group (75 to 84 years), and 13.3% were in the oldest age group (85+ years). The male to female ratio was 1.1:1. The mean age was 73 years (range: 65–96 years) for males and 76 years (range: 65–93 years) for females.

The most common cause for an ED visit was maxillofacial trauma (31.7%), followed by epistaxis (18.7%). Dyspnea (9.7%) and peripheral facial paralysis (9.7%) were the third most frequent causes (Table 1).

Analysis of the main complaints by age showed no significant differences. Maxillofacial traumas were the most common complaint, followed by epistaxis in all age groups. Their distribution among the age groups, however, were different. Maxillofacial traumas constituted 50% of the diagnoses in the eldest group, 29.8% in the intermediate age group, and 28.4% in the youngest age group. The third most common complaint was peripheral facial paralysis in the youngest and intermediate age groups. On the contrary, dyspnea was the third most common complaint in the eldest age group. The distribution of the diagnoses by age groups is shown in Figure 1.

Of the maxillofacial traumas, 79% (n=49) were caused by falls, 17.7% (n=11) were associated with motor vehicle accidents, and 3.2% (n=2) were assault related. There were 59.6% (n=37) simple traumas (such as skin laceration, incision, bleeding, hematoma) not accompanied by a fracture; and 40.3% (n=25) had fractures in one or more of the maxillofacial bones. Simple traumas were managed with wound care, dressing, laceration repair, and medical treatments (analgesic, antibiotics) in the ED. Traumas with fractures were evaluated for any functional or cosmetic deformities, and reduction was planned for displaced fractures. Six patients with displaced nasal fracture underwent closed nasal bone reduction under local anesthesia in the ED and four patients refused reduction. Patients with mandible, skull base, and maxilla fractures needed hospitalization, and interventions were planned in the operating room under general anesthesia. Patients with

Table 1. Distribution of patients by type of emergency disorders

Types of emergency	Number of cases (n)	Percentage (%)
Maxillofacial trauma	62	31.7
Epistaxis	37	18.7
Dyspnea	19	9.7
Peripheral facial paralysis	19	9.7
Head and neck infections	10	5.1
Otalgia	10	5.1
Foreign body	9	4.6
Feeding problems	9	4.6
Vertigo	7	3.5
Hearing loss	5	2.5
Others	8	4.1
Total	195	100

n: Number

non-displaced fractures did not require any intervention. The distribution of the fractures is listed in Table 2.

The second most encountered emergency was epistaxis, accounting for 18.7% of all cases. Hypertension was the most frequent accompanying systemic disease, with a rate of 40.5%, followed by cardiac pathologies (atrial fibrillation, valve diseases) (32.4%). In 27% of the patients, there were no known systemic diseases. The use of anticoagulant medication was reported by 51.5% of the patients. Treatment modalities used for the management of epistaxis are shown in Table 3. Only one patient was hospitalized with posterior nasal packing.

Cases with dyspnea ranked third in prevalence (9.7%). Obstruction of the tracheostomy cannula with a crust or mucous plug was the most common cause of dyspnea (31.5%).

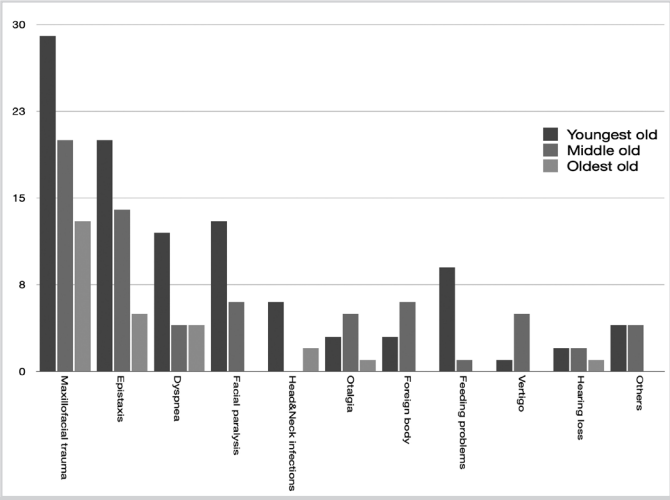


Figure 1. Distribution of cases by age groups

These patients were discharged after tracheobronchial suctioning and removal of stiff plugs. Other causes of dyspnea and the treatment modalities are listed in Table 4. Hospitalization rate was the highest (63%) for dyspnea cases compared to the other emergencies.

Peripheral facial paralysis also accounted for a large number (9.7%) of the emergencies, all of which were evaluated as idiopathic. Corticosteroid treatment were planned, and doses were adjusted according to patients' comorbidities, such as hypertension and diabetes mellitus. Only one patient needed hospitalization because of uncontrolled hypertension.

Head and neck infections accounted for 5.1% of the emergencies. In 40% of these cases, infection had progressed to deep neck space abscesses. These cases all required drainage except for one that had a retropharyngeal abscess. This patient was hospitalized and monitored for regression under intravenous antibiotherapy.

Otalgia was the main complaint of 10 patients, with the most common etiology being acute/chronic otitis media, followed by auricular abscess. A foreign body was a relatively common emergency and mainly located in the larynx (33.3%). Feeding problems were another reason for ORL consultation and mainly secondary to head and neck malignancies (55.5%).

Seven patients diagnosed with dizziness or vestibular impairment were referred for ORL consultation. Of these cases, two with neurological deficits were referred to department of neurology. Two patients showed no vestibular deficit in vestibular examinations. Hearing loss was a less common complaint for ED admission, accounting for 2.5% of the cases. Only one patient had a true emergency with sudden sensorineural hearing loss; the other cases were related to earwax or presbycusis.

Table 2. Numbers of fractures by site and displacement

Cite of fractured bone	Displaced fracture	Non-displaced fracture	Total
Nasal	10	6	16
Maxilla	1	2	3
Mandible	2	0	2
Multiple site	1	2	3
Zygomatic bone	0	1	1
Total	14	11	25

Table 3. Treatment modalities for epistaxis

Treatment modalities	Number of patients
Anterior packing	10
Silver nitrate	10
Medical treatment	8
Absorbable hemostat dressing	5
Electrocautery	3
Posterior packing	1

Table 4. Dyspnea cases according to the etiology, treatment modality and hospitalization need

Etiology of dyspnea	Treatment modality (n)	Hospitalization
Tracheostomy cannula obstruction	Aspiration (6)	No
Laryngeal mass	Direct laryngoscopy and biopsy (4)	Yes
Bilateral vocal fold paralysis	Posterior laser cordotomy (2) Tracheostomy (1)	Yes
Laryngeal edema	Medical treatment (4)	Yes
Oral cavity carcinoma	Tracheostomy (1)	Yes
Hypertrophic thyroid gland	Follow up (2)	No

n: Number

The outcome analysis revealed that 9.7% of the patients required hospitalization. Distribution of the hospitalization rates by diagnoses is shown in Table 5.

Table 5. Hospitalizations by diagnoses

Types of emergency	Hospitalization rate % (n)
Dyspnea	63.1% (n=12)
Others	12.5% (n=1)
Head and neck infections	10% (n=1)
Peripheral facial paralysis	5.2% (n=1)
Maxillofacial trauma	4.8% (n=3)
Epistaxis	2.7% (n=1)
Foreign body	0% (n=0)
Feeding problems	0% (n=0)
Vertigo	0% (n=0)
Hearing loss	0% (n=0)
Otalgia	0% (n=0)

n: Number

Discussion

The geriatric population is the fastest growing segment of society. It is estimated that 12.5% of the world's population will be aged over 65 years by 2030, and all physicians will be required to deal with the effects of this aging population (5). Accordingly, it is reasonable to expect an increase in the number of elderly patients who need emergency otorhinolaryngological care. Extended reviews of ORL emergencies have been conducted before; however, the profile of ORL emergencies in the geriatric population has not been adequately addressed (6-9). Therefore, this study provided a comprehensive analysis of 195 geriatric patients referred to ORL from an ED.

In the presented study, the referral rate of geriatric patients to the ORL physician was found as 1.5%. In our institution, patients do not have direct access to an ORL physician; all patients are first examined and treated by an ED physician. Therefore, this rate reflects not the prevalence of geriatric ORL emergencies, but the geriatric emergency patients referred for evaluation through the triage system. It is difficult to determine the real prevalence of geriatric ORL emergencies since each institution has a different patient flow system, and management and referral protocols can vary according to each hospital's management protocol and the clinicians' approaches.

Maxillofacial traumas were the predominant reason for referral in our cohort. This is in contrast to the study of Dagan et al. (1), in which the most common reason for ORL ED admission among geriatric patients was balance disorders. This may be explained by the different management protocols of the respective institutions. Our study was conducted at a university hospital with a trauma center. Therefore, most of the trauma emergency calls in the city were directed to our hospital, which led to an increased rate of trauma cases. Furthermore, at our institution, the plastic surgery department is situated on another campus, meaning most maxillofacial trauma cases are generally referred to ORL, which also led to increased rates. In our study, most of the traumas were due to falls and more common in the eldest group. The physical changes in the elderly, such as muscle weakness, low levels of physical activity, balance and gait disorders, and visual impairment, could explain this result. The nasal bone was the most common fracture site, followed by the maxilla. Falcone et al. (10) stated similar results but there are different studies those mandible fractures preponderant (11, 12). Reduction was offered for all the displaced fractures, but 28.5% of the patients refused treatment. It is not possible to compare this rate with that of other age groups since there are no data on the treatment refusals in maxillofacial fractures. However, we deem that refusal rates are higher in the geriatric population due to less concerns about cosmetic deformity.

Epistaxis, which was the second most encountered emergency, can be challenging in the elderly, especially because their use of multiple medications and the presence of systemic disease comorbidities compound the difficulties in their treatment. In their analysis of the epidemiology of ORL emergencies, Lammens et al. (6) reported epistaxis as the most frequent diagnosis, accounting for about 25% of their cases. In our study, epistaxis accounted for 18.7% of the

patients, which is slightly lower than the percentage reported by the referred study. This difference can be explained by the study design. In the referred study, all epistaxis cases were assessed under the heading of epistaxis, whereas in our study traumatic epistaxis was included in the maxillofacial trauma group. Prompt management of epistaxis is important for hemodynamic stability, especially in the elderly (13). None of the patients in our study required resuscitation or intensive care unit follow-up. In general, their epistaxis cases were not severe, and anterior nasal packing were sufficient. Only one patient had posterior-based epistaxis that required posterior nasal packing and hospitalization for observation.

Among the most frequent complaints, dyspnea was the third in our study, a finding which differs from other epidemiological studies (7, 8, 14). We assume that the difference is due to our study's geriatric age group in which respiratory distress occurs more frequently than in younger age groups (15). Dyspnea in the elderly is often the consequence of multiple overlapping disorders, but in our study, only the dyspnea cases involving upper airway pathologies were evaluated. The most common etiologies were mainly associated with head and neck malignancies, which are also more commonly seen in this age group (16). Hospitalization need was significantly higher in dyspnea cases than for other emergency cases because airway pathologies need close observation during medical or surgical treatments.

Other causes that are listed in the literature for ORL referrals in the elderly are peripheral facial paralysis, head and neck infections, otalgia, foreign body, feeding problems, balance disorders, and hearing loss. Almost all commonly seen ORL conditions were presented in our results, but the rate of vertigo was found remarkably lower compared to the reports in the literature. This can be explained by the differences in patient admission protocols. In our institution, all patients admitted to the EDs are triaged by emergency medicine specialists, and the decision of whether the patient should be referred to the neurologist or the otorhinolaryngologist is based on the ED physician's clinical judgement. The general approach of the ED physicians is to rule out a neurological emergency, so they usually first refer patients to the neurologist. In the absence of a central pathology, patients are evaluated for peripheral vertigo, in which case, most of the time, symptomatic treatment is applied and ORL outpatient follow-up is recommended. With this algorithm, ORL generally evaluates vertigo patients in outpatient clinics rather than in the emergency unit.

The retrospective design of the study did not allow us to comment on the suitability of the referrals; however, review of the cases showed that most were genuine emergencies. Gallo et al. (17) found that the vast majority of ORL ED admissions were not real emergencies, but their ED working protocol is different from the one at our institution. In the referred study, patients had direct access to ORL ED without any triage system. In our ED, however, all patients are first seen by an ED physician in the triage room, and non-emergency cases are redirected. That the need for ORL consultation is determined by the ED physician, helps reduce unnecessary ORL admissions.

Conclusion

Maxillofacial traumas are the most frequently seen ORL emergencies among geriatric patients, followed by epistaxis. Higher hospitalization rates are seen in dyspnea. The elderly population is physiologically different from younger adults, and they have different needs. Identifying the characteristics of geriatric patients presenting to the ED is important for developing proper management algorithms. Multicenter studies with larger cohorts will better define the epidemiological profile of the geriatric ORL emergencies.

Ethics Committee Approval: Ankara University Ethics Committee for Clinical Investigations (no: 06-298-17, date: 27 March 2017).

Informed Consent: The data collected on the patients did not involve personal information or data that might affect patient privacy, and the study is exempt from the informed consent requirement due to its retrospective nature.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Conception: S.Y., Z.Ç.B., A.M.N.A.O., R.K., G.D., Design: S.Y., Z.Ç.B., A.M.N.A.O., R.K., G.D., Supervision: S.Y., Z.Ç.B., A.M.N.A.O., R.K., G.D., Materials: S.Y., Z.Ç.B., A.M.N.A.O., R.K., G.D., Data Collection and/or Processing: S.Y., A.M.N.A.O., R.K., Analysis and/or Interpretation: S.Y., R.K., Literature Review: S.Y., Writing: S.Y., Critical Review: G.D.

Conflict of Interest: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study received no financial support.

Main Points

- Identifying the characteristics of geriatric patients presenting to the ED is important for developing proper management algorithms.
- In geriatric patients, the most frequently seen ORL emergencies are maxillofacial traumas, followed by epistaxis.
- Higher hospitalization rates were seen in patients with dyspnea.
- The distribution and the prevalence of the cases could differ according to the institutional protocols.

References

1. Dagan E, Wolf M, Migirov LM. Why do geriatric patients attend otolaryngology emergency rooms? Isr Med Assoc J 2012; 14: 633-6. [Crossref]
2. Roberts DC, McKay MP, Shaffer A. Increasing rates of emergency department visits for elderly patients in the United States, 1993 to 2003. Ann Emerg Med 2008; 51: 769-74. [Crossref]
3. Fato M. Geriatric Otolaryngology. Calhoun KH, Eibling DE, editors. Geriatric Otolaryngology. New York: Taylor&Francis Group; 2006.p.1-14.
4. Ozler GS, Yengil E. Why do geriatric patients visit otorhinolaryngology? Ear Nose Throat J 2016; 95: 224-9. [Crossref]
5. Bitto A, Lerner CA, Sell C. The Science of Aging. Sataloff RT, Johns MM, Kost KM, editors. Geriatric Otolaryngology. New York: Thieme Medical Publisher Inc.; 2015.p.1-11.
6. Lammens F, Lemkens N, Laureyns G, Lemmens W, Van Camp L, Lemkens P. Epidemiology of ENT emergencies. B-ENT 2014; 10: 87-92. [Crossref]
7. Raj A, Wadhwa V, Jain A. Epidemiological profile of ENT emergencies: our experience. Indian J Otolaryngol Head Neck Surg 2019; 71: 301-4. [Crossref]
8. Yojana S, Mehta K, Girish M. Epidemiological profile of otorhinolaryngological emergencies at a medical college, in rural area of gujarat. Indian J Otolaryngol Head Neck Surg 2012; 64: 218-24. [Crossref]
9. Garneau JC, Wasserman I, Konuthula N, Malkin BD. Referral patterns from emergency department to otolaryngology clinic. Laryngoscope 2018; 128: 1062-7. [Crossref]
10. Falcone PA, Haedicke GJ, Brooks G, Sullivan PK. Maxillofacial fractures in the elderly: a comparative study. Plast Reconstr Surg 1990; 86: 443-8. [Crossref]
11. Chrcanovic BR, Souza LN, Freire-Maia B, Abreu MH. Facial fractures in the elderly: a retrospective study in a hospital in Belo Horizonte, Brazil. J Trauma 2010; 69: 73-8. [Crossref]
12. Fasola AO, Obiechina AE, Arotiba JT. Incidence and pattern of maxillofacial fractures in the elderly. Int J Oral Maxillofac Surg 2003; 32: 206-8. [Crossref]
13. Yüksel A, Kurtaran H, Kankiliç ES, Ark N, Ugur KS, Gündüz M. Epistaxis in geriatric patients. Turk J Med Sci 2014; 44: 133-6. [Crossref]
14. De Andrade JS, Albuquerque AM, Matos RC, Godofredo VR, Penido Nde O. Profile of otorhinolaryngology emergency unit care in a high complexity public hospital. Braz J Otorhinolaryngol 2013; 79: 312-6. [Crossref]
15. Barbera AR, Jones MP. Dyspnea in the elderly. Emerg Med Clin North Am 2016; 34: 543-58. [Crossref]
16. Mifsud M, Eskander A, Irish J, Gullane P, Gilbert R, Brown D, et al. Evolving trends in head and neck cancer epidemiology: Ontario, Canada 1993-2010. Head Neck 2017; 39: 1770-8. [Crossref]
17. Gallo A, Moi R, Minni A, Simonelli M, de Vincentiis M. Otorhinolaryngology emergency unit care: the experience of a large university hospital in Italy. Ear Nose Throat J 2000; 79: 155-60. [Crossref]

Long-Term Balance Outcomes in Vestibular Ablative Surgeries

Original Investigation

Fakih Cihat Eravcı[1], Metin Yılmaz[1], Ebru Şansal[2], Nagihan Gülhan[1], Recep Karamert[1], Hakan Tutar[1], Mehmet Birol Uğur[1]

[1]Department of Otorhinolaryngology, Gazi University Faculty of Medicine, Ankara, Turkey
[2]Department of Audiology, Gazi University Faculty of Medicine, Ankara, Turkey

Abstract

Objective: To evaluate the long-term balance outcomes of vestibular nerve section (VNS) and labyrinthectomy (L) operations. The indirect outcomes will be the correlation of objective and subjective test results and an analysis of anterior-posterior versus medial-lateral computerized posturography (CP) scores.

Methods: This retrospective study evaluated objective CP and subjective Dizziness Handicap Inventory (DHI) results of patients who underwent VNS and L surgeries for Ménière's disease.

Results: A total of 55 (31 VNS and 24 L) patients were included in the study. The two operation groups were similar in terms of age, and mean time between surgery and the tests (p=0.465 and p=0.616) respectively. The vestibular and global scores at anterior-posterior CP showed statistically significant differences between the groups (p=0.000 and p=0.007) respectively in favor of the VNS group. In addition, the comparison of the vestibular CP scores of anterior-posterior and medial-lateral evaluations of the entire study population was lower in the medial-lateral evaluation (p=0.000). The mean DHI scores did not show statistically significant differences (p=0.359) between operation groups, nor did the correlation analysis between CP and DHI scores reveal statistical significance (p values >0.05).

Conclusion: In the long term, objective balance outcomes are better for VNS patients than for L patients. Additionally, medial-lateral balance outcomes are more affected than anterior-posterior balance outcomes from unilateral ablative surgeries. Subjective balance perception is not different between the two surgery groups, and DHI scores do not show a correlation with CP scores.

Keywords: Ménière's disease, vestibular nerve, labyrinth, surgery, postural balance, dizziness, disability evaluation

ORCID ID of the authors:

F.C.E. 0000-0001-9092-7923;
M.Y. 0000-0002-3382-4220;
E.Ş. 0000-0003-2511-1279;
N.G. 0000-0003-1207-3584;
R.K. 0000-0001-9112-3986;
H.T. 0000-0001-5585-5282;
M.B.U. 0000-0003-2784-015X.

Cite this article as: *Eravcı FC, Yılmaz M, Şansal E, Gülhan N, Karamert R, Tutar H, Uğur MB. Long-Term Balance Outcomes in Vestibular Ablative Surgeries. Turk Arch Otorhinolaryngol 2021; 59(1): 14-9.*

Corresponding Author:
Fakih Cihat Eravcı; fceravci@gmail.com

Received Date: 28.09.2020
Accepted Date: 10.12.2020

DOI: 10.4274/tao.2020.6032

Introduction

Ménière's disease (MD) presents as recurrent episodic vertigo attacks, aural fullness, tinnitus, and sensorineural hearing loss generally accompanies the clinical situation. Although it has a low incidence, it can affect the patient's quality of life and results in serious consequences (1). The strategy for treatment is a stepped approach starting with more conservative

measures, such as dietary modification and oral medication. It is reported that these treatment options are sufficient for 60% to 87% of the patients to maintain their daily activities (2). The next treatment step for patients with ongoing disabling attacks despite conservative treatments are minimally invasive options, such as intratympanic injections and endolymphatic sac decompression. The most successful options, however, are the most invasive—vestibular nerve section (VNS) and labyrinthectomy (L). These ablative surgical options have resulted in over 90% vertigo control in patients with refractory MD (3, 4). Yet, these ablative surgeries result in a unilateral loss of vestibular function, and their actual long-term success depends on sufficient vestibular compensation as impaired vestibular compensation can result in postural instability.

These two ablative surgeries were introduced over 100 years ago and are still being performed due to their success in controlling vertigo attacks (5). Although these operations have morbidities, these are far outweighed by the life-threatening Tumarkin attacks and the clinical presentations in which patients cannot maintain daily activities. Choosing between these two surgical options for relief from severe vertigo attacks depends on the hearing level of the patient and perioperative morbidity risks. Disequilibrium is the main complaint in the long term of patients who have undergone ablative surgeries. If there is a difference in terms of postoperative unsteadiness between these surgeries, it may provide another parameter for deciding on the procedure. Previous studies on vestibular ablative surgeries for MD have generally focused on the success of controlling vertigo attacks; only a few have addressed the balance outcomes of the procedures (6). Unsteadiness after the operation has been reported more frequently from L, at rates ranging from 20% to 28% and with 14% to 20% being after VNS operations (7, 8). A study searching the long-term balance outcomes of both VNS and L surgeries reported a high incidence of incomplete vestibular compensation that did not result in a significant balance handicap, and found no difference in terms of balance between the operations (9). However, another study showed that the L group complained more from subjective dizziness (7). Research on this topic is nearly non-existent, so the controversy continues.

In the presented study, we aimed to evaluate the differences in objective and subjective balance outcomes with computerized posturography (CP) and the Dizziness Handicap Inventory (DHI) in patients who underwent VNS and L procedures. The second outcome will be the chance to explore the relationship between CP and DHI.

Methods

The presented study was conducted in the Department of Otorhinolaryngology, Gazi University Hospital, Ankara, Turkey, approved by the local ethics committee (approval no: 01-09/2019), and carried out in accordance with the principles of the Declaration of Helsinki. All subjects were informed, and consent forms were obtained preoperatively. This retrospective study evaluated the demographic data, CP, and DHI results of the patients that underwent retro-sigmoid VNS and trans-mastoid L for MD between 2008 and 2019. The study criteria included patients aged 18 years and above who underwent one of the mentioned surgical procedures, followed by CP and DHI after one year postoperatively. The criteria excluded patients who had bilateral MD (one patient), central neural system pathology (one patient), those who had not been tested postoperatively (12 patients), and those who had been tested earlier than one year (two patients). Based on these criteria 31 VNS and 24 L patients were included in the study.

Computerized Posturography

The CP used in this study was from Synapsys Posturography Systems (Version 3.0, Marseille, France). The test was administered by an experienced audiologist. The results of the patients' ability to use inputs from vestibular, visual, and proprioceptive systems to control balance were obtained with the sensory organization test (SOT) in a numeric and easily interpretable graph.

The SOT protocols consist of six steps (conditions) assessed separately for anterior-posterior and medial-lateral evaluation and applied in the order of simple to forcible. The platform was static during the first three conditions: eyes were open in the first, closed in the second (Romberg), and the third was applied with a visual environment that was synchronized with postural fluctuation of the patient. The second group of three conditions were performed on a dynamic platform: eyes were open in the fourth, closed in the fifth, and with visual environment in the sixth condition.

Sensory analysis is used to evaluate the loss of function in sensory perception by proportioning the average equilibrium scores in relation to each other. There are five scores: somatosensorial score (condition 1 ÷ condition 2), visual score (condition 4 ÷ condition 1), vestibular score (condition 5 ÷ condition 1), preferential score (condition 3 + condition 6 ÷ condition 2 + condition 5) and global score (overall score incorporating all conditions). In our study, we focused on vestibular score since the somatosensory system is eliminated by a moving platform and the visual system is eliminated with eyes closed. Therefore, this score indicates the patient's ability to use vestibular inputs.

Dizziness Handicap Inventory

DHI is an inventory used to determine the changes in the quality of life in dizzy patients. The Turkish version of the DHI was applied to all patients (10). The inventory comprises 25 statements that investigate the conditions in

daily activities, that are answered with "*yes*", "*sometimes*" or "*no*". These answers are scored as 4, 2, and 0, respectively, and total DHI scores (ranging from 0 to 100) are obtained by summing all scores. Higher scores indicate greater dizziness handicap.

Statistical Analysis

Statistical analyses were performed using the SPSS software (SPSS version 22, Armonk, NY, USA). The results are presented as the mean ± standard deviation (minimum-maximum). The one-sample Kolmogorov-Smirnov test was used to determine the normality. Because this test showed normal distribution for all data, parametric tests were used. The study population was classified according to the two operations, and differences in gender and the side that was operated on were assessed using the chi-square Test. The differences in CP and DHI scores were assessed using the student's two-tailed t-test. Additionally, all CP scores from anterior-posterior and medial-lateral evaluations were compared for the entire study population with the paired t-test. A Pearson's correlation coefficient test was used for correlation analysis between the CP and DHI scores for the entire study population and related correlation coefficient (r) values were shared. In all statistical analyses, a p-value of <0.05 was considered significant.

Results

A total of 55 patients with a mean age of 44.1±12.3 (18–75) years were included in the study. Thirty-one patients had undergone retro-sigmoid VNS and 24 had undergone trans-mastoid L. The mean time between surgery and testing was 3.3±1.5 (1–7) years. The demographic results for each group are summarized in Table 1. The two groups were similar in terms of age, operated side and the mean time between surgery and tests (p=0.465, p=0.464, and p=0.616, respectively). Gender analysis, however, revealed statistical significance (p=0.003).

The mean CP scores in the anterior-posterior evaluation are somatosensorial score, visual score, vestibular score, preferential score, and global score; for the VNS group, they were 91.5±10.0 (58–100), 87.0±11.3 (44–100), 45.3±23.9 (0–83), 84.2±11.1 (66–100), and 58.9±11.3 (28–78), respectively. The CP scores in the anterior-posterior evaluation, in the same order, for the L group were 91.5±11.5 (58–100), 73.3±19.7 (22–96), 22.8±17.1 (0–58), 87.5±11.3 (66–100), and 50.7±10.2 (28–64), respectively. Likewise, the CP scores in medial-lateral evaluation representing the somatosensorial score, visual score, vestibular score, preferential score, and global score for the VNS group were 95.5±6.1 (68–100), 72.1±17.1 (0–91), 17.0±20.2 (0–56), 91.2±15.6 (21–100), and 54.2±11.7 (20–71), respectively. The CP scores in medial-lateral evaluation, in the same order, for the L group were 95.9±6.7 (68–100), 58.6±19.6 (0–80), 8.5±14.2 (0–50), 84.5±19.3 (21–100), and 47.3±9.8 (20–62). These scores are shown in Figure 1. The visual score, vestibular score, and global score from the anterior-posterior evaluation showed statistically significant differences between the groups (p=0.005, p=0.000, and p=0.007, respectively) in favor of the VNS group. Similarly, the visual score, vestibular score, and global score from the medial-lateral evaluation resulted in p=0.011, p=0.075, and p=0.021, respectively, in the statistical analyses, again in favor of the VNS group.

The comparison of the CP scores of anterior-posterior and medial-lateral scores of the entire study population is summarized in Table 2. The vestibular scores were lower at medial-lateral evaluation (p<0.001).

The mean DHI scores of the VNS and L operation groups were 11.4±10.6 (0–44) and 14.6±14.0 (0–50), respectively. These are shown in Figure 2. The DHI score analysis between the two operations did not show any statistical difference (p=0.359).

The correlation analysis of DHI scores with vestibular scores and global scores did not show any statistically significance (p=0.252, r=-0.157; p=0.100, r=-0.224 for anterior-posterior and p=0.303 r=-0.141, p=0.186, r=-0.181 for medial-lateral evaluations, respectively).

Table 1. Demographic results of study groups

	Vestibular neurectomy (n=31)	Labyrinthectomy (n=24)	
Gender			
Male	12 (39%)	19 (79%)	p=0.003+
Female	19 (61%)	5 (21%)	
Operated side			
Right	16 (52%)	10 (42%)	p=0.464+
Left	15 (48%)	14 (58%)	
Mean age (years)	43.0±9.8 (21–59)	45.6±15.1 (18–75)	p=0.465*
Mean follow-up time (years)	3.2±1.0 (1–5)	3.4±2.0 (1–7)	p=0.616*

+Chi-Square Test, *Independent Student t-test, n: Number

Table 2. Computerized posturography (CP) scores in anterior-posterior and medial-lateral evaluations in entire study population

	Anterior-posterior evaluation	Medial-lateral evaluation	
Somatosensorial score	91.5±10.6 (58–100)	95.7±6.3 (68–100)	p<0.001*
Visual score	81.0±16.8 (22–100)	66.2±19.3 (0–91)	p<0.001*
Vestibular score	35.5±23.8 (0–83)	13.3±18.2 (0–56)	p<0.001*
Preferential score	85.6±11.2 (66–100)	88.3±17.5 (21–100)	p=0.316*
Global score	55.3±11.5 (28–78)	51.2±11.4 (20–71)	p<0.001*

*Paired t-test

Significant p-values are shown in bold

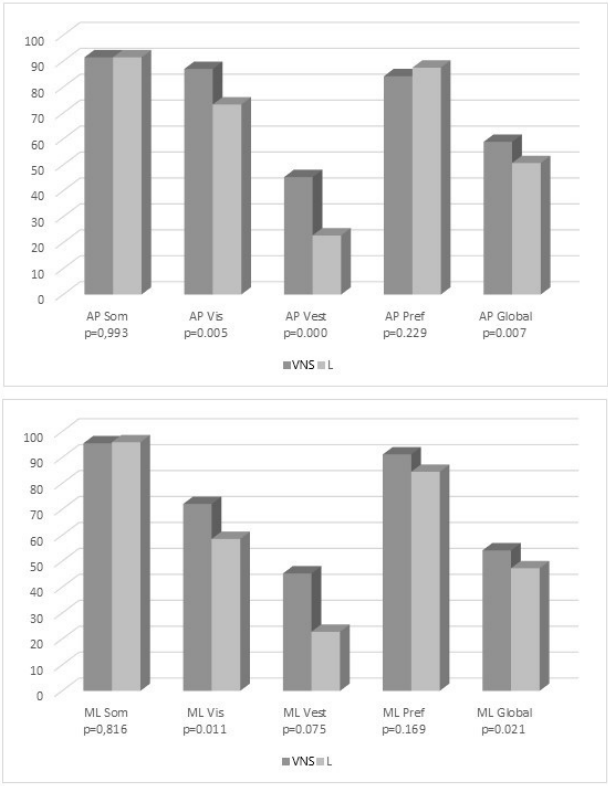


Figure 1. Mean computerized posturography (CP) scores for vestibular nerve section (VNS) and labyrinthectomy (L) group

AP: Anterior-posterior evaluations, ML: Medial-lateral evaluations, Som: Somatosensorial score, Vis: Visual score, Vest: Vestibular score, Pref: Preferential score, Global: Global score

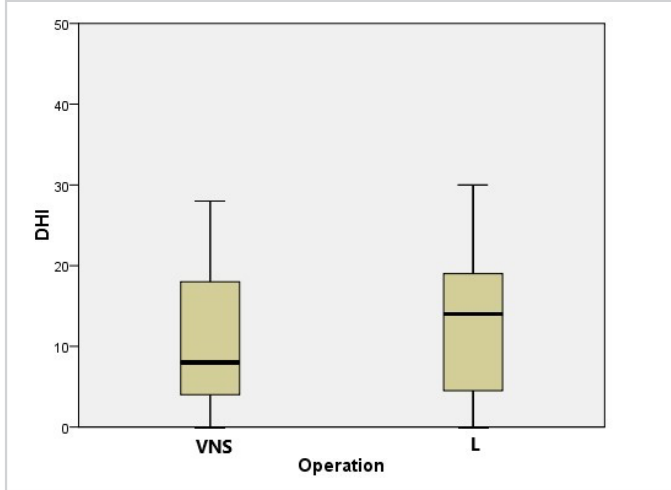


Figure 2. Dizziness Handicap Inventory (DHI) scores for vestibular nerve section (VNS) and labyrinthectomy (L) groups

Discussion

Vestibular ablative surgeries are performed to control the severe vertigo attacks of MD that are intractable to conservative treatment options. These procedures have been performed for over a century. They are reliable and a great deal of experience has been accumulated. Although these procedures are invasive and destructive, recovering from attacks that threaten life and severely disrupt patients' quality of life outweighs the nature of the procedures. In the recent decades, intratympanic aminoglycosides attracted attention for MD treatment as this intervention is a targeted treatment directly to the inner ear with a minimally invasive method and minimal systemic side effects (11). On the other hand, the toxicity of aminoglycosides and lower vertigo control, compared with ablative surgeries, are the chief concerns. Despite being referred to as a destructive procedure, VNS is a hearing-preserving operation. Moreover, in the long term for MD patients, vestibular compensation is determinative of success and can be accomplished in the case of a stabilized vestibular system that rescues the central nervous system from fluctuating vestibular signals, but intratympanic aminoglycoside applications cannot ensure this process because the signals from the inner ear are not totally eliminated. Accordingly, ablative surgeries suggest better vestibular compensation, but unfortunately, this topic requires new studies and elucidation. Even studies about vestibular compensation of ablative surgeries and comparisons between them are scarce. Therefore, in the presented study, we evaluated the objective CP and subjective DHI scores of VNS and L patients. The results revealed that while the subjective DHI scores did not differ between the operations, the VNS group showed better results, confirmed by CP, in objective vestibular and global scores.

Vestibular compensation is a multifactorial process in which age, postoperative time, and surgical differences can affect the results. In the presented study, the two different ablative surgical procedure groups were similar in terms of age and operative time, and therefore we focused on the effect of surgical features on balance outcomes. In theory, there are four different allegations about the differences between VNS and L that can impact the vestibular compensation process. First, L is a preganglionic deafferentation procedure in which ablation is performed peripheral to the ganglion. This is a controversial topic as some allege that this preservation of ganglion plays a role in spontaneous vestibular activity and contributes to the vestibular compensation process (12). Other studies have proposed that this activity may lead to a failure of vertigo control (13). The ambiguity in this issue is whether the ganglion cells survive in the long term or if they later grow as fibrous tissue forming a traumatic neuroma (5). Therefore, the negative or positive impact of ganglion preservation and spontaneous vestibular activity on vestibular compensation is not clear. On the other hand, a total VNS is quite difficult with the retro-labyrinthine approach due to variations in acousticofacial bundle anatomy, and again there is controversy about retained vestibular fibers. Some studies attribute the 10% failure of vertigo control from VNS to these fibers, others speculate that this can contribute to the vestibular compensation process (3, 9, 14).

The other two concerns about retro-sigmoid VNS are that-because it is an intradural procedure-it may delay postoperative mobilization, and retraction of the cerebellum may have a negative effect on vestibular compensation. In our clinic, however, we mobilize patients with VNS as soon as possible, and generally, these patients do not differ from L patients in terms of mobilization time. Additionally, we do not use a cerebellum retractor, rather, we retract delicately with minor surgical instruments until opening the cistern and drainage of the cerebrospinal fluid. These two precautions may have contributed to our VNS results. As we stated, the most common studies related to ablative vestibular surgeries are mainly focused on vertigo control rates. Apart from these, the scarce studies that have focused on vestibular compensation have revealed that there was no difference in terms of disequilibrium between VNS and L, according to self-reported dizziness surveys and posturography performance (9). In contrast, another study revealed that their L group complained more of subjective dizziness, and they attributed this result to the advanced age of the L group (7). In our study, however, we found that the L group's CP scores on the vestibular and global components were lower compared to the VNS group, despite both groups being similar in terms of age. This may be related to the minimal vestibular function in the retained fibers due to incomplete VNS or upregulated proprioceptive inputs (15). Additionally, in our study, thanks to the CP feature, we had the chance to evaluate balance outcomes from anterior-posterior and medial-lateral separately, and to the best of our knowledge, this is the first study finding that medial-lateral motions provoke dizziness more severely in vestibular ablative surgeries.

In contrast to the objective parameters, we did not find a statistical difference in subjective DHI scores between the surgical groups. This subjective dizziness perception is probably affected also by emotional and individual characteristics (16). Additionally, the correlation of objective CP scores and subjective DHI scores are a controversial issue—some studies have found a moderate relation and others found no relation (17, 18). In our study, we did not find statistical significance and considered the results objective; subjective tests do not always correlate with each other since perceptions can vary between individuals.

Studies and evidence on this topic remain scarce, and to the best of our knowledge, the number we reached is the highest in the literature related to ablative surgeries that have been assessed by both objective and subjective tests together. Nevertheless, the study has certain limitations. The retrospective nature of the study hinders gathering additional information, such as the mean mobilization time after surgery, and applying a broad range of objective vestibular tests and establishing the correlation between the two.

Conclusion

In conclusion, the presented study's results show that objective balance outcomes in the long term seem better from VNS than from L ablative surgeries. Further, medial-lateral balance outcomes are more affected than anterior-posterior balance outcomes by unilateral ablative surgeries. Subjective balance perception is not different between the two, and subjective DHI scores do not show a correlation with objective CP scores.

Ethics Committee Approval: The presented study was conducted in the Department of Otolaryngology, Gazi University Hospital, Ankara, Turkey, approved by the local ethics committee (approval no: 01-09/2019).

Informed Consent: All subjects were informed, and consent forms were obtained preoperatively.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: F.C.E., M.Y., N.G., Design: F.C.E., M.Y., E.Ş., Data Collection or Processing: F.C.E., E.Ş., N.G., Analysis or Interpretation: R.K., M.B.U., H.T., Literature Search: F.C.E., N.G., R.K., Writing: F.C.E., N.G., R.K., Critical Review: M.Y., H.T., M.B.U.

Conflict of Interest: The authors declare that they have no conflicts of interest to disclose.

Financial Disclosure: The authors declare that they have no financial support to disclose.

Main Points

- The most successful surgical treatment options in patients with refractory Ménière's disease are vestibular nerve section (VNS) and labyrinthectomy (L).
- These ablative surgeries result in a unilateral loss of vestibular function, and their actual long-term success depends on sufficient vestibular compensation.
- In the presented study, we evaluated the patients with computerized posturography and the dizziness handicap inventory (DHI).
- Results revealed that the VNS group showed better results in objective vestibular and global scores at computerized posturography. However, subjective DHI scores were similar.
- Additionally, computerized posturography results revealed that medial-lateral motions provoke dizziness more severely than anterior-posterior motions in vestibular ablative surgeries.

References

1. Harris JP, Alexander TH. Current-day prevalence of Ménière's syndrome. Audiol Neurotol 2010; 15: 318-22. [Crossref]
2. Claes J. A review of medical treatment for Ménière's disease. Acta Otolaryngol Suppl 2000; 120: 34-9. [Crossref]
3. Schlegel M, Vibert D, Ott SR, Häusler R, Caversaccio MD. Functional results and quality of life after retrosigmoid vestibular neurectomy in patients with Ménière's disease. Otol Neurotol 2012; 33: 1380-5. [Crossref]
4. De La Cruz A, Teufert KB, Berliner KI. Transmastoid labyrinthectomy versus translabyrinthine vestibular nerve section: does cutting the vestibular nerve make a difference in outcome? Otol Neurotol 2007; 28: 801-8. [Crossref]
5. Alarcón AV, Hidalgo LOV, Arévalo RJ, Diaz MP. Labyrinthectomy and vestibular neurectomy for intractable vertiginous symptoms. Int Arch Otorhinolaryngol 2017; 21: 184-90. [Crossref]
6. Badke MB, Pyle GM, Shea T, Miedaner J. Outcomes in vestibular ablative procedures. Otol Neurotol 2002; 23: 504-9. [Crossref]
7. Glasscock III ME, Davis WE, Hughes GB, Jackson CG. Labyrinthectomy versus middle fossa vestibular nerve section in Menière's disease; a critical evaluation of relief of vertigo. Ann Otol Rhinol Laryngol 1980; 89: 318-24. [Crossref]
8. Fisch U. Surgical treatment of vertigo. J Laryngol Otol 1976; 90: 75-86. [Crossref]
9. Eisenman DJ, Speers R, Telian SA. Labyrinthectomy versus vestibular neurectomy: long-term physiologic and clinical outcomes. Otol Neurotol 2001; 22: 539-48. [Crossref]
10. Canbal M, Cebeci S, Duyan G, Kurtaran H, Arslan İ. A study of reliability and validity for the Turkish version of dizziness handicap inventory. TJFMPC 2016; 1: 19-24. [Crossref]
11. Schmerber S, Dumas G, Morel N, Chahine K, Karkas A. Vestibular neurectomy vs. chemical labyrinthectomy in the treatment of disabling Menière's disease: a long-term comparative study. Auris Nasus Larynx 2009; 36: 400-5. [Crossref]
12. Kunkel AW, Dieringer N. Morphological and electrophysiological consequences of unilateral pre-versus postganglionic vestibular lesions in the frog. J Comp Physiol A 1994; 174: 621-32. [Crossref]
13. Langman AW, Lindeman RC. Surgery for vertigo in the nonserviceable hearing ear: transmastoid labyrinthectomy or translabyrinthine vestibular nerve section. Laryngoscope 1993; 103: 1321-5. [Crossref]
14. Leveque M, Seidermann L, Tran H, Langagne T, Ulmer E, Chays A. Vestibular function outcomes after vestibular neurectomy in Meniere disease: Can vestibular neurectomy provide complete vestibular deafferentation? Auris Nasus Larynx 2010; 37: 308-13. [Crossref]
15. Peterka RJ, Statler KD, Wrisley DM, Horak FB. Postural compensation for unilateral vestibular loss. Front Neurol 2011; 2: 57. [Crossref]
16. Pérez N, Martin E, Garcia-Tapia R. Dizziness: relating the severity of vertigo to the degree of handicap by measuring vestibular impairment. Otolaryngol Head Neck Surg 2003; 128: 372-81. [Crossref]
17. Jacobson GP, Calder JH. A screening version of the dizziness handicap inventory (DHI-S). Am J Otol 1998; 19: 804-8. [Crossref]
18. Robertson DD, Ireland DJ. Dizziness handicap inventory correlates of computerized dynamic posturography. J Otolaryngol 1995; 24: 118-24. [Crossref]

A 25-Year Bibliometric Analysis of Allergic Rhinitis Publications from Turkey

Original Investigation

Cüneyt Orhan Kara, Erdem Mengi, Kübra Aktan, Bülent Topuz

Department of Otorhinolaryngology, Pamukkale University Faculty of Medicine, Denizli, Turkey

Abstract

Objective: To analyze the change over the 25 years period in the number of publications on allergic rhinitis from Turkey, and to compare the data of the four major relevant specialties.

Methods: A search was conducted over 25-years between1994 and 2019 using the keywords "allergic rhinitis" and "Turkey" in PubMed®, and "*allerji*", "*alerji*" and "*rinit*" in TRDizin®. The articles were grouped by specialty; namely, "Otorhinolaryngology (ORL)," "Pediatrics," adult "Pulmonary disease" and adult "Allergy/immunology," based on the affiliation of the first author. The total number of publications in each specialty group within the 25-year period were compared using a significance test for a difference in two proportions within the statistical assessment.

Results: The 25-year results revealed 624 and 213 publications in the PubMed® and the TRDizin® databases, respectively. When the number of publications in a specific field in both databases was examined, the highest number of publications were identified in the ORL group, followed by the Pediatrics group. The number of publications in the ORL group was statistically higher than those in the "Pulmonary diseases" and "Allergy/immunology" groups in both the PubMed® and the TRDizin® databases (p=0.0001).

Conclusion: The analysis of the number of 25-year allergic rhinitis publications from Turkey revealed that the academic interest of otolaryngologists in allergic rhinitis was unaffected, despite the challenges experienced in practice, with an increasing number of publications noted. When the number of 25-year publications was examined, ORL recorded the highest number of publications among all specialties.

Keywords: Allergic rhinitis, publication, bibliometrics, PubMed®, TRDizin®, otorhinolaryngology, Turkey

ORCID ID of the authors:

C.O.K. 0000-0003-2219-4283;
E.M. 0000-0001-8813-2443;
K.A. 0000-0001-8622-7182;
B.T. 0000-0001-7895-6190.

Cite this article as: *Kara CO, Mengi E, Aktan K, Topuz B. A 25-Year Bibliometric Analysis of Allergic Rhinitis Publications from Turkey. Turk Arch Otorhinolaryngol 2021; 59(1): 20-5.*

Corresponding Author:
Cüneyt Orhan Kara; cokara@yahoo.com

Received Date: 01.10.2020
Accepted Date: 10.12.2020

DOI: 10.4274/tao.2020.6076

Introduction

Allergic rhinitis (AR) is a common disease, reported to affect 5%–40% of the general population, with evidence of a rising prevalence (1). In Turkey, the prevalence of physician-diagnosed AR is 20.1%, whereas that of self-reported AR is 23.8% in urban areas and 18.4% in rural areas (2, 3). The importance of AR can be attributed to its prevalence, its impact on quality of life and work/school

performance, and its association with other comorbidities (4). Given their prevalence and the morbidity burden, AR and otolaryngic allergies are among the most common fields of interest among otorhinolaryngology (ORL) specialists (5, 6).

In Turkey, too, AR has always been an area of interest for otolaryngologists (7). The number of studies on AR started to increase especially in the 1980s in our country, in line with the global trend. In those years, ORL training clinics began to perform prick tests and to apply immunotherapies as a standard practice in patients with AR, although this increased interest of otolaryngologists in AR has witnessed a gradual decline in recent years (7).

Otolaryngologists and academicians in our country, like their peers around the world, do not only diagnose and treat diseases, but also do research in their fields of interest and publish in national and international journals. There is a lack of data on whether the declining interest of otolaryngologists in AR found reflection in the number of publications on AR from Turkey. Besides otolaryngologists, AR is also a field of interest for specialists of pulmonology, pediatrics, and adult allergy/immunology This bibliometric study analyzes the change in the number of AR publications from Turkey over a 25-year period and determines the impact of the declining interest of otolaryngologists in AR on the number of publications they make. The study further assesses the change in AR publications by other specialties with an interest in the condition and compares the numbers of their publications with the numbers of those by otolaryngologists.

Methods

The study assessed the publications made over the 25-year period from 1994 to 2019 and included in international and national databases, namely, the PubMed®(USA) and the TRDizin®(Turkey). The search in PubMed® was conducted using the keywords "allergic rhinitis" and "Turkey," while the search in TRDizin® was conducted using the keywords "allerji," "alerji" and "rinit." Titles and abstracts of all identified articles were reviewed individually. In cases which the abstract lacked sufficient details, assessment was made by accessing the full text of the article. In addition to AR, the study included also articles with titles such as "immunotherapy and complications" considering such terms as being part of "otolaryngic allergy," and articles that did not mention "allergic rhinitis" in their title but did refer to AR in the text. The study excluded articles that appeared in the search but were not related to AR.

Identified articles were classified into publication groups as "clinical" for studies on disease prevalence, diagnosis, treatment, etc., and "experimental" for studies on animals, and as "case presentations," "reviews" and "guidelines/consensus" according to the method used. And finally, analysis was made over the total number of publications to assess all specialty groups.

"Guidelines/consensus" articles were not included in the specialty group comparison given that these articles involve high numbers of authors from different specialties and their names are listed in alphabetical order (Figures 1, 2 and Table 1). Some of the publications in PubMed® also appeared in TRDizin®, and these were not removed from either of the indices but counted under both.

For specialty group comparisons, all articles were grouped under "Otorhinolaryngology (ORL)," "Pediatrics," adult "Pulmonology" and adult "Allergy/immunology " and listed as "Others" if the first author did not fall under any of these categories. The classification of each publication was determined based on the affiliation of the first author of the study, with the department of the first author garnered from the Affiliations tab in the PubMed® database. When the

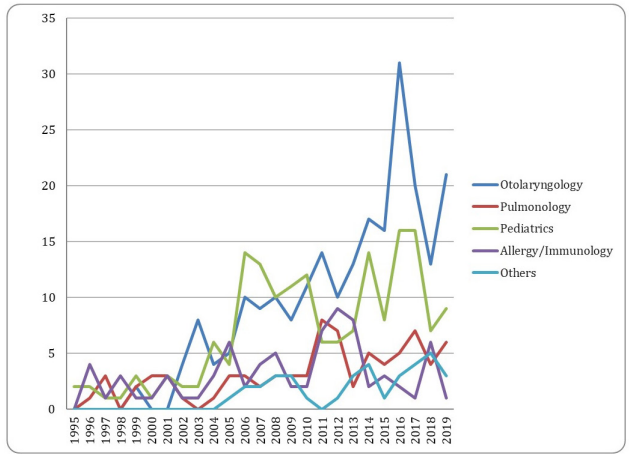


Figure 1. Distribution of "allergic rhinitis" publications from Turkey in PubMed® according to the first author's affiliation and years

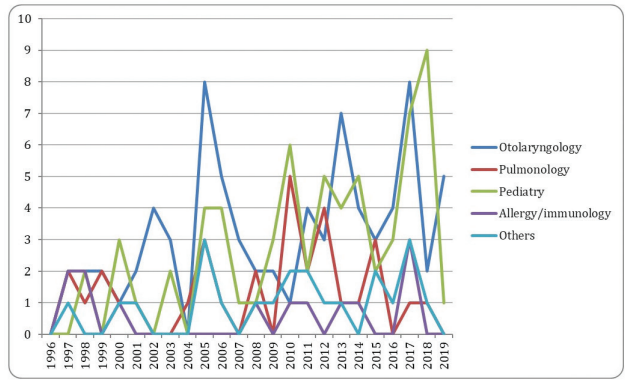


Figure 2. Distribution of "allergic rhinitis" publications from Turkey in TRDizin® according to the first author's affiliation and years

specialty of the first author could not be ascertained using this tab, the affiliation was established by accessing the full text of the article or other publications by the author. In TRDizin®, the first author's affiliation was determined by accessing the full text of the identified article.

A review of affiliations revealed the usage of various terms for pulmonology, pediatrics, and adult allergy/immunology. Of these, Chest Medicine, Pulmonary Diseases (Dis.), Chest Dis. Department (Dept.), Allergic Dis Sub-Dept., Pulmonary Dis.-Allergy Dept., Dept. of Chest Dis., Division (Div.) of Immunology and Allergy, Dept. of Pulmonary Dis.-Allergy, Dept. of Chest Dis. Adult Allergy Unit, and Div. of Allergy and Immunology Dept. of Chest Dis. were classified under the "Pulmonology" group; Dept. of Pediatrics, Dept. of Pediatric Allergy, Dept. of Paediatrics, Pediatric Allergy and Asthma Unit, Dept. of Pediatrics Div. of Allergy, Pediatrics Dept. of Allergy, Dept. of Pediatric Pulmonology, Paediatrics Div. of Allergy and Pulmonology, Dept. of Pediatric Allergy and Pulmonology, Div. of Pediatric Allergy and Pulmonology, Dept. of Pediatrics, Div. of Allergy/Immunology, Dept. Pediatric Allergy and Asthma, Dept. of Pediatrics, Div. of Allergy and Chest Dis. were classified under the "Pediatrics" group; and Internal Medicine, Allergy and Clinical Immunology Unit, Dept. of Clinical Immunology and Rheumatology, Div. of Allergy and Clinical Immunology, Div. of Allergy and Immunology, Internal Medicine Dept. of Allergy, Internal Medicine, Div. of Allergy, Dept. of Immunology, Allergy Div. Dept of Internal Medicine, Dept. of Allergic Dis., Dept. of Internal Medicine, Div. of Immunology and Allergy, Dept. of Internal Medicine and Immunology Div. of Immunology and Allergy, Allergy Div., Dept. of Internal Medicine were classified under the "Allergy/Immunol" group. Table 1 presents the distribution of publications by affiliations. The "Others" group, under which the publications with a first author that did not fall into any of the four groups, consisted of anesthesiology, biochemistry, biology, cardiology, child and adolescent psychiatry, dermatology, endocrinology, environmental engineering, family medicine, gastroenterology, ophthalmology, medical biology, microbiology, molecular biology, nuclear medicine, nursing, occupational medicine, parasitology, pediatrics and infectious dis., pharmaceutical microbiology, pharmaceutical technology, pharmacy, pathology, physiology, rheumatology and urology.

Statistical Analysis

All statistical analyses were performed using the SPSS 25.0 software (IBM SPSS Statistics 25 [Armonk, NY, USA: IBM Corp.]). Categorical data were reported as number and percent. We used significance test for a difference in two proportions. In the interpretation of the comparison results, the Bonferroni correction was used to avoid a decrease in our confidence level. Alpha values as much as the number of paired comparisons (10 paired examinations were made) were arranged (0.05/10=0.005) and significance was interpreted according to this alpha level.

Approval was received from the Ethics Committee of Pamukkale University (60116787-020/71420).

Results

The number of publications identified was 624 in PubMed® and 213 in TRDizin®. Table 1 shows the distribution of publications by their first author's affiliation. Review of the number of publications in both the PubMed® and the TRDizin® databases identified the largest number of

Table 1. Distribution of the total numbers of publications listed in PubMed® and TRDizin® over the 25-year period according to the first author's affiliation

	Otorhinolaryngology	Pediatrics	Allergy/immunology	Pulmonary diseases	Others	**Total
PubMed®	201	177	82*	77*	39*	576
(%)	(34.9)	(30.7)	(14.2)	(13.3)	(6.7)	(100)
TRDizin®	77	65	13*	32*	22*	209
(%)	(36.8)	(31.1)	(6.2)	(15.3)	(10.5)	(100)

There are significant differences between otorhinolaryngology and allergy/immunology, Pulmonary diseases, and others.

*p<0.05 ***"Guidelines/consensus" articles were not included in the specialty group comparison given that these articles involve high numbers of authors from different specialties and their names are usually listed in alphabetical order

Table 2. Distribution of the total number of publications in PubMed® and TRDizin® over the 25-year period according to the article type

	Epidemiological and clinical studies	Experimental studies	Case reports	Reviews	Guides/consensus	Total
PubMed®	494	25	18	39	48	624
(%)	(%79.1)	(%.0)	(%2.8)	(%6.2)	(%7.7)	(100)
TRDizin®	181	2	7	19	4	213
(%)	(%84.9)	(%0.9)	(%3.3)	(%8.9)	(%1.8)	(100)

Table 3. Distribution of publication types by five-year periods

Time periods	Epidemiological and clinical studies	Case reports	Experimental studies	Reviews	Guides/consensus
1995-99	43	2	0	1	0
2000-04	84		1	2	0
2005-09	177	5	0	3	3
2010-14	195	4	-	21*	5
2015-19	176	10	22*	31*	44*
Total	675	25	27	58	52

Numbers of PubMed® and TRDizin® combined (*p<0.05)

publications in the ORL group, followed by the Pediatrics group (Table 1). "Guidelines/consensus" articles were not included in the specialty group comparison given that these articles involve high numbers of authors from different specialties and their names are listed in alphabetical order. Table 2 shows the distribution of the number of publications by types of study and Table 3 shows the breakdown of the types of publications by five-year periods to provide further insight into the trend in the numbers over the 25-year period of our study.

Figures 1 and 2 show the distribution of publications over a 25-year period in the PubMed® and TRDizin® databases by the defined groups and years. The analysis done to identify whether there were any statistical differences among the groups in terms of the total number of publications identified in PubMed® over the 25-year period, the number of articles was found statistically higher in the ORL group than in the Pulmonology (p=0.0001*, p<0.05) and Allergy/immunology (p=0.0001*, p<0.05) groups.

The analysis done to identify whether there were any statistical differences in the total number of publications identified in TRDizin® among the groups over the 25-year period revealed that the number of articles was also statistically higher in the ORL group than in the Pulmonology (p=0.0001*, p<0.05) and Allergy/Immunology (p=0.0001*, p<0.05) groups, while there was no statistical difference between the ORL and Pediatrics groups in terms of the number of publications (p>0.05).

Discussion

AR and otolaryngic allergy are conditions that are diagnosed and treated by otolaryngologists, and these treatment methods have undergone continuous development since the advent of the ORL specialization in Turkey (7). The 1980s witnessed an increasing interest in otolaryngic allergy and AR, and the epidermal skin test and immunotherapy practices that were developed in the 1980s gained momentum in the 2000s (7). In the 2000s, allergy outpatient clinics began to spring up, managed by otolaryngologists, where epidermal skin tests, allergy treatments and immunotherapies were commonly performed. In 2013, such practices were interrupted after hospital administrators started preventing otolaryngologists from providing epidermal skin test and immunotherapy services on the grounds that they were not covered by the Social Security Institution (SSI). Another problem was that AR could be considered within the fields of multiple specialties, diagnosed and treated by ORL, pulmonology, clinical immunology and pediatric departments, and working with the same types of patient groups could sometimes lead to disputes among specialties.

Academic otolaryngologists do research as part of their job, just as other academicians do in their areas of interest and present their research results at congresses and publish in scientific journals to share their findings with the scientific community. Have the SSI practices, which were brought into force in 2013 and partially improved upon in 2016, had any effect on scientific research and the number of publications made? The present study identified an increasing number of publications with otolaryngologists as their first authors since 1994, although no publications were made in certain years, and this was applicable to both the international PubMed® and national TRDizin® databases (Figures 1, 2). It was further ascertained that the restrictive regulations applied to otolaryngologists by the SSI related to AR had no effect on the research and publications on AR. That the academic interest of otolaryngologists in AR has undergone a steady growth over the years suggests that academic otolaryngologists who have taken an active interest in AR at an academic level despite the challenges faced in practice have continued to carry out scientific studies. That said, in Turkey, academicians publish articles not just to contribute to their area of interest, but also to secure academic promotions. It is probable that researchers, although they were not academically interested or had no plans to work in this field, may have selected this field for study because they frequently encounter AR patients.

Another finding of the present study was that the publications on AR were mostly based on patient data (Table 2); in other words, all relevant specialties were seen to have focused on epidemiological and clinical practice rather than experimental laboratory research. It can thus be said that the researchers have had ongoing contact with AR and

AR patients over the 25-year period. An increase, however, was seen in the number of experimental studies over the last 10 years of the study period (Table 3), and this suggests that researchers with an interest in AR are now also engaging in experimental studies.

Another finding of the presented study was that there are a growing number of publications in the literature that were jointly written by many authors from different fields of specialty, such as guidelines or international expert consensus documents (guidelines/consensus) on AR, in the recent years (Table 3). These publications aim at devising international guidelines to steer the building of a common language to be used by all physicians around the world, or to declare consensus as was the case with "Allergic Rhinitis and its Impact on Asthma" (8). Such publications essentially contribute to the development of common guidelines and solutions from a universal perspective, with the cooperation of authors from the different countries around the world. Several authors from Turkey have taken part in these teams, which is clear evidence of the international recognition of our country in the field of AR. There has been a remarkable increase in the number of such mentioned publications in the last five years of the study period (Table 3); however, since these publications cannot be defined as review or research paper, they have been classified under a separate publication category as guidelines/consensus.

An examination of Table 3 reveals a remarkable increase in the numbers of reviews and experimental research papers from Turkey in the last five years, with all (100%) experimental studies and 90% of the reviews conducted over the last 10 years of the study. Based on this finding, it can be suggested that researchers with an interest in AR concluded their clinical research and started to work on experimental studies. Another reason for this finding may be the increasing opportunities that open up in experimental research courses and in experimental research laboratories (9). Regarding the increased number of reviews, it can be suggested that researchers interested in AR have gained sufficient experience and conducted reviews as a means of communicating their own experiences.

The most interesting finding of our study was the distribution of the total number of publications on AR in the 25-year period by the specialties involved in AR (Figures 1, 2 and Table 1). Accordingly, an examination of the total numbers over the 25 years revealed that not only did the number of publications on AR by academic otolaryngologists increase over the years (Figures 1, 2), but were also statistically higher than those authored by the other two specialties (Table 1). Based on this finding, we can suggest that otolaryngologists have a greater academic interest in AR and otolaryngic allergic diseases than the other two specialties involved in adult AR. The natural cause of this may be the fact that patients with AR tend to consult otolaryngologists when experiencing nasal complaints rather than other specialties.

One limitation of the presented study was its failure to include academicians from all related specialties. The number of medical faculties is increasing every year in Turkey, leading to an increase in the number of academicians, and this may also be behind the increasing number of publications on AR (10). Another limitation was that the study assessed only the number of publications, with no qualitative analysis of their content. An analysis of all AR publications by relevant specialties in our country identified no studies in "The top 100 most influential articles in AR from 1970 to 2018" (11). Based on the previous studies analyzing the quality-related problems of the publications from Turkey and looking into their scientific contributions, it can be suggested that these problems may be attributable to several reasons, such as the prevalence of publications made for only academic promotion purposes, the lack of research infrastructure, the low level of research funding/support and the lack of a research tradition (10). All of these topics, however, fall outside of the scope of the presented study and should be examined in further studies.

Conclusion

The analysis of the number of 25-year AR publications from Turkey revealed that the academic interest of otolaryngologists in AR was unaffected, despite the challenges experienced in practice, with an increasing number of publications noted. When the number of 25-year publications was examined, ORL recorded the highest number of publications among all specialties.

Ethics Committee Approval: Approval was received from the Ethics Committee of Pamukkale University (60116787-020/71420).

Informed Consent: It is not necessary for this study.

Peer-review: Externally peer-reviewed.

Conflict of Interest: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Authorship Contributions

Conception: C.O.K, E.M., K.A., B.T., Design: C.O.K, B.T., Supervision: C.O.K., B.T., Materials: C.O.K., E.M., K.A., Data Collection and/or Processing: C.O.K., E.M., K.A., Analysis and/or Interpretation: C.O.K., E.M., K.A., B.T., Literature Review: C.O.K., K.A., B.T., Writing: C.O.K., E.M., B.T., Critical Review: C.O.K., B.T.

Main Points

- Academic interest of otolaryngologists in research of allergic rhinitis was unaffected, despite the challenges experienced in practice.
- The number of allergic rhinitis publications by otolaryngologists has increased steadily over the 25-year period.
- Otorhinolaryngologists recorded the highest number of allergic rhinitis publications among all specialties in the 25 years.

References

1. Bousquet J, Van Cauwenberge P, Khaltaev N, Aria Workshop Group, World Health Organization. Allergic rhinitis and its impact on asthma. J Allergy Clin Immunol 2001; 108: 147-334. [Crossref]
2. Topuz B, Kara CO, Ardiç N, Zencir M, Kadiköylü S, Tümkaya F. [The prevalence of allergic rhinitis in the adult urban population of Denizli]. Kulak Burun Bogaz Ihtis Derg 2005; 14: 106-9. [Crossref]
3. Cingi C, Topuz B, Songu M, Kara CO, Ural A, Yaz A, et al. Prevalence of allergic rhinitis among the adult population in Turkey. Acta Otolaryngol 2010; 130: 600-6. [Crossref]
4. Johansson SG, Hourihane JO, Bousquet J, Bruijnzeel-Koomen C, Dreborg S, Haahtela T, et al. A revised nomenclature for allergy. An EAACI position statement from the EAACI nomenclature task force. Allergy 2001; 56: 813-24. [Crossref]
5. Logbook Oto-Rhino-Laryngology-Head and Neck Surgery (revision 2018) Training Programme. Available from: http://www.http://orluems.com//gestor/upload/LOGBOOK%20REVISED%20FINAL%202018.pdf (Accessed: March 2020).
6. https://www.kbb.org.tr/menu/ucep-28/ (Accessed: March 2020).
7. Topuz B, Kara CO, Çanakçıoğlu S, Günhan K, Uslu Coşkun B, Keleş E, et al. [How are we in the field of otorhinolaryngologic allergy?] KBB-Forum 2020; 19: 161-8. [Crossref]
8. Bousquet JJ, Schünemann HJ, Togias A, Erhola M, Hellings PW, Zuberbier T, et al. Next-generation ARIA care pathways for rhinitis and asthma: a model for multimorbid chronic diseases. Clin Transl Allergy 2019; 9: 44. [Crossref]
9. Başer A, Şahin H. Atatürk'ten günümüze tıp eğitimi. Tıp Eğitimi Dünyası 2017; 48, 70-83. [Crossref]
10. Erdağ TK, Kurtoğlu G. The 100 most cited Turkish papers in the otorhinolaryngology journals of Web of Science. Turk Arch Otorhinolaryngol 2015; 53: 112-9. [Crossref]
11. Wu Q, Zheng R, Wang W, Qiu H, Huang X, Yang Q. The top 100 most influential articles in allergic rhinitis from 1970 to 2018: a bibliometric analysis. J Int Med Res 2019; 47: 6315-36. [Crossref]

The Effect of Curcumin on the Prevention of Myringosclerosis in Rats

Original Investigation

Özlem Akkoca[1], Selda Kargın Kaytez[1], Nihat Yumuşak[2], Akif Sinan Bilgen[1], Ali Kavuzlu[1], Ramazan Öcal[1], Hatice Çelik[1], Necmi Arslan[1]

[1]Department of Otorhinolaryngology, University of Health Sciences Ankara Training and Research Hospital, Ankara, Turkey
[2]Department of Pathology, Harran University Faculty of Veterinary Medicine, Şanlıurfa, Turkey

Abstract

Objective: The aim of this study was to investigate the preventative effect of oral curcumin (CMN) on myringosclerosis (MS) in an experimental rat model.

Methods: The study included 21 female Wistar albino rats randomly separated into three groups. Group 1 was given no treatment (control group). In Group 2 and Group 3, the tympanic membrane (TM) was perforated using a sterile ear pick. The rats in Group 3 were administered oral CMN 200 mg/kg/day. All rats were sacrificed after 16 days. Otomicroscopic and histopathologic examinations were performed on the tympanic membranes.

Results: Histopathologic examinations revealed that there were statistically significant differences between Group 2 and Group 3 in terms of MS degrees ($p<0.001$) and mean thicknesses of TMs ($p<0.001$), but there were no differences between Group 1 and Group 3. In respect of MS detected by otomicroscopy, a statistically significant difference was determined between Groups 1 and 2 ($p<0.001$) and between Groups 2 and 3 ($p<0.01$), but there was no significant difference between Group 1 and Group 3 ($p=0.575$).

Conclusion: Orally administered CMN can prevent myringosclerosis formation in experimentally induced myringotomies.

Keywords: Myringosclerosis, curcumin, tympanic membrane, rats, histology, microscopy, animal experiment

ORCID ID of the authors:
Ö.A. 0000-0002-1030-3692;
S.K.K. 0000-0002-8683-7076;
N.Y. 0000-0002-9299-2902;
A.S.B. 0000-0001-5532-2654;
A.K. 0000-0002-0071-4914;
R.Ö. 0000-0002-9087-4806;
H.Ç. 0000-0001-8951-2755;
N.A. 0000-0002-5650-1475.

Cite this article as: *Akkoca Ö, Kargın Kaytez S, Yumuşak N, Bilgen AS, Kavuzlu A, Öcal R, et al. The Effect of Curcumin on the Prevention of Myringosclerosis in Rats. Turk Arch Otorhinolaryngol 2021; 59(1): 26-32.*

Corresponding Author:
Özlem Akkoca; o.ozturkakkoca@gmail.com

Received Date: 01.08.2020
Accepted Date: 14.11.2020

DOI: 10.4274/tao.2020.5827

Introduction

Myringosclerosis (MS) is an irreversible degeneration characterized by dystrophic calcification and hyalinization in the fibrous layer of the tympanic membrane (TM) (1). It is caused by middle ear infections or surgical intervention to the TM (2). Especially in the treatment of otitis media with effusion in children, the incidence of MS has been reported as 28%-61% depending on the frequency of ventilation tube application (3, 4). Recent studies have shown that hyperoxidative

damage and free oxygen radicals may be the main cause of MS formation (1, 5). It is therefore thought that with the application of anti-inflammatory or antioxidant agents, which can prevent the harmful effects of oxygen-derived free radicals, it may be possible to reduce or prevent the development of MS (1, 4).

Curcumin (CMN) (diferuloylmethane) is a natural polyphenol product obtained from the rhizomes of the Curcuma longa plant (6). In recent years, it has been reported that CMN, which has been used in medical preparations and food coloring for centuries, has strong antioxidant and anti-inflammatory effects (6, 7). It is a safe, non-toxic, and well tolerated agent even at high doses (8). There are studies showing that intraperitoneal, oral, and topical CMN application has a positive effect on wound healing in different parts of the body (8, 9). There are, however, no studies that have investigated the effect of oral CMN administration for the prevention of MS development.

The aim of this study was to investigate whether CMN has a beneficial effect in preventing MS development. To evaluate the effectiveness of CMN, MS was experimentally induced in rats and the results were presented with histopathological parameters.

Methods

Approval and Animals

Approval for this experimental study was obtained from the Experimental Animal Research Ethics Committee of University of Health Sciences, Ankara Training and Research Hospital (Approval Date: September 17, 2019; Approval Number: 596). The procedures required for the care and treatment of all animals were carried out in accordance with the ethical principles of animal experiments and the laws related to animal protection. The animals were housed in standard cages under a 12-hour light/dark cycle, at a stable temperature of 20˚±2 ˚C and humidity of 60%±5%, with food and water ad libitum.

Curcumin Preparation

CMN was administered orally via a feeding tube as 200 mL/kg/day (Sigma-Aldrich Chemical Co.; St. Louis, MO, USA) diluted with 1 mL saline. CMN doses were chosen based on previous experimental studies (10-12).

Experimental Design and Surgical Procedure

A total of 21 female Wistar albino rats, aged 10-12 weeks, each weighing 250 g, were used in the study. All rats were anesthetized with ketamine hydrochloride (50 mg/kg, intramuscular) (New York, NY, USA) preoperatively, then examined with an otomicroscope (Opmi 1; Zeiss, Germany). Only rats with normal TMs examination were included in the study. Rats with TM perforation, myringosclerosis, and infection in the external auditory canal and/or TM were excluded from the study. Myringotomy was performed bilaterally, approximately 2 mm in the upper posterior quadrant of the TMs, by the same researcher, under the otomicroscope, using a sterile ear pick and ear speculum. No signs of ear infection were detected in any animal during the study.

The rats were randomly separated into three groups of 7 (Groups 1, 2, 3). Myringotomy was performed in Group 2 and Group 3 using a sterile ear pick. The groups were treated as follows:

Group 1 (control group): normal TM was confirmed, and no treatment was applied,

Group 2: myringotomy was performed,

Group 3: myringotomy was performed followed by oral CMN solution 200 mg/kg/day administered with a feeding tube for 15 days as treatment.

Only one rat in Group 1 died during this experiment and was excluded from the study.

Otomicroscopic Examination

On the 16th day of the study, the TMs of 20 rats (40 ears) were evaluated by otomicroscopy under anesthesia with ketamine, and then the rats were sacrificed. Myringosclerotic lesions were scored semi-quantitatively using a 4-point scale; 0: no visible myringosclerotic plaques, 1: MS that can be seen at certain intervals with white halo around umbo, 2: Moderate MS containing white halo around umbo, and visible along the manubrium mallei and the anulus, 3: Severe MS with horseshoe-like whitish deposits along the anulus.

Histopathological Examination

After otomicroscopic evaluation, the rats were sacrificed with a high dose of pentobarbital (80 mg/kg, intraperitoneal injection). After decapitation, the head and jaw muscles of the rats were cleaned. Then, the middle ear was removed with the help of bone scissors with the bulla. The tissues taken were decalcified in EDTA solution for 7 days. Then TMs were separated under the stereomicroscope and placed in neutral formal with the bulla and fixed for histopathological analysis. Histopathological evaluation was performed under a light microscope by a pathologist blinded to the groups. All tissues were fixed overnight with a 10% buffered neutralized formalin solution, followed by decalcification with a 10% nitric oxide solution. Routine pathology procedures were applied, and the samples were embedded in paraffin blocks after passing through graded alcohol (50%, 75%, 96%, 100%) and xylol series. Sections were taken from the parts of the TM where myringotomy was performed. Sections of 5 μ thickness obtained from the prepared blocks were taken

on the slides of a Leica RM 2125 RT including the first three sections and every tenth section. The preparations were stained with hematoxylin-eosin (H&E) after treatment with alcohol and xylol. Sclerotic changes in the connective tissue of the lamina propria were evaluated with Masson Trichrome staining. All samples were examined under a high-resolution light microscope (Olympus DP-73 camera, Olympus BX53-DIC microscope; Tokyo, Japan).

Sclerotic changes and density of fibroblast proliferation (FP) in the TM lamina propria were separately quantitatively rated; 0: no visible myringosclerosis/FP, 1: mild myringosclerosis/FP, 2: moderate myringosclerosis/FP, 3: severe myringosclerosis/FP. TM thickness (TMT) was measured using the H&E stained sections of the preparations. The images obtained under the microscope were digitalized with a camera (Olympus BX50, Olympus Optical Co., Tokyo, Japan) and transferred to a computer environment. The TMTs in 10 different areas were measured in micrometers. For statistical analysis, the mean of these 10 values was accepted as the TMT value.

Statistical Analysis

Statistical analyses of the data obtained in the study were made using the IBM Statistical Package for the Social Sciences v20 (IBM SPSS Corp.; Armonk, NY, USA) software. Descriptive statistics were stated as mean±standard deviation (SD), median, minimum, and maximum values for continuous data. Kruskal-Wallis Variance Analysis was used in the analysis of the differences of the variables in three groups. The group/groups from where the difference originated was/were determined using the Kruskal-Wallis Multiple Comparison test. A value of $p<0.05$ was accepted as statistically significant.

Results

In the otomicroscopic examination on the 16th day all the TM perforations were observed to have healed in all three groups. The myringosclerotic lesions were evaluated in 4 grades. In the histopathological examination, sclerotic changes, FP, and mean TMT were determined (Table 1, Table 2).

Otomicroscopic Examination

In Group 2, myringosclerosis was detected in 12 ears (85.7%) as grade 3, and in two ears (14.3%) as grade 1, and in Group 3 in four ears (28.6%) as grade 1, in two ears (14.3 %) as grade 2 and in eight ears there were no sclerotic changes (57,1%). No sclerotic changes were detected in Group 1 (Table 1). In respect of the myringosclerosis groups detected with otomicroscopy, the differences between Groups 1 and 2 ($p<0.001$), and between Groups 2 and 3 ($p<0.01$) were determined to be statistically significant. There was no significant difference between Groups 1 and 3 ($p=0.575$).

Histopathological Examination

Sclerotic changes in the TM lamina propria were shown in Table 2 and Figures 1-3. A statistically significant difference was found between the groups in terms of sclerotic changes in the lamina propria detected in histopathological examination ($p<0.001$). Statistically significant difference was determined between Groups 1 and 2 ($p<0.001$), and between Groups 2 and 3 ($p<0.01$). The difference between Groups 1 and 3 was not statistically significant ($p=0.538$).

FP in lamina propria of TM was detected as follows: in Group 2 severe (71.4%) in 10 ears, moderate (14.3%) in two ears, and mild (14.3%) in two ears; in Group 3 mild in eight ears (57.1%), and in Group 1 mild in two ears (16.7%).

Table 1. Otomicroscopic examination of myringosclerosis

Group	Myringosclerosis (MS) Scale (Point)				
	Ear number	0	1	2	3
1 (Control)	12	12 (100%)	0 (0%)	0 (0%)	0 (0%)
2 (No treatment)	14	0 (0%)	2 (14.3%)	0 (0%)	12 (85.7%)
3 (Treatment)	14	8 (57.1%)	4 (28.6%)	2 (14.3%)	0 (0%)

Table 2. Histopathologic examination of sclerosis

Group	Myringosclerosis (MS)				
	Ear number	No MS	Mild MS	Moderate MS	Severe MS
1 (Control)	12	10 (83.3%)	2 (16.7%)	0 (0%)	0 (0%)
2 (No treatment)	14	0 (0%)	2 (14.3%)	0 (0%)	12 (85.7%)
3 (Treatment)	14	4 (28.6%)	6 (42.8%)	4 (28.6%)	0 (0%)

Statistically significant difference in FP in the lamina propria was found between Groups 1 and 2 ($p<0.001$), and between Groups 2 and 3 ($p<0.01$). There was no significant difference between Groups 1 and 3 ($p=0.176$).

The average TMT was determined in Group 1 as 12.5 µm (range, 9-38), in Group 2 as 178.5 µm (range, 13-196), and in Group 3 as 41 µm (range, 29-131) (Table 3) (Figures 1, 2, 3). Statistically significant difference was determined between Groups 1 and 2 ($p<0.001$), between Groups 2 and 3 ($p<0.05$), and between Groups 1 and 3 ($p<0.01$) (Table 3).

Discussion

Based on otomicroscopic and histopathological findings, the results of this study demonstrated that oral administration of CMN, a nutrient known to have antioxidant and anti-inflammatory effects, prevents the development of experimentally induced MS.

MS is a non-specific, irreversible chronic inflammatory condition characterized by calcium deposition and hyalinization in the lamina propria layer of the TM, typically presenting as white sclerotic lesions (4, 5). Although MS is observed especially in children due to myringotomy and ventilation tube applications, factors such as chronic middle ear infections and trauma have also been held responsible in the etiology (5). Mattsson et al. (13) reported that MS had developed in nine hours after myringotomy in pars tensa and in 12 hours in pars flaccida. In otomicroscopic examination, lesions seen as white calcified plaques of variable shapes and sizes in the TM have been observed in histopathological examination to be mineralized aggregates with calcium phosphate content located in irregular collagen fibers in the lamina propria of sclerotic lesions (14, 15). Following acute TM perforation, TM thickness increases due to edema, inflammation, and new vessel formation in the fibrous layer. It also shows increased fibroblastic activity and epithelial proliferation in TM (16).

Although the formation mechanism is not fully known, recent studies have shown that a hyperoxic environment formed in the middle ear as a result of TM trauma and perforations, and subsequently, free oxygen radicals (ROS) appear (1, 2, 4, 5).

In humans and animals, the middle ear cavity contains 5.5-12.1% oxygen (17). After myringotomy, atmospheric air enters the middle ear cavity and the O2 level increases in the middle ear. Then ROS formation increases in the mitochondria and the endoplasmic reticulum (18). Polymorphonuclear cells and macrophages migrate to the inflammation site, leading to phagocytosis and increased arachidonic acid metabolism. Thus, increasing amounts of ROS contribute to the development of MS (16).

Table 3. Thickness of tympanic membrane

Group	Thickness of tympanic membrane (micrometer)			
	Ear number	Min	Max	Mean
1 (Control)	12	9	38	12.5
2 (No treatment)	14	13	196	178.5
3 (Treatment)	14	29	131	41

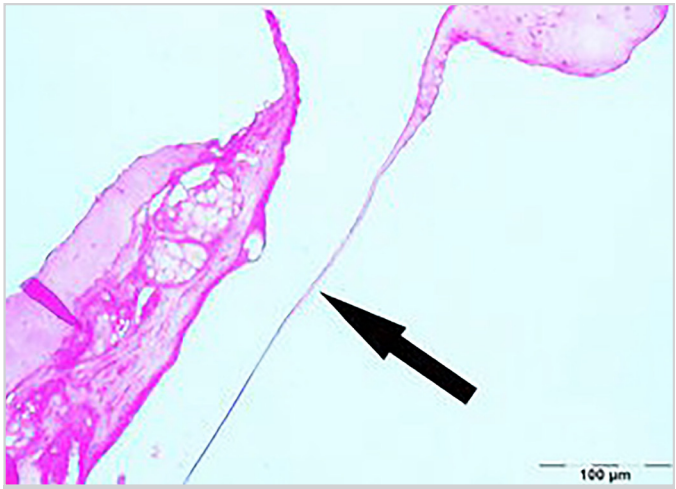


Figure 1. View of normal tympanic membrane (0 point scale) in (hematoxylin and eosin, original magnification x200)

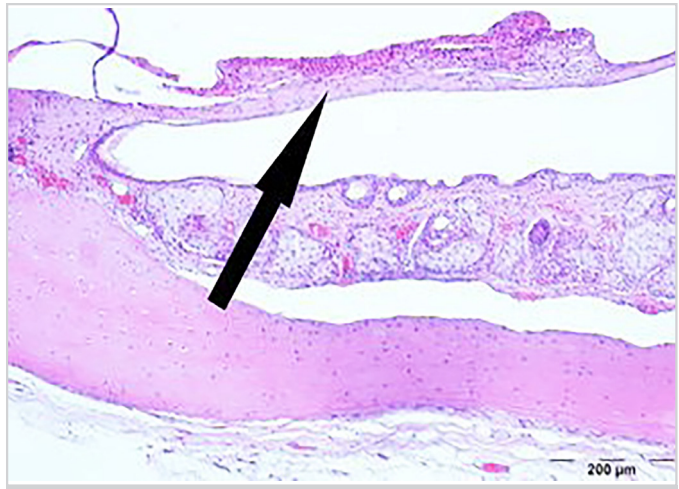


Figure 2. Sclerotic areas and thickness in the tympanic membrane from Group 2

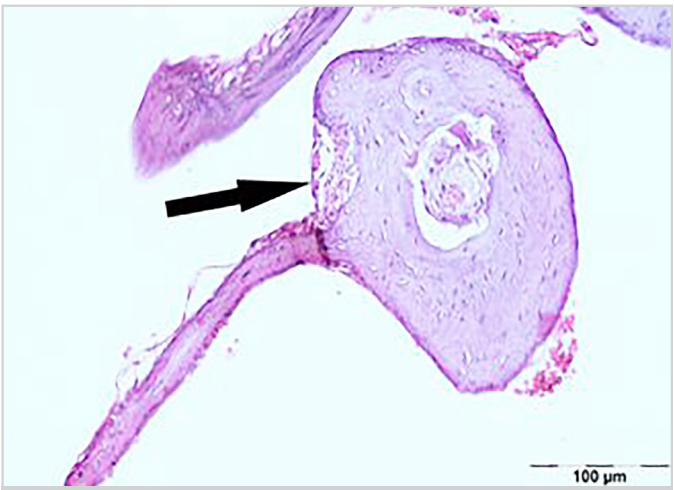


Figure 3. Sclerotic areas and thickness in the tympanic membrane from Group 3

The ROS formed lead to the development of MS by initiating the inflammatory process and tissue damage, creating irregular collagen synthesis, hyaline degeneration, and calcification (19). ROS can be neutralized by substances with antioxidant properties. There are many studies which show that MS formation can be prevented by applying antioxidant, anti-inflammatory, and ROS scavenging agents (1-4, 16, 20-22).

Eğilmez et al. (1) reported that oral or topical administration of Hypericum perforatum extract after myringotomy decreased the inflammation and fibroblastic activity in the lamina propria of the TMs of the rats. Dündar et al. (2) demonstrated that ascorbic acid and/or N-acetylcysteine treatments reduced the development of MS by reducing inflammation scores and cellular infiltration. Üstündağ et al. (3) found that topical application of dexamethasone in rats after myringotomy has positive effects in reducing both the severity and prevalence of MS. Kargin Kaytez et al. (4) used montelukast orally and topically in rats after myringotomy and reported that it reduced FP and TM thickness. Kazikdas et al. (20) suggested that the prevalence of myringosclerotic plaques was less in rats receiving alpha-tocopherol intramuscularly. Park et al. (21) proved that sodium thiosulphate reduced the tympanic membrane thickness after myringotomy in rats and reduced the formation of MS by preventing calcium accumulation. Görür et al. (22) observed in a study that intraperitoneal selenium administration during the closure period of the perforation following myringotomy in rats reduced the occurrence of MS. Vuralkan et al. (16) concluded that FP and TM thickness decreased with both local and intraperitoneal application of L-carnitine. However, there are no studies showing the effect of oral CMN administration on MS development. Our study is the first study in the literature, demonstrating that oral CMN administration after myringotomy in rats decreases both FP and TM thickness in the lamina propria.

CMN is a type of spice that is commonly used in South Asian cuisines. In recent years it has been shown to have anti-inflammatory, antioxidant, wound-healing, hypoglycemic and antimicrobial properties. It is used to prevent and treat diseases related to the digestive system, the cardiovascular system, the liver, and the skin, as well as those of the endocrine system such as diabetes, and has positive effects on wound healing (8, 9). In rat studies, it has been found that orally administered CMN increases the activity of antioxidant enzymes such as superoxide dismutase, catalase, and glutathione peroxidase (23). These antioxidant enzymes have a protective effect on human cells against the harmful effects of toxic reactive oxygen radicals. It has also been shown that CMN inhibits the production of proinflammatory cytokines released from monocytes and macrophages, such as tumor necrosis factor alpha and interleukin-1, which are known to play important role in regulating inflammatory responses (24). In the early phase of wound healing, CMN also increases the speed of healing by inducing apoptosis of inflammatory cells and shortens the inflammatory process. CMN has an enhancing effect on collagen synthesis and has an effect on the differentiation of fibroblasts and facilitating migration to the wound site (25).

There are many studies which show that CMN, known to have significant antioxidant and anti-inflammatory effects, can be used as a wound-healing agent, especially when administered topically (9, 25, 26). However, there are few studies that discuss its oral administration (10, 27). In a literature review, a study was found which evaluated the improvement in TM after paracentesis using topical CMN, but no other study could be found that examined the effect of CMN on oral administration and MS formation. In a study by Birdane et al. (26) topical CMN was used in the form of drops and it was found that TMs healed close to normal in rats after paracentesis similar to normal TMs. In the same study, it was reported that TMT and sclerosis level were significantly lower in the CMN group compared to the control group. In our study, CMN was administered orally 200 mg/kg/day diluted with 1ml saline via a feeding tube to the rats in Group 3 for 15 days as has been described in previous studies (10-12). Correlations were determined between otomicroscopic and histopathologic examination results. In both examinations, statistically significant difference was found between Groups 1 and 2 ($p<0.01$), and between Groups 2 and 3 ($p<0.01$), but there was no significant difference between Groups 1 and 3 ($p=0.575$, $p=0.538$) (Tables 1, 2). However, when comparing the numbers of ears detected with sclerosis and the grades in both examinations (Tables 1 and 2), it was seen that mild sclerosis could be detected in the histopathologic examination but not in the otomicroscopic examination. In Group 3, histopathologic examination found moderate sclerosis in four ears (28.6%) and mild sclerosis in six ears (42.9%), while otomicroscopic examination found MS grade 1 in four ears (28.6%) and

grade 2 in two ears (14.3%). Although otomicroscopy has 80% sensitivity and 75% specificity, as stated by Santos et al. (28), it can also be seen from the findings of our study that histolopathological examination is a better method to evaluate MS. Sclerosis in the lamina propria and FP in rats that were administered oral CMN had similar levels of TM characteristics as the rats in the control group, and only the mean TMT was higher (Figures 1, 2). The mean TMT value was found to be highest at 178.5 μm (13-196) in Group 2, and lowest at 12.5 μm (9-38) in Group 1. Although no difference in sclerosis and FP was determined between Group 1 (control group) and Group 3 (oral CMN group), TMT was at a higher level in Group 3, which may have resulted from the effect of CMN enhancing myofibroblasts, fibroblasts, and macrophages migration and angiogenesis in the post-traumatic healing process (29).

In this study, we found that orally administered CMN can prevent the occurrence of experimental MS. Therefore, CMN, which is known as an important nutrient, should be part of the daily diet, and topical use should be considered in those with infection caused by a ventilation tube or myringotomy. There is a need for further clinical studies in this field.

Conclusion

Oral administration of CMN, which is known and used as a spice, can prevent experimental MS. These effects of CMN may be due to the antioxidant and/or anti-inflammatory properties. However, there is a need for clinical trials which can reveal the effects of CMN on MS.

Ethics Committee Approval: Ethics committee approval was received for this study from the Experimental Animal Research Ethics Committee of University of Health Sciences, Ankara Training and Research Hospital (Approval Date: September 17, 2019; Approval Number: 596).

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - S.K.K.; Design - A.S.B.; Supervision - A.K.; Resources: R.Ö.; Materials - H.Ç.; Data Collection and/or Processing - S.K.K.; Analysis and/or Interpretation - N.Y.; Literature Search - Ö.A.; Writing - Ö.A.; Critical Reviews - N.A.

Conflict of Interest: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Main Points

- Oral curcumin has an inhibitory effect on sclerotic changes and fibroblast proliferation in the lamina propria layer of the tympanic membrane in experimental myringosclerosis.
- Oral intake of curcumin in experimental myringosclerosis has a decreasing effect on tympanic membrane thickness.
- Curcumin can prevent experimental myringosclerosis, due to its antioxidant and/or anti-inflammatory effects when administered orally.

References

1. Eğilmez OK, Kökten N, Ekici AI, Kalcıoğlu MT, Yesilada E, Tekin M. The effect of Hypericum perforatum L. (St. John's Wort) on prevention of myringosclerosis after myringotomy in a rat model. Int J Pediatr Otorhinolaryngol 2015; 79: 1128-34. [Crossref]
2. Dündar R, İnan S, Muluk NB, Cingi C, İlknur AE, Katılmış H. Inhibitory effect of N-acetyl cysteine and ascorbic acid on the development of myringosclerosis: an experimental study. Int J Pediatr Otorhinolaryngol 2014; 78: 1019-25. [Crossref]
3. Üstündağ M, Koçyiğit M, Bulut E, Altaner Ş, Taş A, Yağız R. Effect of topical dexamethasone for preventing experimentally induced myringosclerosis. Turk Arch Otorhinolaryngol 2017; 55: 3-9. [Crossref]
4. Kargin Kaytez S, Kavuzlu A, Yumusak N, Oçal R, Akkoca O. Is there any effect of montelukast on prevention of myringosclerosis after myringotomy in a rat model? Eur Arch Otorhinolaryngol 2019; 276: 57-62. [Crossref]
5. Özdemir D, Ağrı İ, Bakirtaş M, Ağrı A, Mehel DM, Çelebi M, et al. The effect of rosmarinic acid on the prevention of myringosclerosis. Int J Pediatr Otorhinolaryngol 2019; 126: 109597. [Crossref]
6. Birdane L, Muluk NB, Cingi C, Burukoglu D, Fidan V, Incesulu A. Evaluation of the efficacy of curcumin in experimentally induced acute otitis media in rats. Ann Otol Rhinol Laryngol 2014; 123: 325-32. [Crossref]
7. Mirzaei H, Shakeri A, Rashidi B, Jalili A, Banikazemi Z, Sahebkar A. Phytosomal curcumin: a review of pharmacokinetic, experimental and clinical studies. Biomed Pharmacother 2017; 85: 102-12. [Crossref]
8. Bucak A, Ozdemir C, Ulu S, Gonul Y, Aycicek A, Uysal M, et al. Investigation of protective role of curcumin against paclitaxel-induced inner ear damage in rats. Laryngoscope 2015; 125: 1175-82. [Crossref]
9. Çakan D, Aydın S, Demir G, Başak K. The effect of curcumin on healing in an animal nasal septal perforation model. Laryngoscope 2019; 129: E349-E54. [Crossref]
10. Safali S, Aydin BK, Nayman A, Ugurluoglu C. Effect of curcumin on bone healing: an experimental study in a rat model of femur fracture. Injury 2019; 50: 1915-20.[Crossref]

11. AlBasher G, Abdel-Daim MM, Almeer R, Ibrahim KA, Hamza RZ, BungauS, et al. Synergistic antioxidant effects of resveratrol and curcumin against fipronil-triggered oxidative damage in male albino rats. Environ Sci Pollut Res Int 2020; 27: 6505-14. [Crossref]
12. Hocking AJ, Elliot D, Hua J, Klebe S. Administering fixed oral doses of curcumin to rats through voluntary consumption. J Am Assoc Lab Anim Sci 2018; 57: 508-12.[Crossref]
13. Mattsson C, Johansson C, Hellström S. Myringosclerosis develops within 9 h of myringotomy. ORL J Otorhinolaryngol Relat Spec 1999; 61: 31-6. [Crossref]
14. Selçuk A, Ensari S, Sargın AK, Can B, Dere H. Histopathological classification of tympanosclerotic plaques. Eur Arch Otorhinolaryngol 2008; 265: 409-13. [Crossref]
15. Doner F, Yariktas M, Dogru H, Uzun H, Aydin S, Delibas N. The biochemical analysis of tympanosclerotic plaques. Otolaryngol Head Neck Surg 2003; 128: 742-45. [Crossref]
16. Vuralkan E, Tokgöz SA, Simsek G, Koybasioglu F, Han U, Caliskan M, Besalti O, Akin I. Effect of local use of L-carnitine after myringotomy on myringosclerosis development in rats. J Laryngol Otol 2013; 127: 468-72. [Crossref]
17. Sadé J, Luntz, M. Dynamic measurements of gas composition in the middle ear. II: steady state value. Acta Otolaryngol 1993; 113: 353-7. [Crossref]
18. Akbaş Y, Pata YS, Görür K, Polat G, Polat A, Ozcan C, Unal M. The effect of L-carnitine on the prevention of experimentally induced myringosclerosis in rats. Hear Res 2003; 184: 107-12. [Crossref]
19. Dogan E, Erdag TK, Sarioglu S, Ecevit MC, Ikiz AO, Güneri EA. The preventive effect of N-nitro L-arginine methyl ester in experimentally induced myringosclerosis. Int J Pediatr Otorhinolaryngol 2011; 75: 1035-9. [Crossref]
20. Kazikdas KC, Uguz MZ, Erbil G, Tugyan K, Yilmaz O, Guneli E, et al. The anti-oxidant effect of alpha-tocopherol in the prevention of experimentally induced myringosclerosis. Otol Neurotol 2006; 27: 882-6. [Crossref]
21. Park YH, Park CH, Kim HJ. The effect of topical sodium thiosulfate in experimentally induced myringosclerosis. Laryngoscope 2010; 120: 1405-10. [Crossref]
22. Görür K, Ozcan C, Polat A, Unal M, Tamer L, Cinel I. The anti-oxidant and anti-apoptotic activities of selenium in the prevention of myringosclerosis in rats. J Laryngol Otol 2002; 116: 426-9. [Crossref]
23. Akbik D, Ghadiri M, Chrzanowski W, Rohanizadeh R. Curcumin as a wound healing agent. Life Sci 2014; 116: 1-7. [Crossref]
24. Wu NC, Wang JJ. Curcumin attenuates liver warm ischemia and reperfusion-induced combined restrictive and obstructive lung disease by reducing matrix metalloprotease 9 activity. Transplant Proc 2014; 46: 1135-8. [Crossref]
25. Barchitta M, Maugeri A, Favara G, Magnano San Lio R, Evola G, Agodi A, et al. Nutrition and wound healing: an overview focusing on the beneficial effects of curcumin. Int J Mol Sci 2019; 20: 1119. [Crossref]
26. Birdane L, San T, Muluk NB, Burukoglu D, Cingi C. Efficacy of curcumin in the healing of paracentesis in rats. Int J Pediatr Otorhinolaryngol 2014; 78: 280-4. [Crossref]
27. Soyalıç H, Gevrek F, Karaman S. Curcumin protects against acoustic trauma in the rat cochlea. Int J Pediatr Otorhinolaryngol 2017; 99: 100-6. [Crossref]
28. Santos PF, Leal MC, Peixoto C, Neto SC, Rosas ST. Otomicroscopic and histologic findings of induced myringosclerosis in rats: a critical study of an experimental model. Braz J Otorhinolaryngol 2005; 71: 668-74. [Crossref]
29. Sidhu GS, Singh AK, Thaloor D, Banaudha KK, Patnaik GK, Srimal RC, et al. Enhancement of wound healing by curcumin in animals. Wound Repair Regen 1998; 6: 167-77. [Crossref]

A Herbal Formula in the Therapy of Acute Postviral Rhinosinusitis

Original Investigation

Aleksandar Peric[1], Dejan Gacesa[2], Aleksandra Barac[3], Aneta Peric[4]

[1]Department of Otorhinolaryngology, Military Medical Academy Faculty of Medicine, University of Defence, Belgrade, Serbia
[2]Ear Nose and Throat Hospital "Doctor Zutic", Belgrade, Serbia
[3]Department of Infectious and Tropical Diseases, Belgrade University School of Medicine, Belgrade, Serbia
[4]Institute of Pharmacy, Military Medical Academy Faculty of Medicine, University of Defence, Belgrade, Serbia

Abstract

Objective: To assess the effects and adverse events of preparation Sinulan forte® containing extracts of five medicinal plants in comparison to mometasone furoate nasal spray (MFNS) in therapy of acute postviral rhinosinusitis (APRS).

Methods: We included 46 APRS patients in this prospective investigation and randomized to two groups. The patients in group 1 (n=23) received MFNS 200 μg two times/day for ten days, and patients in group 2 (n=23) received Sinulan forte®, tablets 225 mg per os, two times/day also for ten days. We evaluated the total symptom score (TSS), the separate scores for individual symptoms (nasal congestion, rhinorrhea, postnasal discharge, facial pain, impaired sense of smell), the quality-of-life outcome, and the findings from nasal endoscopy (edema of the nasal mucosa, nasal secretion) prior and after the therapy.

Results: Significantly lower absolute post-treatment scores and better relative improvement were identified for TSS, nasal congestion, facial pain, loss of the sense of smell, edema of the mucosa and nasal secretion in patients receiving herbal preparation (group 2). However, lower absolute post-treatment score and better relative improvement were found for rhinorrhea and postnasal drip in group 1. Clinically important differences were found regarding the TSS and endoscopic findings, with no adverse effects in group 2, but in group 1 two patients had mild nasal bleeding and two had sensation of dryness in the nasal mucosa.

Conclusion: Herbal product Sinulan forte® can be a safe and effective treatment for APRS. Our results suggest no adverse events of this herbal preparation in comparison to intranasal corticosteroid spray therapy.

Keywords: Rhinitis, herbal medicine, inflammation, nasal steroid, sinusitis, quality of life, endoscopy

ORCID ID of the authors:

A.P. 0000-0002-8453-7272;
D.G. 0000-0002-5377-1525;
A.B. 0000-0002-0132-2277;
A.P. 0000-0002-4187-7584.

Cite this article as: *Peric A, Gacesa D, Barac A, Peric A. A Herbal Formula in the Therapy of Acute Postviral Rhinosinusitis. Turk Arch Otorhinolaryngol 2021; 59(1): 33-42.*

Corresponding Author:
Aleksandar Peric, aleksandarperic1971@gmail.com

Received Date: 28.10.2020
Accepted Date: 12.12.2020

DOI: 10.4274/tao.2020.6098

Introduction

Acute rhinosinusitis (ARS) is an acute inflammatory disorder of the sino-nasal mucosa, and in more than 98% of the patients is caused by rhinoviruses, coronaviruses, influenza, and adenoviruses (1-3). This inflammation, usually known as common cold, can pass in 7-10 days with the appropriate symptomatic therapy. In some cases, however, it can be followed by acute postviral rhinosinusitis (APRS) with prolonged duration of nasal symptoms, requiring the use of medications (2-4). Inflammation caused by bacteria is found in only 0.5 to 2% of ARS patients, requiring antibiotic treatment (2-4). According to the current European guidelines for diagnostics and treatment of rhinosinusitis, there is a recommendation for use of intranasal corticosteroid sprays (INCS) and drops especially in the therapy of patients with APRS (5). A clinical trial conducted by Meltzer et al. (6) showed that the treatment of patients with uncomplicated ARS with mometasone furoate nasal spray (MFNS) was effective and relatively safe in a full dose of 400 μg daily. This is very important for the reduction of antibiotic prescriptions in these patients. However, there are evidenced problems with the use of INCS in patients with diabetes, enhanced intraocular pressure, cataract, arterial hypertension, and other disorders (6).

Herbal medicinal products have been used around the world for the treatment of many inflammatory diseases. In 2011, the World Health Organization estimated that 70–90% of the population of developing countries and almost 20% of the United States used herbal drugs, whereas in Europe these percentages are estimated to 10–20% (7, 8). *Andrographis paniculata* (creat or green chiretta) is an annual plant of the family *Acanthaceae,* native to South Asia, having antimicrobial and anti-inflammatory effects (9, 10). Several controlled clinical trials showed that this plant can be an effective and safe option in the treatment of uncomplicated upper airway inflammations (9-12). Sinulan forte® is a trademarked herbal preparation, available in tablets and composed of five herbal extracts: green chiretta (*Andrographis paniculata*, leaf), elder (*Sambucus nigra*, flower), common mullein (*Verbascum thapsus*, flower), European vervain (*Verbena officinalis*, herb), and gentian (*Gentiana lutea*, root). Herbal preparation with *Andrographis paniculata* extract is recommended in the European Position Paper on Rhinosinusitis and Nasal Polyps 2020 (EPOS 2020) for the treatment of common cold, but we found no randomized studies regarding the use of this herbal compound in the treatment of APRS (5). Our comparative study was designed to evaluate the effects and the safety of the herbal product Sinulan forte® and the intranasal corticosteroid MFNS in the treatment of patients with APRS.

Methods

Study Design

This was a randomized, prospective, open-label and non-inferiority study on the treatment of APRS. The study was conducted according to the Helsinki Declaration, from January through December 2019 in our Department of Otorhinolaryngology. The protocol for investigation is approved by the Ethics Committee of the Military Medical Academy, Belgrade, Serbia (MMA no: 05/2019). Written informed consent was obtained from every patient.

Inclusion and Exclusion Criteria

Forty-six subjects with APRS were recruited for participation in this study. In line with the EPOS 2012 (13), patients had inflammatory changes in the nasal cavity and sinuses, increased symptoms (nasal obstruction/congestion, rhinorrhea, postnasal drip, facial pain/pressure, and loss of the sense of smell) after five days or persistent complaints after 10 days, but no longer than 12 weeks. Endoscopic examination of the patients showed edematous nasal mucosa and increased middle meatal secretion.

Criteria for exclusion were: patients aged <18 and >65 years, having chronic rhinosinusitis (CRS), previous surgery in the sinonasal region, deformation of the nasal septum and turbinate hypertrophy that significantly disrupt the nasal airflow and INCS application, different systemic disorders that can affect the nose and sinuses (non-eosinophilic and eosinophilic granulomatosis with polyangiitis, Kartagener's syndrome, cystic fibrosis, etc.), immunologically associated diseases (multiple sclerosis, polyarthritis, rheumatoid arthritis, diabetes mellitus), sensitivity to non-steroid anti-inflammatory drugs, seasonal allergic rhinitis, bronchial asthma, allergic reactions to medicines used in this study. Also, patients who had used oral or topical antihistamines, corticosteroids, and antibiotics a month prior to the study and patients who used sympathomimetics and mucolytics within the seven days before the study were also excluded. Current cigarette smoking, pregnancy and lactation were also criteria for exclusion. Patients who had complaints of common cold within five days resolution and severe bacterial ARS, with fever higher than 38 °C, severe facial pain and mucopurulent discharge with unilateral predomination were excluded. To exclude the patients with bacterial ARS, aspirate from the middle meatus was taken from every patient and samples were cultivated on blood agar (HiMedia™ Laboratories, Mumbai, India) for pathogenic bacteria.

Randomization

The patients were randomly divided according to the CONSORT statement. Sixty-five subjects with diagnosis of APRS were recruited for this study. Five patients did not accept to participate, and fourteen subjects did not meet

the inclusion criteria. Finally, forty-six (n=46) patients were selected and assigned to group 1 (n=23) and group 2 (n=23). Computer-generated random allocation was used for assignment of patients into two groups. The participants were deemed eligible by the researcher. The researcher then informed the nurse about the eligibility and she assigned the participants to group 1 or 2. Figure 1 presents the study profile.

Treatment

Group 1 (n=23) received MFNS (Mometazon Sandoz®, Lek Pharmaceuticals D.D., Verovskova 57, 1526 Ljubljana, Slovenia) 200 µg two times daily (two sprays in both nostrils in the morning and in the evening) for 10 days. These patients were informed about the correct application of INCS. Group 2 (n=23) received herbal preparation Sinulan forte® 225 mg tablets (Walmark, A.S., Oldrichovice 44, 73961 Trinec, Czech Republic), two times daily for 10 days. The drugs were provided to the patients after randomization. Both the researchers and patients knew which treatment was being administered.

Clinical Evaluation

Levels of ARS symptoms were evaluated at the start of the study (visit 1) and within two days after the end of therapy (visit 2) using a 10 cm visual analogue scale (VAS) (0–10

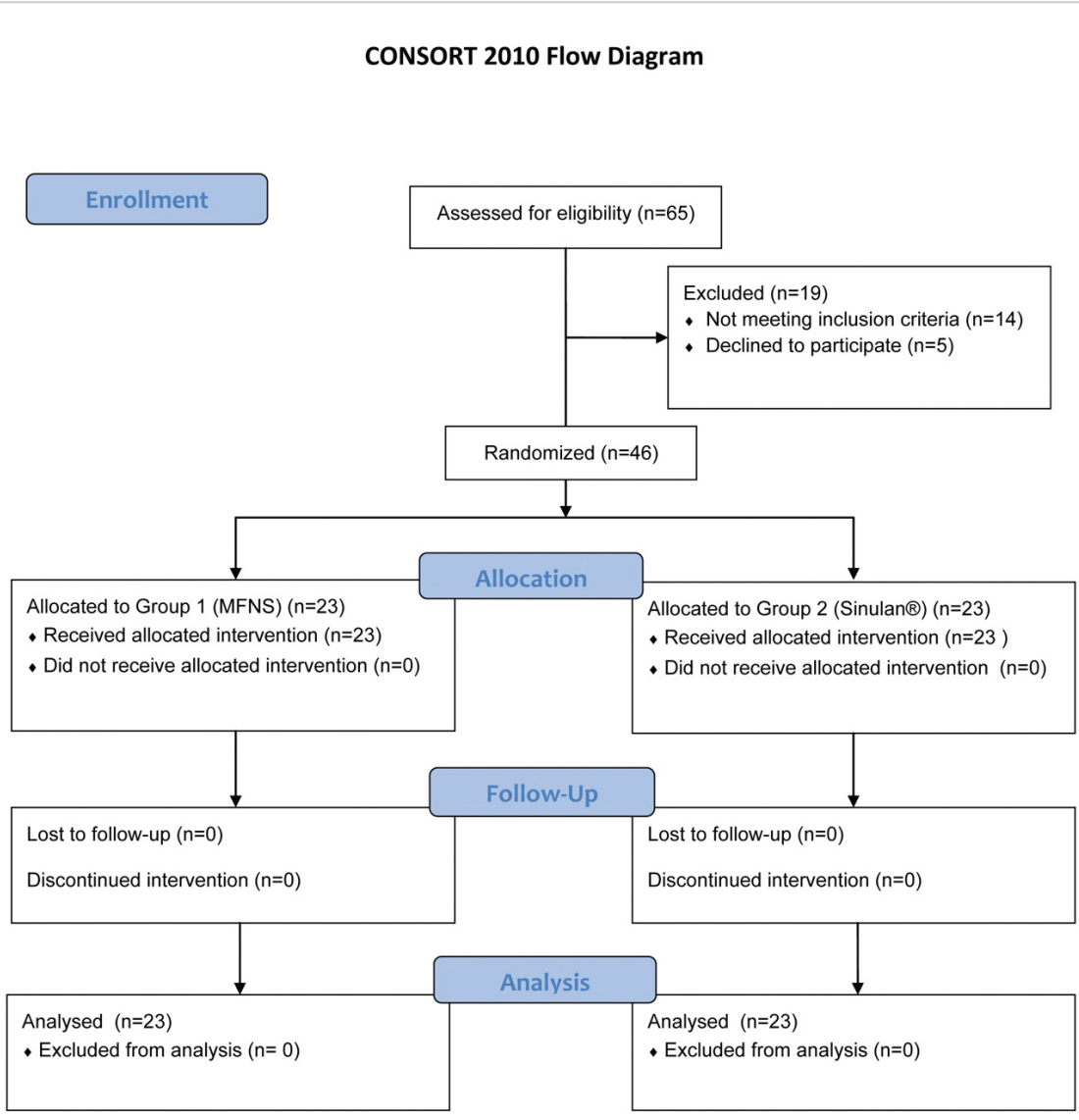


Figure 1. Randomization was performed in accordance with the CONSORT statement. Sixty-five patients (n=65) diagnosed with APRS were found eligible for the study. Five (n=5) patients refused to participate and fourteen (n=14) did not meet the inclusion criteria. Forty-six (n=46) patients were thus enrolled and randomized to groups 1 (n=23) and 2 (n=23)

CONSORT: Consolidated Standards of Reporting Trials, APRS: Acute postviral rhinosinusitis, n: Number

cm; from 0=absence of symptom to 10=maximum symptom intensity). The use of VAS was applied and explained to the patients by the nurse after the randomization. Patients self-reported the intensity of their symptoms. Symptoms scored from 0 to 3 were indicated as "mild ARS;" symptoms scored from 4 to 7 were indicated as "moderate ARS." Participants with "severe ARS," i.e., scored from 8 to 10 and reported fever higher than 38 °C were excluded. The participants self-assessed the intensity of their symptoms and noted the therapy use on diary cards, two times daily, after the taking their medication. At visit 2, the researcher recorded the scores and evaluated the patients' treatment compliance based on their diary cards. The health-related quality of life (QoL) score was evaluated at visits 1 and 2 with the Sino-Nasal Outcome Test 20 (SNOT-20). This 20-item questionnaire can be used for the assessment of social and emotional consequences of ARS symptoms. At visits 1 and 2, two independent rhinologists used a 4 mm 0° endoscope (Storz SE & Company, Tuttlingen, Germany) to evaluate the presence of mucosal edema and nasal secretion in the middle meatus on the same patient. A four-point scale described by Pfaar et al. (14) was used for the evaluation of mucosal edema and nasal secretion. Presence of edema was scored from "no edema" (0) to "severe edema" (3); nasal secretion from "none" (0) to "profuse" (3). The maximum bilateral score for separate endoscopic sign is 6. Following the EPOS 2012 guideline (13), we did not use radiological examinations (X-ray, computed tomography, magnetic resonance imaging) for the diagnosis and the evaluation of the treatment outcomes.

The efficacy endpoints were mean total symptom score (TSS); sum of the scores for 5 symptoms, individual symptom scores, scores for endoscopic findings (edema, nasal secretion), and SNOT-20 score at the visit 1 and visit 2.

Follow-up

All patients were asked to come for the follow-up visit on days 10th and 20th, and TSS and endoscopic parameters were evaluated due to the potential risk of recurrence.

Safety

Reported adverse effects were noted during the study, including the follow-up period, by grading their severity as mild, moderate, and severe. At visit 2, we performed laboratory tests, evaluation of vital signs and nasal examination (rhinoscopy, endoscopy). The participants were informed about the possible adverse effects of both medications. All possible complications of severe form of ARS (orbital, intracranial or bony) were noted during the study.

Sample Size Calculation

Calculation of sample size was based on a requirement to reach the minimal differences in TSS and endoscopic findings between the two treatment options. According to Meltzer et al. (15), the calculation of minimal clinically important difference (MCID) is based on a proposal provided by the Agency for Healthcare Research and Quality. This distribution-based method relied on the statistical distributions of data concerning the TSS and endoscopic findings. The calculation is performed by the formula: MCID=0.5 (50%) of the sum of pre-treatment standard deviations (SDs) of TSS/endoscopic signs in both treatment groups. The sufficient total sample sizes providing at least 80% power of study, at level of significance of 0.05 to reach a MCID in TSS of 1 and endoscopic score of 1 were 23 participants in each group.

Statistical Analysis

The parameters were expressed as mean ± SD. For between-group comparison, we used the non-parametric Mann-Whitney U test. For paired comparisons within a group, we used the Wilcoxon's test. To calculate the relative improvement of each parameter weighed with the pretherapeutic value, we used the formula: post-therapeutic value - pretherapeutic value/pretherapeutic value * 100. The statistical significance (p) is set at the level of 0.05. The analysis was performed using the version 15.0 of the Statistical Package for the Social Sciences (SPSS) software (SPSS Inc., Chicago, USA).

Results

Demographic Data

Forty-six participants (27 males and 19 females) aged 19 to 63 years (mean age: 41.37±32.65) suffering from APRS were enrolled in the study. Demographic characteristics of participants are presented in Table 1.

Clinical Data

Data presenting pre- and post-treatment TSS, individual scores for each nasal symptom, SNOT-20 and endoscopic

Table 1. Demographic characteristics of the study population

Parameter	Group 1 (MFNS) (n=23) Mean ± SD (range)	Group 2 (Sinulan forte®) (n=23) Mean ± SD (range)	p-value
Male/female	13/10	14/9	1.000
Age	43.78±3.08 (18–61)	42.48±2.73 (18–61)	0.547

MFNS: Mometasone furoate nasal spray, SD: Standard deviation, n: Number

findings are presented in Table 2. Results related to all parameters' relative changes after the two different therapies are presented in Table 3.

At the start of study (visit 1), we found no differences regarding the TSS and individual symptom scores between the two treatment groups. We also found no differences between the treatment groups regarding SNOT-20, mucosal edema, and nasal secretion (Table 2).

After the treatment, we found a significant decrease in all parameters, including a SNOT-20 score in both groups of patients.

At visit 2, comparing the post-treatment levels of parameters, we observed lower TSS and lower scores for nasal obstruction/congestion, facial pain/pressure, impaired sense of smell, as well as endoscopically assessed mucosal edema and nasal secretion in group 2. We did find, however, lower post-treatment rhinorrhea and postnasal drip scores in

Table 2. Clinical parameters before and after treatment

Parameter	Group 1 (MFNS) (n=23) Mean ± SD (range)	Group 2 (Sinulan forte®) (n=23) Mean ± SD (range)	p-value
Nasal obstruction (V1)	6.52±0.18 (5–7)	6.23±0.31 (4–7)	0.312
Nasal obstruction (V2)	3.10±0.16 (2–4)	2.07±0.14 (2–3)	<0.001
Rhinorrhea (V1)	6.65±0.14 (6–7)	6.42±0.18 (5–7)	0.096
Rhinorrhea (V2)	3.41±0.22 (2–5)	4.21±0.19 (3–5)	0.004
Postnasal drip (V1)	6.52±0.17 (4–7)	6.47±0.18 (5–7)	0.708
Postnasal drip (V2)	2.79±0.13 (2–4)	3.38±0.16 (2–5)	0.024
Facial pain/pressure (V1)	6.84±0.19 (4–7)	6.56±0.20 (6–7)	0.063
Facial pain/pressure (V2)	3.14±0.22 (2–4)	2.27±0.15 (1–3)	0.006
Impaired sense of smell (V1)	6.43±0.21 (5–7)	6.32±0.20 (5–7)	0.424
Impaired sense of smell (V2)	3.12±0.15 (2–4)	2.13±0.19 (1–3)	<0.001
Total symptom score (V1)	32.57±1.97 (29–35)	30.87±2.94 (26–34)	0.082
Total symptom score (V2)	15.17±1.92 (12–19)	13.30±1.46 (12–16)	0.003
SNOT-20 (V1)	27.65±2.52 (22–29)	29.02±3.24 (21–30)	0.427
SNOT-20 (V2)	12.87±1.03 (11–14)	13.14±2.04 (11–14)	0.202
Mucosal edema (V1)	5.70±0.53 (5–6)	5.63±0.67 (4–6)	0.691
Mucosal edema (V2)	3.21±0.19 (1–4)	2.49±0.51 (2–3)	0.005
Nasal secretion (V1)	4.73±0.31 (4–6)	4.63±0.61 (4–6)	0.551
Nasal secretion (V2)	2.36±0.19 (2–4)	1.47±0.31 (1–3)	0.002

MFNS: Mometasone furoate nasal spray, SD: Standard deviation, V1: Visit 1 (before treatment), V2: Visit 2 (after treatment), SNOT: Sino-nasal outcome test

Table 3. Differences in the relative improvement of the clinical parameters after the treatment with two different preparations

Parameter	MFNS (n=23)	Sinulan forte® (n=23)	p-value
Nasal obstruction*	53.52%	63.48%	0.002
Rhinorrhea*	50.21%	34.14%	<0.001
Postnasal drip*	55.30%	49.61%	0.026
Facial pain/pressure*	55.80%	65.83%	<0.001
Impaired sense of smell*	51.84%	68.01%	<0.001
Total symptom score*	53.46%	56.84%	0.017
SNOT-20*	51.20%	51.90%	0.255
Mucosal edema*	51.74%	58.99%	0.013
Nasal secretion*	39.06%	64.49%	<0.001

MFNS: Mometasone furoate nasal spray, SNOT: Sino-nasal outcome test, *: relative improvement (%) = post-therapeutic value - pretherapeutic value/pretherapeutic value x 100

APRS patients treated with MFNS (group 1) compared to those treated with herbal preparation (group 2). However, we found no post-treatment differences in SNOT-20 between the two groups (Table 2).

When we compared the relative improvement for each parameter, we found significantly higher relative improvement for TSS, nasal obstruction/congestion, facial pain/pressure, loss of sense of smell, and for mucosal edema and nasal secretion in group 2. However, relative improvement for rhinorrhea and postnasal drip score was better in group 1. We found no differences in SNOT-20 relative improvement between two groups (Table 3) (Figure 2).

We found that the MCID for TSS between the two groups after the treatment should be 1.23. The difference between post-treatment values was: 15.17–13.3=1.87. As our difference was higher than 1.23, this meant clinically important difference in TSS. We also found that the MCID for the sum of endoscopic findings between two groups should be 0.53. The difference between post-treatment values in endoscopic findings was: 5.57–3.96=1.61. As our difference is much higher than 0.53, this, too, meant clinically important difference in endoscopic findings.

Follow-up

All patients were proceeded to the follow-up for the evaluation of TSS, mucosal edema and nasal secretion. As presented in Table 4, we found no important changes in the trends of the differences between the two treatment groups on day 10th and day 20th following visit 2.

Safety

The patients from the herbal preparation group (group 2) did not report any adverse effects, whereas from the MFNS group (group 1) two patients reported mild epistaxis and two reported mild dryness sensation of the nasal mucosa. No participants were found with disturbed vital signs and laboratory findings.

Discussion

This is the first randomized study comparing the efficacy and safety of an herbal preparation with dry extracts of five medicinal plants with *Andrographis paniculata* extract as a main constituent to INCS treatment on nasal symptoms, endoscopic findings and QoL in patients with APRS. The

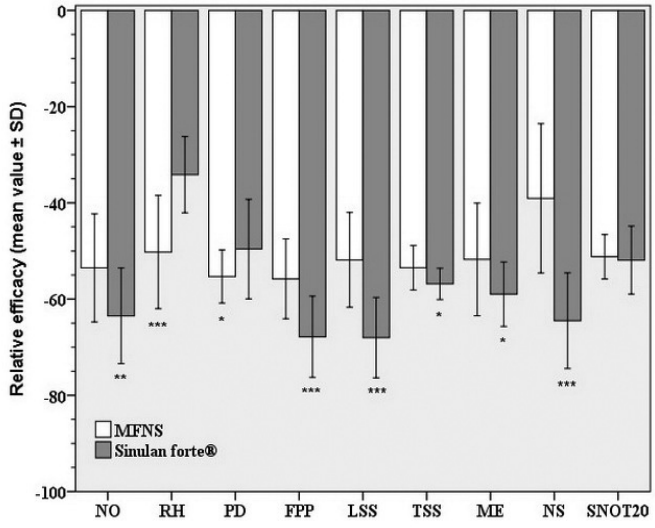


Figure 2. Differences in the relative improvement of the clinical parameters after the treatment with two different preparations.
NO: Nasal obstruction, RH: Rhinorrhea, PD: Postnasal drip, FPP: Facial pain/pressure, LSS: Loss of the sense of smell, ME: Mucosal edema, NS: Nasal secretion, TSS: Total symptom score, SNOT20: Sino-nasal outcome test 20.

***p<0.001 vs corresponding group, **p<0.01 vs corresponding group, *p<0.05 vs corresponding group

Table 4. The main clinical parameters during the follow-up

Parameter	Group 1 (MFNS) (n=23) Mean ± SD (range)	Group 2 (Sinulan forte®) (n=23) Mean ± SD (range)	p-value
Total symptom score (V2)	15.17±1.92 (12–19)	13.30±1.46 (12–16)	0.003
Total symptom score (Day 10th)	15.84±2.35 (12–19)	13.67±1.58 (12–16)	0.004
Total symptom score (Day 20th)	16.03±2.05 (12–19)	13.72±1.73 (12–16)	0.004
Mucosal edema (V2)	3.21±0.19 (1–4)	2.49±0.51 (2–3)	0.005
Mucosal edema (Day 10th)	3.35±0.24 (1–4)	2.56±0.73 (2–3)	0.005
Mucosal edema (Day 20th)	3.62±0.33 (1–4)	2.78±0.86	0.006
Nasal secretion (V2)	2.36±0.19 (2–4)	1.47±0.31 (1–3)	0.002
Nasal secretion (Day 10th)	2.41±0.22 (2–4)	1.51±0.28 (1–3)	0.002
Nasal secretion (Day 20th)	2.44±0.31 (2–4)	1.53±0.34 (1–3)	0.002

MFNS: Mometasone furoate nasal spray, SD: Standard deviation, V2: Visit 2 (after treatment), Day 10: 10th day of follow-up, Day 20: 20th day of follow-up

result demonstrated that both the herbal medicinal product and INCS reduced all symptoms and endoscopic signs and improved QoL in patients with APRS. However, our results suggest slightly better relative improvement in all clinical parameters, except for rhinorrhea and postnasal drip scores, in patients treated with Sinulan forte® than in those treated with MFNS. Finally, our results showed clinically important post-treatment differences in both TSS and endoscopic findings between the groups.

Herbal medicinal products, which contain extract of green chiretta (*Andrographis paniculata*) as their main compound are reported to improve the symptoms in patients with common cold (9-12). The main active ingredient of *Andrographis paniculata* leaf has not been fully identified, but it is generally assumed to be andrographolide. This lactone has strong effects against viruses, and acts against *Streptococcus pneumoniae, Staphylococcus aureus* and *Escherichia coli* (16). Andrographolide has strong anti-inflammatory effects. It inhibits lipopolysaccharide-stimulated nitric oxide (NO) and pro-inflammatory cytokine production in the inflamed tissue of the nasal mucosa (16). Andrographolide significantly inhibits interleukin-6 and interleukin-17 production in monocytes isolated from CRS patients with nasal polyp (17).

However, other constituents in Sinulan forte® also show strong antiviral and anti-inflammatory activities. The flower of common mullein has many bioactive substances (glycosides, saponins and terpenoids) that exhibit strong anti-influenza virus activity, as well as anti-*Staphylococcus aureus*, antioxidant, and wound-healing activity (18). European vervain, gentian and elder have anti-inflammatory effect that can be attributed to the antiviral effect of bioflavonoids, especially on rhinoviruses, adenoviruses, corona viruses, coxsackie and influenza virus (19). Bioflavonoids inhibit neuraminidase, an enzyme of great importance for replication of viruses (19). These three plants also have bacteriostatic action (19). These anti-inflammatory, antiviral, and antibacterial effects of Sinulan forte® constituents results to a stronger improvement of nasal obstruction/congestion, rhinorrhea, facial pain/pressure, and loss of sense of smell in comparison to patients treated with MFNS monotherapy. The better resolution of endoscopically evaluated nasal secretion from the middle meatus in our patients treated with the herbal preparation can also be explained by the antiviral and bacteriostatic actions of these constituents (19).

Following the treatment, at visit 2, the patients treated with MFNS had lower scores for rhinorrhea and postnasal discharge, and better relative improvement in rhinorrhea and postnasal drip scores than the patients treated with herbal preparation. These findings are not in accordance with the lower nasal secretion scores and better relative improvement in nasal secretion scores seen in in group 2 following the treatment. We could explain this unusual feature with the stimulative effect of European vervain, gentian and elder have on mucociliary clearance (20). ARS is characterized by disturbance in mucociliary clearance caused by infection and inflammatory changes in the nasal mucosa. This mucosal clearance depends on the active transport of chloride ions (Cl-) through the respiratory epithelium, strongly regulated by bioflavonoids, the main pharmacological constituents in European vervain, gentian and elder. This increased transepithelial transport results in better hydration of the mucus and reduction of its viscosity (20). So, three constituents from Sinulan forte® stimulate mucociliary clearance, resulting in higher rhinorrhea and postnasal discharge scores in these patients. Therefore, intranasal corticosteroids have an anti-inflammatory action, resulting in the inhibition of secretion from the mucosal glands (21). So, the patients treated with the herbal product have higher scores of rhinorrhea and postnasal discharge after the treatment compared to those treated with MFNS.

Although majority of the studies recommend intranasal corticosteroid therapy for 14-15 days, there is no clear recommendation in the European (EPOS 2012) or the American (ICAR 2016) guidelines regarding the duration of intranasal corticosteroid therapy in patients with ARS, particularly in those suffering from APRS (3, 6, 13, 22, 23). The duration and nature of APRS symptoms were the main reasons why we decided to treat our patients for 10 days. First, we wanted to coordinate the duration of treatment with Sinulan forte® with the duration of the MFNS treatment. Our results showed no compromise in the efficacy of MFNS as the patients had very good improvement in terms of clinical parameters. However, our results suggest that oral therapy with the herbal preparation have slightly better clinical efficacy than topical corticosteroid therapy. As APRS has more persistent symptoms than common cold, the duration of the herbal treatment was prolonged. In a study by Saxena et al. (11), the patients with common cold were given the preparation with *Andrographis paniculata* (KalmCold™) two times daily for 5 days, whereas the patients in our study were treated for 10 days. The patients in group 1 from our study were given 200 μg of MFNS twice daily for 10 days, 400 μg daily in total. According to the study by Meltzer et al. (6), MFNS 200 μg once daily and twice daily (400 μg) for 15 days was significantly superior to placebo in the treatment of patients with mild-to-moderate ARS. Finally, from a safe standpoint, our results of the 20-day follow-up after the end of medication use could be an apology for our choice of 10-day treatment. The results showed that there appeared to be no greater risk of recurrence of bigger exacerbation of APRS symptoms after MFNS treatment compared to Sinulan forte® treatment.

According to our results, treatment by herbal preparation and INCS almost equally reduces the SNOT-20 score.

We found no post-treatment absolute differences and no difference in relative improvement in QoL between the two groups. However, TSS and individual symptom scores were significantly lower after the treatment with herbal drugs than with MFNS. VAS is a psychometric measurement instrument to subjectively quantify patients' symptom severity. The SNOT-20 is a questionnaire designed for the assessment of QoL in patients with rhinosinusitis (24). According to papers published in the past ten years, correlation between VAS and QoL tests (SNOT-20, SNOT-22) is well established for patients with CRS (25). However, we found no papers concerning such correlation in patients with ARS, especially in those with APRS. One possible conclusion could be that in patients with APRS, improvement in nasal symptoms assessed with VAS does not follow the improvement in the QoL, estimated by SNOT-20.

While previous studies reported no serious adverse effects of *Andrographis paniculata* and other herbal constituents of Sinulan forte®, the minor adverse events reported were mainly gastrointestinal, such as nausea and diarrhea, and allergic reactions to the preparation constituents (9-12). We encountered no adverse effects in our patients that were treated with the herbal preparation, whereas in the group treated with MFNS two patients reported mild nasal bleeding and two reported mild sensation of dryness in the nasal cavity. As previously noted, INCS decrease the activity of glands situated in the nasal mucosa (21). The most common local adverse effects of INCS use include epistaxis and nasal dryness (26). Rate of epistaxis has been reported to be about 5% in patients treated with INCS. According to a recent systematic review of the literature, nasal bleeding can be a result of small mechanical trauma of the nasal mucosa by nasal applicator tip of the INCS device against the nasal septum rather than a result of mucosal atrophy (26).

The presented study has limitations, since it was not a multi-center study and the sample size was relatively small. The evaluation of nasal symptoms was dependent on the subjective sensation of the patients. On the other hand, we used endoscopic examination for the objective assessment of the local findings in the nasal cavity. Although randomized and prospective, our study was conducted as an open label study. Evidence for the clinical effects of herbal medicines in the treatment of common cold and APRS is limited in the medical literature and only several placebo-controlled studies investigating the efficacy of *Pelargonium sidoides* (EPs® 7630), five herbal compounds (BNO 1016), Myrtol standardized (GeloMyrtol®), and *Cyclamen europaeum* (Nasodren®) reported benefit of treatment versus placebo, with significantly reduced severity and duration of disease, and without serious side-effects (27-30). So, there is a need for further placebo-controlled studies that can provide better evidence of the effects of Sinulan forte® and other herbal preparations in the treatment of APRS.

Conclusion

Our results demonstrated statistically significant and clinically relevant improvement in TSS after the treatment with the herbal product Sinulan forte® compared to MFNS. Further, the herbal preparation had better effects on nasal congestion, facial pain, and loss of the sense of smell, and on endoscopic signs in patients with APRS compared to MFNS. We found no adverse effects in patients treated with herbal preparation, suggesting that this treatment can be safer compared to INCS treatment in patients with this uncomplicated form of ARS.

Acknowledgements

This investigation was conducted as a part of scientific project of the Military Medical Academy Faculty of Medicine, Belgrade, Serbia (MFVMA 02 /19-21/).

The authors thank Professor Dubravko Bokonjić from Institute for Toxicology of the Military Medical Academy, Belgrade, Serbia for his valuable support during the statistical analysis and interpretation of results.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of the Military Medical Academy, Belgrade, Serbia (MMA No 05/2019).

Peer-review: Externally peer-reviewed.

Author Contributions: Concept: A.P., D.G., Design: A.P., A.B., A.V.P., Supervision: A.P., A.V.P., Resources: A.P., D.G., A.B., A.V.P., Materials: A.P., D.G., A.B., A.V.P., Data Collection and/or Processing: A.P., D.G., A.B., A.V.P., Analysis and/or Interpretation: A.P., D.G., A.B., A.V.P., Literature Search: A.P., A.V.P., Writing Manuscript: A.P., A.B., Critical Review: A.P., D.G., A.B., A.V.P.

Conflict of Interest: The authors have no conflict of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Main Points

- Herbal preparation with *Andrographis paniculata* extract is recommended in the current European guidelines for treating common cold, but we found no studies regarding the use of this herbal compound in the treatment of acute postviral rhinosinusitis (APRS).
- The aim of our study was to evaluate the efficacy and safety of the combined herbal medicinal product Sinulan forte®, which contains the extracts of five medicinal plants with *Andrographis paniculata* as a main constituent, in comparison to mometasone furoate nasal spray (MFNS) when treating the patients with mild to moderate APRS.
- Our results showed statistically significant and clinically relevant improvement in the total symptom scores (TSS) of the patients treated with the herbal product compared to those of the patients treated with MFNS.
- The herbal preparation has better effects on nasal obstruction, facial pain/pressure, and impaired sense of smell, as well as on endoscopic findings in comparison to MFNS.
- No adverse events were encountered in patients treated with herbal preparation, suggesting that this treatment can be a safe treatment option in patients with APRS.

References

1. Alobid I, Mullol J. Management of rhinosinusitis today. Clin Pulm Med 2008; 15: 332-41. [Crossref]
2. Klossek JM, Mesbah K. Presentation and treatment of acute maxillary sinusitis in general practice: a French observational study. Rhinology 2011; 49: 84-9. [Crossref]
3. Orlandi RR, Kingdom TT, Hwang PH, Smith TL, Alt JA, Baroody FM, et al. International consensus statement on allergy and rhinology: rhinosinusitis. Int Forum Allergy Rhinol 2016; 6: S22-209. [Crossref]
4. Park JJ, Bachert C, Dazert S, Kostev K, Seidel DU. Current healthcare pathways in the treatment of rhinosinusitis in Germany. Acta Otolaryngol 2018; 138: 1086-91. [Crossref]
5. Fokkens WJ, Lund VJ, Hopkins C, Hellings PW, Kern R, Reitsma S, et al. European position paper on rhinosinusitis and nasal polyps 2020. Rhinology 2020; 58: 1-464. [Crossref]
6. Meltzer EO, Bachert C, Staudinger H. Treating acute rhinosinusitis: comparing efficacy and safety of mometasone furoate nasal spray, amoxicillin, and placebo. J Allergy Clin Immunol 2005; 116: 1289-95. [Crossref]
7. Eğilmez OK, Kökten N, Kalcıoğlu MT, Doğan Ekici AI, Şerifler S, Yeşilada E. Investigation of the protective effect of Nigella sativa oil in cisplatin induced oral mucositis: an experimental study. Turk Arch Otorhinolaryngol 2020; 58: 10-5. [Crossref]
8. Laccourreye O, Werner A, Laccourreye L, Bonfils P. Benefits, pitfalls and risks of phytotherapy in clinical practice in otorhinolaryngology. Eur Ann Otorhinolaryngol Head Neck Dis 2017; 134: 95-9. [Crossref]
9. Coon JT, Ernst E. Andrographis paniculata in the treatment of upper respiratory tract infections: a systematic review of safety and efficacy. Planta Med 2004; 70: 293-8. [Crossref]
10. Gabrielian ES, Shukarian AK, Goukasova GI, Chandanian GL, Panossian AG, Wikman G, et al. A double blind, placebo-controlled study of Andrographis paniculata fixed combination Kan Jang in the treatment of acute upper respiratory tract infections including sinusitis. Phytomedicine 2002; 9: 589-97. [Crossref]
11. Saxena RC, Singh R, Kumar P, Yadav SC, Negi MPS, Saxena VS, et al. A randomized double blind placebo controlled clinical evaluation of extract of Andrographis paniculata (KalmCold™) in patients with uncomplicated upper respiratory tract infection. Phytomedicine 2010; 17: 178-85. [Crossref]
12. Hu XY, Wu RH, Logue M, Blondel C, Lai LYW, Stuart B, et al. Andrographis paniculata (Chuān Xīn Lián) for symptomatic relief of acute respiratory tract infections in adults and children: a systematic review and meta-analysis. PLoS ONE 2017; 12: e0181780. [Crossref]
13. Fokkens WJ, Lund VJ, Mullol J, Bachert C, Alobid I, Baroody F, et al. European position paper on rhinosinusitis and nasal polyps 2012. Rhinology 2012; 50: 1-12. [Crossref]
14. Pfaar O, Mullol J, Anders C, Hörmann K, Klimek L. Cyclamen europaeum nasal spray, a novel phytotherapeutic product for the management of acute rhinosinusitis: a randomized double-blind, placebo-controlled trial. Rhinology 2012; 50: 37-44. [Crossref]
15. Meltzer EO, Wallace D, Dykewitz M, Shneyer L. Minimal clinically important difference (MCID) in allergic rhinitis: Agency for Healthcare Research and Quality or anchor-based thresholds. J Allergy Clin Immunol Pract 2016; 4: 682-8.e6. [Crossref]
16. Abu-Ghefreh AA, Canatan H, Ezeamuzie CI. In vitro and in vivo anti-inflammatory effect of andrographolide. Int Immunopharmacol 2009; 9: 313-8. [Crossref]
17. Kou W, Sun R, Wei P, Yao HB, Zhang C, Tang XY, Hong SL. Andrographolide suppresses IL-6/Stat3 signaling in peripheral blood mononuclear cells from patients with chronic rhinosinusitis with nasal polyps. Inflammation 2014; 37: 1738-43. [Crossref]
18. Riaz M, Zia-Ul-Haq M, Jaafar HZE. Common mullein, pharmacological and chemical aspects. Rev Bras Farmacogn 2013; 23: 948-59. [Crossref]
19. Passali D, Cambi J, Passali FM, Bellussi LM. Phytoneering: a new way of therapy for rhinosinusitis. Acta Otorhinolaryngol Ital 2015; 35: 1-8. [Crossref]
20. Kreindler JL, Chen B, Kreitman Y, Kofonow J, Adams KM, Cohen NA. The novel dry extract BNO 1011 stimulates chloride transport and ciliary beat frequency in human respiratory epithelial cultures. Am J Rhinol Allergy 2012; 26: 439-43. [Crossref]
21. Meltzer EO, Teper A, Danzig M. Intranasal corticosteroids in the treatment of acute rhinosinusitis. Curr Allergy Asthma Rep 2008; 8: 133-8. [Crossref]

22. Keith PK, Dymek A, Pfaar O, Fokkens W, Kirby SY, Wu W, et al. Fluticasone furoate nasal spray reduces symptoms of uncomplicated acute rhinosinusitis: a randomized placebo-controlled study. Prim Care Respir J 2012; 21: 267-75. [Crossref]

23. Meltzer EO, Gates D, Bachert C. Mometasone furoate nasal spray increases the number of minimal-symptom days in patients with acute rhinosinusitis. Ann Allergy Asthma Immunol 2012; 108: 275-9. [Crossref]

24. Sohu HG, Park SJ, Ryu IS, Lim HW, Song YJ, Yeo NK. Comparison of clinical presentation and surgical outcomes between recurrent acute rhinosinusitis and chronic rhinosinusitis. Ann Otol Rhinol Laryngol 2018; 127: 763-9. [Crossref]

25. Doulaptsi M, Prokopakis E, Seys S, Pugin B, Steelant B, Hellings P. Visual analogue scale for sino-nasal symptom severity correlates with sino-nasal outcome test 22: paving the way for a simple outcome tool of CRS burden. Clin Transl Allergy 2018; 8: 32. [Crossref]

26. Verkerk MM, Bhatia D, Rimmer J, Earls P, Sacks S, Harvey RJ. Intranasal steroids and the myth of mucosal atrophy: a systematic review of original histological assessments. Am J Rhinol Allergy 2015; 29: 3-18. [Crossref]

27. Bachert C, Schapowal A, Funk P, Kieser M. Treatment of acute rhinosinusitis with the preparation from Pelargonium sidoides EPs 7630: a randomized, double-blind, placebo-controlled trial. Rhinology 2009; 47: 51-8. [Crossref]

28. Jund R, Mondigler M, Stammer H, Stierna P, Bachert C. Herbal drug BNO 1016 is safe and effective in the treatment of acute viral rhinosinusitis. Acta Otolaryngol 2015; 135: 42-50. [Crossref]

29. Paparoupa M, Gillissen A. Is Myrtol® standardized a new alternative toward antibiotics. Pharmacogn Rev 2016; 10: 143-6. [Crossref]

30. Ponikau JU, Hamilos DL, Barreto A, Cecil J, Jones SW, Manthei SE, et al. An exploratory trial of Cyclamen europaeum extract for acute rhinosinusitis. Laryngoscope 2012; 122: 1887-92. [Crossref]

Three-Dimensional Analysis of Round Window Membrane in the Chinchilla Model with Acute Otitis Media Induced with *Streptococcus Pneumoniae* 7F

Original Investigation

Nevra Keskin Yılmaz[1,2], Hasan Albasan[3], Mehmet Kazım Börkü[1], Michael Mauro Paparella[2], Sebahattin Cüreoğlu[2]

[1]Department of Internal Medicine, Ankara University, Faculty of Veterinary Medicine, Ankara, Turkey
[2]Department of Otorhinolaryngology, Head and Neck Surgery, University of Minnesota Medical School, Minneapolis/Minnesota, USA
[3]Pet Depot Veterinary Group, La Verne, California, USA

Abstract

Objective: The purpose of this study was to investigate the morphological changes of round window membrane (RWM) in chinchillas with *Streptococcus pneumoniae (S. pneumoniae)* serotype 7F induced acute otitis media (AOM) by two dimensional (2D) and three dimensional (3D) measurements.

Methods: Temporal bone specimens taken from 12 chinchillas were divided into two groups. The control group consisted of healthy animals that were injected with intrabullar saline. The subjects in the experimental group were induced with AOM by intrabullar injection of *S. pneumoniae* 7F. The 2D and 3D measurements of RWM were compared between the groups.

Results: Dramatic changes were noted in the RWM of the experimental group compared to the control group. The thickness [mean ± standard deviation (SD)] of the RWM was significantly ($p<0.05$) increased in the experimental group compared to the control group by 2D measurements taken at three different points of RWM. Moreover, 3D measurements revealed that the volume (mean ± SD) of RWM was significantly ($p=0.009$) increased in the experimental group.

Conclusion: The results of our study, which indicated significant change in RWM in both 2D and 3D measurements, may shed light on the relationship between AOM and inner ear diseases. Based on our results, we recommend evaluating 3D analyses of RWM, which provide useful data, to better understand the changes in the membrane.

Keywords: Acute otitis media, pathology, cochlear round window, *Streptococcus pneumoniae*, cellular morphology

ORCID ID of the authors:

N.K.Y. 0000-0002-6287-1157;
H.A. 0000-0003-1192-6506;
M.K.B. 0000-0002-5621-1208;
M.M.P. 0000-0002-2727-1674;
S.C. 0000-0001-9220-7073.

Cite this article as: *Keskin Yılmaz N, Albasan H, Börkü MK, Paparella MM, Cureoğlu S. Three-Dimensional Analysis of Round Window Membrane in the Chinchilla Model with Acute Otitis Media Induced with Streptococcus Pneumoniae 7F. Turk Arch Otorhinolaryngol 2021; 59(1): 43-8.*

Corresponding Author:
Nevra Keskin Yılmaz; keskinnevra@gmail.com

Received Date: 18.09.2020
Accepted Date: 23.01.2021

DOI: 10.4274/tao.2021.5998

Introduction

Acute Otitis media (AOM), which defines the inflammation of the tympanic cavity, the Eustachian tube, the mastoid process and the mucoperiosteum surrounding the mastoid air cells, is recognized as one of the most important animal and human health threatening infectious diseases

across the world (1, 2). Given the anatomical localization of the ear, AOM should be evaluated in terms of many different complications, extracranial and/or intracranial (3-6).

The round window membrane (RWM), which separates the middle ear and the scala tympani of the basal turn of the cochlea, has an important role in several pathologies involving the middle and the inner ears in that it is a semi-permeable membrane allowing bacterial toxins, inflammatory mediators, and antibiotics to pass through (7, 8). As RWM takes part in the body's defense system and plays a role in the transport of mechanical energy between the ear ossicles and the inner ear fluid; the structural changes that occur in the RWM with the thickening of the membrane give rise to the pathology of many diseases involving the middle and the inner ears including hearing loss (3, 8-10). Therefore, analyzing any changes in RWM plays an important role in determining the pathogenesis of possible complications that may arise from otitis media and labyrinthitis.

Three-dimensional (3D) analysis of different anatomical regions is a field that is increasingly investigated as it helps to better understand and evaluate the detailed structure of the focused area. Although many studies have been conducted to examine the changes in the RWM, to our knowledge, there is no study that examined the morphological changes in the membrane in three dimensions and revealed the relationship of these measurements with the two-dimensional (2D) analyses of the entire surface of the membrane. The aim of this study was to assess any morphological changes of the RWM by 2D and 3D measurements in the chinchilla model with *Streptococcus pneumoniae* (*S. pneumoniae*) serotype 7F induced acute otitis media (AOM).

Methods

Design and Setting

The study used 12 Chinchillas divided into two groups. In the experimental group (n=6), the superior bullas of the chinchillas were bilaterally shaved after anesthesia with ketamine-HCl (20 mg/kg, intramuscular). After the region was cleaned in accordance with the asepsis-antisepsis rules, *S. pneumoniae* serotype 7F ($2x10^1$ bacteria/bulla) was injected bilaterally into the middle ears of the chinchillas. The bacteria used to create AOM was obtained by preparing a sample from a patient diagnosed with OM originating from *S. pneumoniae* serotype 7F at the University of Minnesota Medical School, Department of Otorhinolaryngology Head and Neck Surgery, by culturing and reproducing it in a blood agar. Otoscopic examination was performed in all subjects during the study and the animals were euthanized with the injection of high-dose ketamine-HCl seven days after inoculation. To our knowledge, this is the first study to make the 3D analysis of the chinchilla RWM. Therefore, right and left temporal bone samples were compared to each other to reveal whether there was difference between the contralateral ears in the experimental group; and the right temporal bone samples of the two groups were compared to determine the difference between the experimental and control groups. To ensure uniformity in the comparisons between the two groups, the same amount of saline solution was also injected into the right ears of the chinchillas in the control group (n=6) and the subjects were euthanized seven days after the injection.

After the animals were euthanized, all temporal bones in both groups were removed for further processing and histopathological examination. This temporal bone study was approved by the Institutional Review Board of the University of Minnesota (#0206M26181).

Histopathological Assessment

After euthanasia, all temporal bones were removed, perfused in Heidenhain's Susa solution, fixed in formalin, decalcified, and embedded in celloidin, and serially sectioned in the horizontal plane at a thickness of 20 μm. Every 10^{th} section was stained with hematoxylin-eosin and studied by light-microscopy using digital camera and image analysis software (SPOT Advanced; SPOT Imaging Solutions, Sterling Heights, MI, USA).

The round window thickness was determined by taking the average of the measurements made from three to five sections where the membrane was the widest. Each section was measured from three different points. The first measurement was made from the center of the round window, while the other two measurements were performed 0.2 mm anterior and inferior (10, 11).

We performed 3D reconstruction of the RWM by using the reconstruction software (Amira 3D Software for Life Sciences; FEI, Hillsboro, OR, USA) on the scanned sections with a high-resolution scanner (PathScan Enabler IV; Meyer Instruments, Houston, TX, USA) including the mid-modiolar level, as well as on the adjacent two to four sections where the RWM is best observed and could be digitized.

Statistical Analysis

To determine the sample size, we conducted power analysis with G*Power software version 3.1.9.2. (University of Kiel; Kiel, Germany) by taking the type I-α error rate 0.05 and calculating the power of the test as 0.80 and the groups were evaluated for statistical significance by using the Mann-Whitney U test with MedCalc Statistical Software version 12.7.7 (MedCalc Software Bvba; Ostend, Belgium). Significance was defined as $p<0.05$.

Results

The results of our study revealed severe inflammatory cell infiltration, bacterial invasion, and dense fibrous structure in the middle ear cavity in the experimental group. Moreover, the round window niche was filled with serous exudate and polymorphonuclear leukocytes (PMNs) were seen in intense amounts in all temporal bone specimens in the experimental group. Severe inflammatory cell invasion was also observed in the scala tympani of the lower basal turn of the cochlea (Figure 1).

When examined morphologically, there were no differences between the right and the left RWMs in the experimental group, whereas there were significant changes in the experimental group compared to those in the control group (Figure 2a). RWM was found to be thicker at the anterior and posterior ends of the RWM and thinner at the center in the control group and the membrane was positioned convexly towards the scala tympani of the basal fold of the cochlea. In the experimental group, however, there was pronounced thickening of the membrane both in the right and the left ears that was most intense on the epithelial surface and edematous enlargement in the fibrous middle layer (Figure 2b). The convex shape of the membrane was more flattened in the experimental group.

The membrane thickness measurements taken at three different points did not reveal significant differences between the right and the left ear measurements in the experimental group in 2D analysis (p>0.05). However, we found significant differences between the experimental and the control groups. In the measurements, anterior was 17.6 µm, center was 15.32 µm, and inferior was 18.31 µm in the control group, while anterior was 31.26 µm, center was 32.52 µm, and inferior was 36.57 µm in the experimental group. Membrane thicknesses were significantly higher in the anterior (p=0.009); in the center (p=0.015), and in the inferior (p=0.041) of the experimental group compared to those of the control group. Moreover, the mean thickness of the three points [mean ± standard deviation (SD)]; 33.5±16.7 µm) in the experimental group was significantly (p=0.009) higher compared to those (mean ± SD; 16.4±2.4 µm) of the control group. In the 3D analysis, the mean volume of the RWM was significantly (p=0.009) higher (mean ± SD; 0.106±0.038 mm^3) in the experimental group compared to that (mean ± SD; 0.066±0.008 mm^3) of the control group (Figure 3). As in the 2D analysis, we found no significant differences in 3D analysis between the right and the left ears in the experimental group (p>0.05).

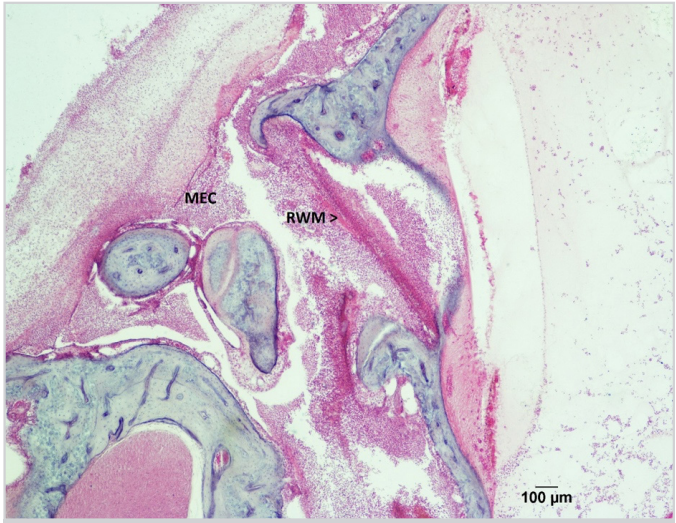


Figure 1. Round window niche is filled with inflammatory cells accompanied with thickened round window membrane (x2)

MEC: Middle ear cavity, RWM: Round window membrane (H&E), H&E: Hematoxylin-eosin

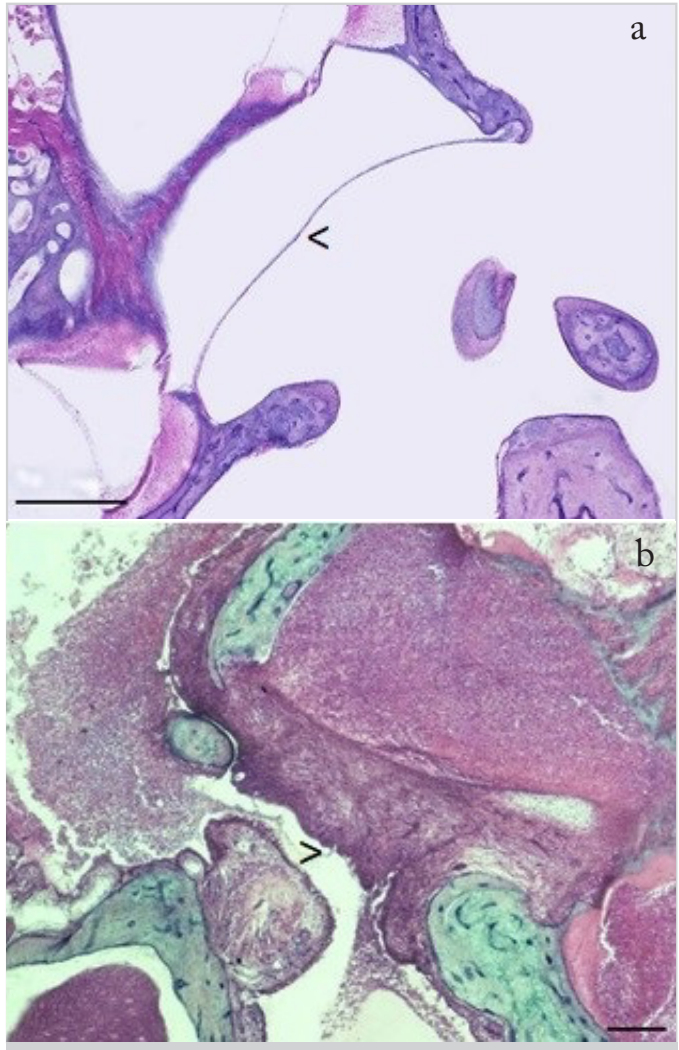


Figure 2a. The normal structure of the RWM in the control group, b. Severe thickening of RWM in the experimental group due to intracellular edema and cell proliferation. Arrow heads: RWM (scale bar: 500 µm, H&E)

RWM: Round window membrane, H&E: Hematoxylin-eosin

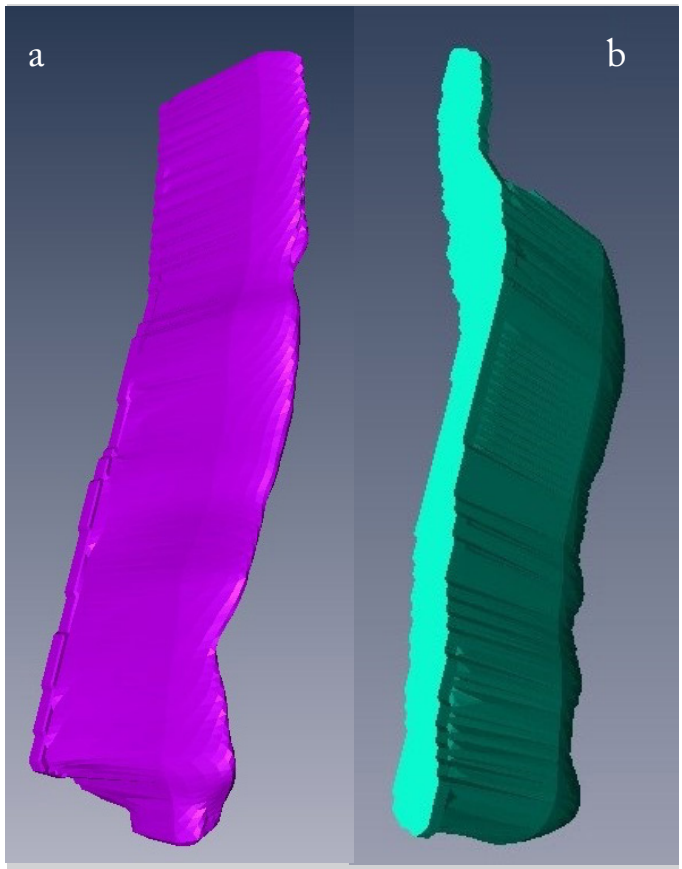


Figure 3. Representative photos of 3D reconstruction of the RWMs. a. Healthy RWM from control group, b. Thickened RWM from experimental group

RWM: Round window membrane

Discussion

AOM is a commonly seen disease which decreases the quality of life, requires patients to frequently present to clinics because of high recurrence rates and complications. The round window niche is a region that has been studied by many researchers due to its proximity to vital structures such as the tympanic segment of the facial nerve, the jugular vein, and the RWM that forms the middle ear-perilymph barrier (12-14).

In this study, we observed that after inoculating the bacteria via intrabullar injection into the middle ear, dense accumulation of purulent exudate occurred, especially in front of the round window niche and in the scala tympani of the basal turn of the cochlea. Previous studies have shown that free radicals, bacterial exotoxins, antioxidants, antibiotics, local antiseptics, and bacteria in the round window niche can penetrate the RWM and pass through the inner ear, and the material from the middle ear cavity may spread to inner ear. If this material affects the inner ear, it may lead to the development of sensorineural hearing loss, labyrinthitis and even otogenic meningitis (3, 8, 12, 15-18).

In our study, the cross-sections of RWM showed differences in the shape of the membrane in the experimental group. While a normal chinchilla RWM has a more convex shape, the RWM of the infected ears showed a more flattened shape in our study, in accordance with the findings of previous studies (10, 12). Most researchers assume that this difference in the shape of RWM is related with the negative middle ear pressure due to inflammatory cell and exudate infiltration in the tympanic cavity due to acute onset of OM as well as with the inflammatory changes in the layers of the membrane (10, 19). But in all circumstances, the contraption involving the change in the shape of RWM may affect the whole interaction between the middle and the inner ears, hence the hearing mechanism.

Although the pathologies caused by *S. pneumoniae* in the RWM have been examined in many histopathology studies, to our knowledge, the quantitative data on membrane thickness have not been studied (12, 20). Considering that the number and species of the microorganisms used, and the duration of inoculation significantly affect the changes in membrane thickness, a better understanding of the pathological process by quantitative measurements support the results of the experiments. In the presented study, we found in the 2D measurements that the thickness of the RWM was significantly higher in the experimental group compared to those in the control group. In accordance with our results, Jiang et al. (10) observed that the membrane was significantly thickened in the chinchillas with AOM created by *Haemophilus influenzae* inoculation compared to the control group in four days after inoculation. In both their and our studies, the thickening of the RWM, which may be explained by the intracellular edema and cell proliferation occurring in the membrane, may be interpreted as part of the body's defense system to protect the inner ear and other related structures from inflammation in the middle ear. However, the exact mechanism to understand the underlying pathology should be evaluated further.

The thickening of the RWM is directly related with the changing mechanism of membrane permeability. Numerous studies show that the permeability of RWM relatively increases in the early stages of OM, whereas it tends to decrease in the later stages (12, 20-23). In a study conducted on 25 cats with OM with Eustachian tube obstruction, it was observed that the transition within three days following the obstruction was similar to the transition from normal RWM, but the permeability of the membrane was greatly reduced after one to two weeks of occlusion (21). Similarly, a study in guinea pigs inoculated with *Pseudomonas aeruginosa* showed a gradual increase in permeability one week after OM was induced; however, permeability decreases when the inflammatory processes associated with OM are prolonged for more than two weeks (22). Based on these studies and our findings, it could be concluded that the increase in

RWM permeability in the early period of OM may be due to the degenerative changes in the epithelial cells of the membrane. As the inflammatory reaction is prolonged, however, permeability decreases due to increased fibrosis in the middle layer of the membrane and effusion in the round window niche on either side of the membrane and the presence of PMNs (21, 22).

3D reconstruction of the temporal bone is an increasingly used method as it helps the surgeon to better understand the anatomical structure in the diagnosis and treatment of otologic diseases and in ear operations (24, 25). Although it is possible to distinguish and analyze the anterior, inferior, and center of the RWM in 2D analyses on temporal bone sections, in 3D analysis the membrane cannot be examined in this way and can be analyzed as a single structure. In the present study, however, when the temporal bone samples in the experimental group were examined, the thickening that occurred at all three points of the membrane could be clearly observed in 3D visuals. Therefore, performing a 3D reconstruction, enabled us to display the status and understand the changing angle of the RWM, and helped to track the thickness of the membrane.

Understanding the anatomical position of the RWM and the changes in its structure in three dimensions has importance for pharmacokinetic research (26). Recent studies show that local drug delivery is a more efficient option than systemic antibiotic therapy in the treatment of inner ear diseases (26, 27). In this direction, as it acts as a gateway between the middle and the inner ears, and because it is a metabolically active membrane, RWM may play an active role in the transfer of drugs intended to reach the inner ear (26-28). However, changes in the permeability of the membrane can complicate the manipulation of the drugs that are planned to be delivered to the inner ear, and the efficiency of the treatment may decrease (28). Therefore, determining the morphological changes and the 3D display of the angle and the location of the membrane may affect the treatment methods and results. Although there are only a few reports studying the reconstruction of RWM, 3D analysis of the membrane by using in-vivo visualization techniques may be a helpful method to better understand and analyze the morphology of the membrane and related structures and to direct the treatment protocols.

Conclusion

In our study, it was determined that the results obtained by the 3D measurements of the RWM were compatible with those of 2D measurements. In parallel with 2D measurements, 3D reconstruction results also showed that the volume of RWM in the experimental group was increased compared to those in the control group. These results show that the measurement of the membrane with 3D methods for pathologic illumination may significantly contribute to the outcomes in patients whose RWM permeability or stiffness are thought to be affected.

Acknowledgements

The authors thank to the Scientific and Technological Research Council of Turkey (TUBITAK). This study is a part of the first author's Ph.D. dissertation. A portion of this study was delivered as a poster presentation at the American College of Veterinary Internal Medicine (ACVIM) Forum, June 6th-8th, 2019, Phoenix, Arizona.

Ethics Committee Approval: This temporal bone study was approved by the Institutional Review Board of the University of Minnesota (#0206M26181).

Informed Consent: Experimental study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: N.K.Y., M.M.P., S.C., Concept: N.K.Y., H.A., M.K.B., M.M.P., S.C. Design: N.K.Y., H.A., M.M.P., S.C., Data Collection or Processing: N.K.Y., M.M.P., S.C., Analysis or Interpretation: N.K.Y., H.A., H.A., M.K.B., M.M.P., S.C., Literature Search: N.K.Y., H.A., M.K.B., M.M.P., S.C., Writing: N.K.Y., H.A., M.K.B., M.M.P., S.C., Critical Review: N.K.Y., H.A., M.K.B., M.M.P., S.C.

Conflict of Interest: The authors declared that there is no conflict of interest.

Financial Disclosure: This research was funded by International Hearing Foundation, 5M Lions International and, Starkey Hearing Foundation.

Main Points

- This study provides a detailed histopathological description and quantitative information on the morphological changes of the RWM in AOM induced with *S. pneumoniae* serotype 7F.
- The results showed that the shape and the thickness of RWM changes within seven days after *S. pneumoniae* injection into the middle ear.
- The results of 2D and 3D analyses of the RWM were compatible; and the 3D reconstruction of the RWM may be a helpful tool to understand and analyze the changes in the membrane caused by AOM.

References

1. Schauer LL. Otitis media. Garfunkel LC, Kaczorowski J, Christy C, editors. Pediatric clinical advisor e-book: instant diagnosis and treatment. Elsevier Health Sciences; 2007.p.419-20.

2. Koçyiğit M, Giran Örtekin S, Çakabay T. Otitis media, classification and principles of treatment approach [Article in Turkish] İKSST Derg 2016; 8: 65-70. [Crossref]
3. Cureoglu S, Schachern PA, Rinaldo A, Tsuprun V, Ferlito A, Paparella MM. Round window membrane and labyrinthine pathological changes: an overview. Acta Otolaryngol 2005; 125: 9-15. [Crossref]
4. Joglekar S, Morita N, Cureoglu S, Schachern PA, Deroee AF, Tsuprun V, et al. Cochlear pathology in human temporal bones with otitis media. Acta Otolaryngol 2010; 130: 472-6. [Crossref]
5. Penido ND, Chandrasekhar SS, Borin A, Maranhão AS, Testa JR. Complications of otitis media – a potentially lethal problem still present. Braz J Otorhinolaryngol 2016; 82: 253-62. [Crossref]
6. Kaya S, Tsuprun V, Hızlı Ö, Schachern PA, Paparella MM, Cureoglu S. Cochlear changes in serous labyrinthitis associated with silent otitis media: a human temporal bone study. Am J Otolaryng 2016; 37: 83-8. [Crossref]
7. Goycoolea MV, Paparella MM, Goldberg B, Schlievert PM, Carpenter AM. Permeability of the middle ear to staphylococcal pyrogenic exotoxin in otitis media. Int J Pediatr Otorhinolaryngol 1980; 1: 301-8. [Crossref]
8. Paparella MM, Morizono T, Le CT, Choo YB, Mancini F, Lidén G, et al. Sensorineural hearing loss in otitis media. Ann Otol Rhinol Laryngol 1984; 93: 623-9. [Crossref]
9. Schachern PA, Paparella MM, Hybertson R, Sano S, Duvall AJ 3rd. Bacterial tympanogenic labyrinthitis, meningitis, and sensorineural damage. Arch Otolaryngol Head Neck Surg 1992; 118: 53-7. [Crossref]
10. Jiang S, Seale TW, Gan RZ. Morphological changes in the round window membrane associated with Haemophilus influenzae-induced acute otitis media in the chinchilla. Int J Pediatr Otorhinolaryngol 2016; 88: 74-81. [Crossref]
11. Sahni RS, Paparella MM, Schachern PA, Goycoolea MV, Le CT. Thickness of the human round window membrane in different forms of otitis media. Arch Otolaryngol Head Neck Surg 1987; 113: 630-4. [Crossref]
12. Schachern P, Tsuprun V, Cureoglu S, Ferrieri P, Briles D, Paparella M, et al. The round window membrane in otitis media: effect of pneumococcal proteins. Arch Otolaryngol Head Neck Surg 2008; 134: 658-62. [Crossref]
13. Sun W, Wang W. Advances in research on labyrinth membranous barriers. J Otol 2015; 10: 99-104. [Crossref]
14. Li Z, Cai Z, Li J, Shen J, Tao B, Zhang G. 3D quantitative measurement for multi-spiral CT images of round window area related structure. Int J Clin Exp Med 2017; 10: 3510-6. [Crossref]
15. Paparella MM, Schachern PA, Choo YB. The round window membrane: otological observations. Ann Otol Rhinol Laryngol 1983; 92: 629-34. [Crossref]
16. Nomura Y. Otological significance of the round window. Adv Otorhinolaryngol 1984; 33: 1-162. [Crossref]
17. Goycoolea MV, Lundman L. Round window membrane. Structure function and permeability: a review. Microsc Res Tech 1997; 36: 201-11. [Crossref]
18. Goycoolea MV. Clinical aspects of round window membrane permeability under normal and pathological conditions. Acta Otolaryngol 2001; 121: 437-47. [Crossref]
19. Wang X, Nakmali D, Gan RZ. Complex modulus of round window membrane over auditory frequencies in normal and otitis media chinchilla ears. Int J Exp Comput Biomech 2015; 3: 27-44. [Crossref]
20. Schachern PA, Tsuprun V, Cureoglu S, Ferrieri PA, Briles DE, Paparella MM, et al. Effect of apolactoferrin on experimental pneumococcal otitis media. Arch Otolaryngol Head Neck Surg 2010; 136: 1127-31. [Crossref]
21. Schachern PA, Paparella MM, Goycoolea MV, Duvall AJ 3rd, Choo YB. The permeability of the round window membrane during otitis media. Arch Otolaryngol Head Neck Surg 1987; 113: 625-9. [Crossref]
22. Kim CS, Cho TK, Jinn TH. Permeability of the round window membrane to horseradish peroxidase in experimental otitis media. Otolaryngol Head Neck Surg 1990; 103: 918-25. [Crossref]
23. Saber AK. Round window membrane and delivery of biologically active agents into the cochlea. Institutionen för klinisk neurovetenskap/Department of Clinical Neuroscience, Doctoral Thesis. 2010. [Crossref]
24. Jun BC, Yeo SW, Chang KH. The PACS and three-dimensional reconstruction of temporal bone in middle ear surgery. Otolaryng Head Neck 2004; 131: 268. [Crossref]
25. Lee CF, Chen PR, Lee WJ, Chen JH, Liu TC. Three-dimensional reconstruction and modeling of middle ear biomechanics by high-resolution computed tomography and finite element analysis. Laryngoscope 2006; 116: 711-6. [Crossref]
26. Patel J, Szczupak M, Rajguru S, Balaban CD, Hoffer ME. Inner ear therapeutics: an overview of middle ear delivery. Front Cell Neurosci 2019; 13: 261. [Crossref]
27. Salt AN, Plontke SK. Local inner-ear drug delivery and pharmacokinetics. Drug Discov Today 2005; 10: 1299-306. [Crossref]
28. Mikulec AA, Hartsock JJ, Salt AN. Permeability of the round window membrane is influenced by the composition of applied drug solutions and by common surgical procedures. Otol Neurotol 2008 29: 1020-6. [Crossref]

Incidence and Management of Delayed Epistaxis Following Endoscopic Skull Base Surgery

Original Investigation

Zahide Mine Yazıcı[1], Ömür Günaldı[2], Osman Tanrıverdi[2], Selçuk Güneş[1], Filiz Gülüstan[1], Recep Haydar Koç[1], İbrahim Sayın[1]

[1]Department of Otorhinolaryngology, University of Health Sciences Turkey, Bakırköy Dr. Sadi Konuk Training and Research Hospital, İstanbul, Turkey
[2]Department of Neurosurgery, Bakırköy Mazhar Osman Mental Health and Neurological Diseases Training and Research Hospital, İstanbul, Turkey

Abstract

Objective: Among other complications of endoscopic skull base surgery, delayed epistaxis has not been given much importance. This report presents postoperative delayed nosebleed cases in a large number of patients who underwent an endoscopic endonasal transsphenoidal approach to the sellar region for resection of lesions.

Methods: Three hundred and sixty three patients who were reached to the sellar region by endoscopic endonasal transsphenoidal route and operated was included in the study. Retrospective chart reviewing of these patients was performed. The correlation between the duration of nosebleeds, bleeding location, treatment methods and comorbidities of the patients were evaluated.

Results: Ten patients (3.6%) reported delayed epistaxis in the postoperative period and were referred to the otolaryngology department. Postoperative epistaxis occurred between days 7th and 33th (mean 16.5) days. The treatment consisted of chemical silver nitrate cauterization in two patients, return to the operating room in three patients, nasal packing in five patients.

Conclusion: Delayed postoperative epistaxis often has no obvious etiology, and intervention requires teamworking. Well-coordinated teamworking of the neurosurgeon with other specialities such as neuroradiology and otorhinolaryngology is needed to achieve better results.

Keywords: Epistaxis, skull base, endoscopic surgical procedure, complication

ORCID ID of the authors:

Z.M.Y. 0000-0002-4164-3438;
Ö.G. 0000-0001-5071-1319;
O.T. 0000-0002-4846-4213;
S.G. 0000-0001-9458-5799;
F.G. 0000-0003-4857-214X;
R.H. 0000-0002-8394-5290;
İ.S. 0000-0003-3388-7835.

Cite this article as: *Yazıcı ZM, Günaldı Ö, Tanrıverdi O, Güneş S, Gülüstan F, Koç RH, Sayın İ. Incidence and Management of Delayed Epistaxis Following Endoscopic Skull Base Surgery. Turk Arch Otorhinolaryngol 2021; 59(1): 49-53.*

Corresponding Author:
Mine Zahide Yazıcı; minezahide@yahoo.com

Received Date: 05.09.2020
Accepted Date: 17.01.2021

DOI: 10.4274/tao.2021.5918

Introduction

Today, all surgical techniques are directed towards minimally invasive techniques. Since its introduction in the 1990s, endoscopic endonasal sellar and parasellar surgery has rapidly gained acceptance in otolaryngology and neurosurgery. Endoscopic-guided transsphenoidal surgery applications have been standardized by Carrau et al. (1) and

Cappabianca et al. (2). In the following years, endoscopic skull base surgery (ESBS) has become more widespread and is used in many centers today.

Although many complications related to ESBS have been discussed in the literature, epistaxis is a seldom reported complication that can increase morbidity and mortality. The rate of epistaxis after ESBS ranges from 1.7% to 10% within the first 30 days (3).

Epistaxis after ESBS shows different features compared to other etiology of epistaxis. We evaluated the patients' nosebleeds that occurred within the first 6 weeks after discharge as delayed epistaxis. Postoperative bleeding is ideally preferred to be stopped at the same hospital of surgery, but this may not be possible in the late postoperative bleeding. Different points of late postoperative epistaxis were tried to be emphasized in this article.

In this study, we performed a retrospective analysis of delayed nasal bleeding in a group of patients who have underwent surgery for resection of sellar lesions with ESBS.

Methods

This study was approved by the Local Ethics Committee of Dr. Sadi Konuk Training and Research Hospital (2019/318). Informed consent was obtained from all patients who met the inclusion criteria. The study was conducted with patients who underwent ESBS for intracranial pathology at the Department of Neurosurgery, Bakırköy Mazhar Osman Mental Health and Neurological Diseases Training and Research Hospital, İstanbul between March 2014 and May 2019. All endoscopic approaches were performed by the same author (Ö.G.). The endoscopic approach to skull base was described previously in the literature (4). The patients who presented to the Emergency Department (ED) with epistaxis within six weeks after discharge from the neurosurgery clinic after transnasal endoscopic surgery were evaluated as patients with delayed epistaxis and were included for the study. Patients were excluded if an expanded skull base procedure was performed or if a nasal septal Hadad flap was used during the procedure. Also, patients whose medical records could not be accessed were excluded from the study.

Expanded skull base procedures used for accessing the ventral skull base have been classified into various anatomically based modules. In this classification scheme, the modules are defined based on their location on the sagittal and coronal/parasagittal planes. The approaches to access the median skull base (along the sagittal plane) include transfrontal, transcribriform, transplanum/transtuberculum, transclival, and transodontoid. To standardize our surgical technique, in our study, we excluded the operations in which we used the parasagittal or the coronal modules and included those which we used the transsellar approach in pathologies localized to the sellar region.

Epistaxis in the initial surgery room or before discharge were considered immediate and not included in this study. Medical records were analyzed for events during admission or ED visits. Details concerning the management of epistaxis were reviewed from medical records, including topical medicinal sprays, use of hemostatic agents, nasal packing, or surgical intervention. Common risk factors for epistaxis, including hypertension and blood thinner use were also noted.

Results

A total of 383 consecutive patients were identified. Twenty patients' medical records could not be accessed, and these patients were excluded from the study. In total, the medical charts of 363 patients were analyzed. Among all patients, 166 of the patients in the study were male (45.8%), 197 were female (%54.2). The average subject age was 46.2 years (range: 15 to 81). Endoscopic skull base operation indications were: 330 pituitary adenomas (126 functional adenomas, 36 recurrent adenomas, 168 nonfunctional adenomas), eleven chordomas, nine pseudotumor cerebri cases, six craniopharyngiomas, five Rathke cleft cysts, and two other pathologies. Endocrinological diagnoses in functional adenomas were: 73 acromegaly, 28 Cushing's syndrome, 11 prolactinoma, and 14 other types of cases. Ten patients reported delayed epistaxis in the postoperative period (3.6%), presenting to an otolaryngology emergency service on mean postoperative day 16.5 (range: 7–33 days). Features of delayed epistaxis patients are listed in Table 1. Among 10 patients with bleeding, seven were female, five had high blood pressure, and four were using blood thinners. None of the patients had underlying coagulopathy indicated on their clinical history or biochemical test records. All patients were cross matched for transfusion needs.

Seven of the 10 patients who presented with epistaxis had pituitary adenoma (four acromegaly, two Cushing's syndrome, one nonfunctional adenoma). Other indications were optic nerve decompression, arachnoid cyst in the sellar region, and rhinorrhea repair in the sphenoid sinus.

Treatments included chemical silver nitrate cauterization in two patients, return to the operating room (OR) in three, and nasal packing in five patients. In the OR, decision was made to stop the bleeding and invite the neurosurgeon who performed the first skull base surgeries of these patients to the OR. The neurosurgeon attended the operation to prevent intracranial complications while the otolaryngologist intervened to stop the bleeding. None of our patients required embolization or a blood transfusion. We preferred the sphenopalatine artery (SPA) bipolar cautery for two subjects and posterior septal bipolar cautery for one subject among these three patients. We used Merocel (Medtronic Xomed Surgical

Table 1. Summary of delayed epistaxis patients

Patient, age, sex	Pathology	HT	Tobacco	Alcohol	Blood thinner	POD	Treatment	Bleeding site
KY 25, M	Arachnoid cyst	-	-	-	-	19	Merocel nasal tampons	Right middle turbinate and posterior septum
ŞÇ 37, F	PA (Cushing)	-	-	-	-	20	Return to the operating room	Posterior septal artery
NY 21, F	Optic nerve decompression	-	-	-	-	33	Return to the operating room	SPA
HY 60, F	PA (Nonfunctional)	+	-	-	+	11	Silver nitrate	Anterior septum
MH 33, M	PA (Cushing)	-	+	+	-	16	Merocel nasal tampons	Posterior septum mucosal edges
AB 57, F	PA (Acromegaly)	+	-	-	-	7	Merocel nasal tampons	Middle turbinate inferior
HY 45, F	PA (Acromegaly)	-	-	-	-	9	Return to the operating room	SPA
NC 70, F	PA (Acromegaly)	+	-	-	+	11	Merocel nasal tampons	Septum
MD 67, M	Rhinorrhea	+	+	+	+	26	Merocel nasal tampons	Not identified
AT 63, F	Recurrent PA (Acromegaly)	+	-	-	+	13	Silver nitrate	Anterior septum

HT: Hypertension, POD: Postoperative day, F: Female, M: Male, PA: Pituitary adenoma, SPA: Sphenopalatine artery

Products, Jacksonville, FL, USA) nasal tampons since they are made of synthetic open-cell foam polymer that provides a tissue-compatible and less susceptible environment for *Staphylococcus aureus* than traditional nasal gauze (5). We coated the tampons with antibiotic ointment and placed on the floor of the nasal cavity. Tampons were expanded with saline. After placing the tampons, it is necessary to observe the presence of any postnasal bleeding in the pharynx. If there was no bleeding within 48 hours, we removed the tampons and inspected the source of the bleeding. Although not statistically significant, as previously mentioned in the literature, the tendency to hemorrhage was higher in acromegaly cases compared to other pituitary adenomas (6). Although we do not have objective statistical data on this subject, our clinical observation is in this direction.

Discussion

The posterior septal artery is a branch of SPA that runs along the lower face of the sphenoid sinus and can bleed if not cauterized in sphenoid sinus surgery. Meticulous elevation of the mucosa and bipolar coagulation of the artery before the bone work can prevent bleeding in this vessel. Most of the delayed bleeding is caused by the SPA or one of its branches (7). In case of bleeding from the SPA or its branches, electrocauterization or vascular clips can be used under OR conditions.

Excessive bleeding and deficits, especially in cranial nerves may be a warning for carotid artery bleeding (3-6). It is important to remember that not all internal carotid artery (ICA) injuries manifest intraoperatively. The formation of vasospasm in the ICA following skull base surgery has been reported from a few hours up to one month after surgery (8). One of the most common complications after cavernous ICA rupture is the development of pseudoaneurysm. Pseudoaneurysm is caused by a leak or hematoma in the peripheral fibrous wall of the ICA (9). Traumatic pseudoaneurysms of the ICA resulting in epistaxis usually occur within the three weeks after the initial injury (88%) (10). Pseudoaneurysm formation is a common complication after cavernous ICA trauma. Regular angiographic screening is required in all suspected patients since there is a high risk of bleeding in the postoperative period. Fortunately, there was no carotid hemorrhage or pseudoaneurysm in our series of patients, but this does not mean that it will not happen. In this study, we evaluated this issue in detail since otolaryngologists are not very familiar.

Most ICA injuries can be prevented by observing the surgical anatomy and findings of radiologic examinations. Putting in place a clear action plan for the surgical team before intervening in such injuries can save important time and improve results. The key to treatment is controlling the initial bleeding, maintaining normotension, as well as radiologic evaluation by angiography and embolization by neuroradiology (6). Despite the many technological advances, mortality in major ICA injuries is still around 17%. The overall complication rate with balloon occlusion is between 8% and 20% (11).

Most postoperative bleeding develops within two to four weeks after surgery and there is a risk of bleeding up to five to six weeks postoperatively when the middle turbinate is resected (12). Although some authors limit nose bleeding to delayed epistaxis up to 4 weeks, we accepted 6 weeks as did Zimmer and Andaluz (3). Our neurosurgery team does not prefer resecting the middle turbinate, and when they have to, they take care to indicate this point in detail in the operation note, as this information is important when preventing stump bleeding.

Once the general condition of the patient has been stabilized, adrenaline guide pads are useful for both removing the blood clots and vasoconstricting the nasal mucosa. It is important to identify both the site and cause of the bleeding, so it can be stopped, and the cause can be treated. It is important to contact the institution where the skull base operation was done or to contact the neurosurgeon who did the initial surgery. If neither is possible, at least the medical records should be evaluated in detail. Especially, if the intervention for bleeding is done at a hospital different to the one where the initial surgery was done, it is beneficial for the two teams to communicate to obviate the complications that may occur while managing the epistaxis. During surgery, before proceeding with the intervention, it is essential to understand whether there is dehiscence on the carotid artery or to know which reconstruction method was used in the skull base surgery, the sella is reconstructed with abdominal fat, septal cartilage, middle turbinate, and other reconstructive techniques.

Thompson et al. (13) found a 3% rate for postoperative epistaxis in 30 days. While they managed most of the patients with nasal packing, one patent required chemical cautery, and five patients were treated in the OR. The authors reported that bleeding patients were elderly, male, and hypertensive.

De Los Reyes et al. (14) described 551 pituitary adenoma cases that included 457 endoscopic approaches with a postoperative epistaxis rate of 3.5%. Among their patients with delayed epistaxis, mean postoperative bleeding day was 10.8 days. Of the 12 cases with delayed epistaxis, two did not require nasal packing, the remaining 10 cases were first treated with nasal packing of different types. However, this approach was unsuccessful in five cases who were then treated with embolization. They recommended this approach in delayed epistaxis cases with no obvious etiology.

Zimmer and Andaluz (3), in their 434 consecutive endoscopic transsphenoidal patient series, found 4.1% incidence rate for epistaxis in six weeks of surgery. Treatment methods were in-office cautery in seven patients, cautery at the OR in five patients, nasal packing in three patients, embolization in two patients and use of intranasal hemostatic agents in one patient. Epistaxis that shows symptoms with deficits in the cranial nerves should be intervened in OR conditions. If the site of bleeding cannot be controlled, angiography with embolization was recommended in the referred study.

One possible bias of our study is that cases were excluded if an expanded skull base procedure was performed or if a nasal septal Hadad flap was used during the procedure. This means that the incidence of our delayed epistaxis cases after skull base surgery was 3.6%.

We manage our cases with nasal packing, cautery, and surgical exploration. The most important step in our treatment algorithm is to try to find the source of bleeding with an endoscopic nasal examination. Initial attempts should aim to control the bleeding with chemical cautery or nasal tampons, but hospitalization and surgical intervention may be needed if bleeding persists. Cranial nerve deficits are important signs in skull base epistaxis and the attending physician must be vigilant about this condition. Such patients may need angiography with embolization.

Conclusion

To achieve better outcomes in skull base surgery, well-coordinated teamworking of the neurosurgeon with other specialities (neuroradiology, otorhinolaryngology, and others who specialize in endoscopic surgery) is needed.

It is important to reach the epicrisis and contact the surgeon while intervening in the nasal bleeding of the patient who underwent skull base operation.

Ethics Committee Approval: This study was approved by the Local Ethics Committee of Dr. Sadi Konuk Training and Research Hospital (2019/318).

Informed Consent: Informed consent was obtained from all patients who met the inclusion criteria.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Conception: Z.M.Y., Design: Z.M.Y., F.G., Supervision: Z.M.Y., S.G., Materials: Ö.G., O.T., F.G., Data Collection and/or Processing: Ö.G., O.T., R.H.K., Literature Reviewing: S.G., R.H.K., Writing: Z.M.Y., Critical Review: İ.S.

Conflict of Interest: The authors declare that they have no conflict of interest.

Financial Disclosure: The authors declared that this study received no financial support.

Main Points

- Delayed epistaxis after skull base surgery can be seen up to 45 days postoperatively.
- As always, all patients presenting with postoperative epistaxis should be evaluated by nasal endoscopy to determine the bleeding site.
- Particular attention should be paid to the findings of abnormal bleeding amount and cranial nerve deficits in patients undergoing skull base surgery.

References

1. Carrau RL, Jho HD, Ko Y. Transnasal-transsphenoidal endoscopic surgery of the pituitary gland. Laryngoscope 1996; 106: 914-8. [Crossref]
2. Cappabianca P, Alfieri A, de Divitiis E. Endoscopic endonasal transsphenoidal approach to the sella: towards functional endoscopic pituitary surgery (FEPS). Minim Invasive Neurosurg 1998; 41: 66-73. [Crossref]
3. Zimmer LA, Andaluz N. Incidence of epistaxis after endoscopic pituitary surgery: proposed treatment algorithm. Ear Nose Throat J 2018; 97: 44-8. [Crossref]
4. Kiraz M, Gunaldi O, Tanriverdi O, Erdim İ, Postalci LS, Tugcu B et al. Comparison of sinonasal complications of microscopic and endoscopic aproaches for transsphenoidal hypophyseal surgery: prospective study. Turk Neurosurg 2018; 28: 915-22. [Crossref]
5. Breda SD, Jacobs JB, Lebowitz AS, Tierno PM Jr. Toxic shock syndrome in nasal surgery: a physiochemical and microbiologic evaluation of Merocel and NuGauze nasal packing. Laryngoscope 1987; 97: 1388-91. [Crossref]
6. Valentine R, Wormald PJ. Carotid artery injury after endonasal surgery. Otolaryngol Clin North Am 2011; 44: 1059-79. [Crossref]
7. Stankiewicz JA. Nasal endoscopy and control of epistaxis. Curr Opin Otolaryngol Head Neck Surg 2004; 12: 43-5. [Crossref]
8. Laws ER Jr. Vascular complications of transsphenoidal surgery. Pituitary 1999; 2: 163-70. [Crossref]
9. Kalapatapu VR, Shelton KR, Ali AT, Moursi MM, Eidt JF. Pseudoaneurysm: a review. Curr Treat Options Cardiovasc Med 2008; 10: 173-83. [Crossref]
10. Chen D, Concus AP, Halbach VV, Cheung SW. Epistaxis originating from traumatic pseudoaneurysm of the internal carotid artery: diagnosis and endovascular therapy. Laryngoscope 1998; 108: 326-31. [Crossref]
11. Koitschev A, Simon C, Löwenheim H, Naegele T, Ernemann U. Management and outcome after internal carotid artery laceration during surgery of the paranasal sinuses. Acta Otolaryngol 2006; 126: 730-8. [Crossref]
12. Ramakrishnan VR, Kingdom TT, Nayak JV, Hwang PH, Orlandi RR. Nationwide incidence of major complications in endoscopic sinus surgery. Int Forum Allergy Rhinol 2012; 2: 34-9. [Crossref]
13. Thompson CF, Wang MB, Kim BJ, Bergsneider M, Suh JD. Incidence and management of epistaxis after endoscopic skull base surgery. ORL J Otorhinolaryngol Relat Spec 2012; 74: 315-9. [Crossref]
14. De Los Reyes KM, Gross BA, Frerichs KU, Dunn IF, Lin N, Rincon-Torroella J et al. Incidence, risk factors and management of severe post-transsphenoidal epistaxis. J Clin Neurosci 2015; 22: 116-22. [Crossref]

Evaluation of the Association between Paranasal Sinus Osteomas and Anatomic Variations Using Computed Tomography

Original Investigation

Ceyhun Aksakal[1], Murat Beyhan[2], Erkan Gökçe[2]

[1]Gaziosmanpaşa University Faculty of Medicine, Department of Otorhinolaryngology, Tokat, Turkey
[2]Gaziosmanpaşa University Faculty of Medicine, Department of Radiology, Tokat, Turkey

Abstract

Objective: The pathogenesis of paranasal sinus osteoma (PSO) has not been fully elucidated. It is thought that both embryological and developmental factors play a role in the etiology. The aim of the present study was to investigate the association of frequency and localization of PSOs detected on computed tomography (CT) examination with osteoma presence.

Methods: In this retrospective study conducted in December 2017 through March 2020 in Gaziosmanpaşa University Faculty of Medicine, images of a total of 18,867 patients who underwent paranasal sinus, maxillofacial CT and brain CT angiography were reviewed for the presence of PSOs. Sizes of PSOs and accompanying mucosal pathologies were identified. Associations between PSOs and paranasal sinus variations were evaluated statistically compared to the control group (200 patients without PSO).

Results: A total of 176 patients (0.92%) were found to have PSO. Average age of the patients with PSO was 59.9 years (range: 18–93). PSOs were unilateral in 152 patients while 24 patients had multiple osteomas. Female/male ratio was 1.1/1. PSOs were most commonly located in the frontal sinuses. Frequencies of vertical concha bullosa, secondary middle turbinate, twisted uncinate, supraorbital ethmoid cell, intersinus septal cell, ethmoidomaxillary cell, Haller's cell, frontal sinus hypoplasia and sphenoid sinus hypoplasia were significantly higher in the patient group compared to the control group.

Conclusion: Higher or lower incidence rates of some anatomic variations in the patients with PSO could be explained by the possible effects of genetic and/or environmental factor. Additional studies are needed to evaluate these possible associations.

Keywords: Osteoma, paranasal sinus, variation, computed tomography

ORCID ID of the authors:

C.A. 0000-0001-9770-1513;
M.B. 0000-0002-8630-4632;
E.G. 0000-0003-3947-2972.

Cite this article as: *Aksakal C, Beyhan M, Gökçe E. Evaluation of the Association between Paranasal Sinus Osteomas and Anatomic Variations Using Computed Tomography. Turk Arch Otorhinolaryngol 2021*

Corresponding Author:
Ceyhun Aksakal; ceyhunaksakal0@hotmail.com

Received Date: 24.07.2020
Accepted Date: 30.11.2020

DOI: 10.4274/tao.2020.5811

Introduction

Osteomas are well-limited, slowly growing osseous tissue tumors usually located in the skull, the paranasal sinuses and the mandible (1). The frequency rate of paranasal sinus osteomas (PSOs) on standard radiography and computed tomography (CT) varies from 0.42 to 3% (1-3). They are most commonly localized to the frontal and ethmoid sinuses, and quite rare in the sphenoid and maxillary sinuses (1, 4, 5). They are more common in males, with a male/female ratio ranging from 1.08:1 to 2.6:1 (5-7). About 10% of the PSOs, which develop slowly, become symptomatic and they are mostly observed as incidental events in CT (4). CT is the best examination modality to determine the presence and localization of small-sized PSOs in paranasal sinuses. In CT, they appear as dense, compact, homogeneous, round or oval-shaped and well-limited masses (4, 5, 8). Osteomas are generally solitary, and multiple osteomas are quite rare. That multiple osteomas are often seen in Gardner's syndrome indicates the effects of genetic factors in the formation of osteomas (9).

Paranasal sinus development continues in the first three decades of life. It was argued that genetic and environmental factors could cause anatomic variations during growth and development (10). Chaiyasate et al. (11) compared monozygotic and dizygotic twins for anatomic variations and found that some variations such as concha bullosa and infraorbital cell were more common in monozygotic twins, whereas other variations such as frontal type 3 and type 4 cell were more common in dizygotic twins. These findings imply that both genetic and environmental factors could affect the anatomic variations.

The associations between PSO and clinical conditions, especially such as mucosal sinus diseases, mucoceles and nasal polyps, were investigated in earlier studies. However, studies investigating the relationship of PSO with paranasal sinus variations are quite limited. The aim of the present study was to investigate the demographic and clinical characteristics of patients whose CT examinations showed PSO, and to determine the localizations and the numbers of PSOs, as well as their associations with paranasal sinus variations.

Methods

Study Design and Patient Selection

The study was conducted in the Gaziosmanpaşa University Faculty of Medicine Training and Research Hospital with 18,868 consecutive patients older than 18 years of age who underwent paranasal sinus, brain, maxillofacial CT or brain CT angiography scan for various reasons from December 2017 through March 2020. All radiological examinations were retrospectively examined and unanimously evaluated by an otorhinolaryngologist experienced in head-neck radiological anatomy and two radiologists. Axial, coronal, and sagittal reformat images of 1.25 mm slice thickness were created from helical screening of 2.5 or 5.0-mm slice thickness in axial plane using 128-slice (Optima 660, 2016, GE) or 32-slice (Supria, 2019, Hitachi) CT machines. Images that did not include the paranasal sinuses or low-quality images with artifacts that could not be evaluated radiologically, and images of the patients with trauma, tumor or surgical history that deformed the paranasal sinuses were excluded during the comparison with the control group. An analysis of the medical records revealed that CT indications included suspect for cerebral hemorrhage and investigating the etiology of headache (brain CT), to investigate a suspected stroke (brain CT angiography), trauma and presurgical examinations for maxillofacial surgery (maxillofacial CT) and investigating paranasal sinus diseases (sinusitis, tumors, etc.) (paranasal sinus CT). The control group consisted of patients whose paranasal CT scans were performed in the period from December 2017 through March 2020 for various indications (sinusitis and paranasal tumor suspicions, etc.) and who were not found to have osteoma. The control group was determined by retrospective evaluation of these patients. While determining the control group, first, the file numbers of the 200 consecutive patients aged over 18 years who had their paranasal CT scans in the mentioned period were recorded. Then, in a second more detailed examination, paranasal variations were evaluated using the CT images of these patients. Excluded patients were illustrated by the flow diagram in Figure 1. Localization, side, size (from the axial and coronal slice), and presence of accompanying sinus diseases, polyps or mucocele were evaluated in 176 patients who were identified to have PSOs. In addition, demographic data of the patients (age and gender distribution) and the medical records of the patients were analyzed.

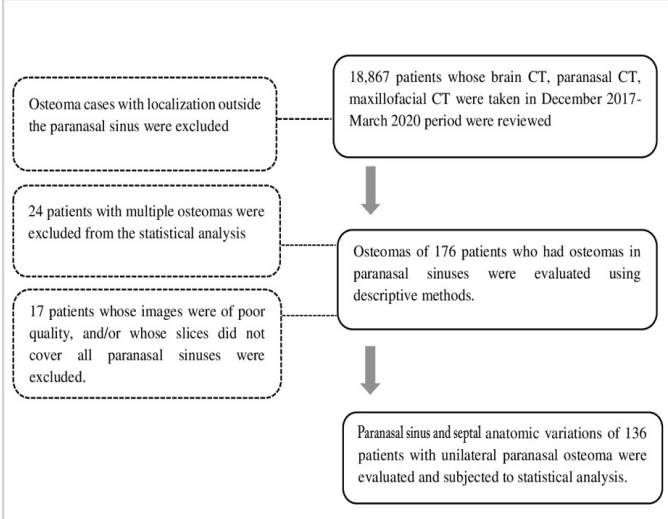


Figure 1. Flow diagram of patient selection
CT: Computed tomography

Evaluation of Anatomic Variations

Anatomic variations were evaluated in patients with unilateral osteomas whose images revealed all paranasal sinus structures. Anatomic variations were also evaluated in 200 consecutive patients who underwent paranasal sinus CT examination in our hospital in the study period and had not undergone any rhinologic surgery or had nasal trauma history (control group). The anatomic variations that were evaluated are septum deviation, septum pneumatization, concha bullosa (vertical, bulbous), paradoxical middle turbinate (MT), secondary MT, pneumatized superior turbinate, pneumatized inferior turbinate, paradoxical inferior turbinate, twisted uncinate process, atelectatic uncinate process, pneumatized uncinate process, lamina papyracea dehiscence, agger nasi cell, Haller's cell, Kuhn's cells (type 1, 2, 3, 4), supraorbital ethmoid cell (SOEC), frontal bullar cell, intersinus septal cell (ISSC), Onodi cell, maxillary sinus hypoplasia, septated maxillary sinus, ethmoidomaxillary cell (EMC), accessory ostium, frontal sinus aplasia, frontal sinus hypoplasia, frontal sinus hyperaeration, frontal sinus pneumosinus dilatans, crista galli pneumatization, sphenoid sinus agenesis, sphenoid sinus hypoplasia, anterior clinoid process pneumatization (ACPP), pterygoid process pneumatization (PPP) and greater sphenoid wing pneumatization (GSWP).

The number and localization of paranasal sinus variations were determined in both groups. All anatomic variations were recorded individually for both sides. Then, the associations of above-mentioned variations with osteoma in 136 patients with unilateral osteomas were evaluated statistically.

As a second analysis, the frequencies of anatomic variations in 136 patients with osteoma were statistically compared to the frequencies in the control group of 200 individuals. In this comparison, presence of the above-mentioned variations for at least once in patients with PSO and in patients of the control group were evaluated as "present."

Statistical Analysis

The study had a descriptive design and included the demographic characteristics, and the average and standard data of the patients. Quantitative variables were expressed as mean and standard deviation, while qualitative variables were expressed as frequency and percentage. Statistical analyses were performed using SPSS software (IBM SPSS Statistics 22, SPSS Inc., IBM Co., Armonk, NY, United States). Fisher's Exact test was used for the analysis of qualitative data. The study was approved by the clinical research ethics committee of Gaziosmanpaşa University Faculty of Medicine (approval no: 20-KAEK-109). Informed consent was obtained from all individual participants included in the study.

Results

Patients

Out of a total of 337 patients with osteoma in craniofacial region, 176 patients with osteoma were identified using the flow diagram in Figure 1. Multiple osteomas were detected in 24 of 176 patients with at least one osteoma. PSO detection frequency with CT was 0.92% (176/18,867). Eighty-two of the patients with PSO were male (46.5%) and 94 were female (53.4%). Average age was 59.9 years (range: 18–93). The female/male ratio was 1.1/1. The difference between the genders for the osteoma frequency was not statistically significant based on Fisher's Exact test ($p>0.05$). The measurement of the PSOs at the largest dimension varied from 2 to 50 mm. Average osteoma sizes by dimensions were as follows: anteroposterior 6.2±3.9, mediolateral 6.07±4.65 and craniocaudal 6.7±4.57 mm. As for the comorbidities seen in CT images, 21 (11.9%) patients had sinusitis findings, while nine (5.1%) patients had nasal polyp and one patient (0.5%) had mucocele in addition to osteoma (Table 1).

A further analysis of the 152 patients with unilateral osteomas revealed that the osteomas were located in the frontal sinus (Figure 2) in 74 patients (48.6%), in the anterior ethmoid sinus in 57 (37.5%), in the posterior ethmoid sinus

Table 1. Association of osteoma localizations with sinonasal mucosal pathologies

Variables	Frontal	Anterior ethmoid	Posterior ethmoid	Sphenoid	Maxillary
None	91 (89.2)	64 (80)	17 (85)	9 (100)	4 (66.6)
Sinusitis	7 (6.8)	11 (13.7)	2 (10)	-	1 (1.6)
AWOL	3 (42.8)	7 (63.6)	0 (0)	-	0 (0)
NAWOL	4 (57.1)	4 (36.3)	2 (100)	-	1 (100)
Nasal polyp	3 (2.9)	5 (6.2)	1 (5)	-	-
AWOL	1 (33.3)	5 (100)	1 (100)	-	-
NAWOL	2 (66.6)	0 (0)	0 (0)	-	-
Mucocele	1 (0.9)	-	-	-	-
AWOL	0 (0)	-	-	-	-
NAWOL	1(100)	-	-	-	-

AWOL: associated with osteoma localization, NAWOL: non-associated with osteoma localization

in 15 (9.8%), in the sphenoid sinus in 3 (1.9%) and in the maxillary sinus in 3 (1.9%). PSOs were found in 65 different localizations in 24 patients with multiple PSOs (Figures 3, 4). Gardner's syndrome was observed in one patient with multiple osteomas. Of the 217 osteoma localizations, 105 (48.3%) were on the left and 112 (51.6%) were on the right (Table 2).

The control group had a similar gender distribution (47.3% male and 52.6% female) with a mean age of 39.1±12.3 years. Statistical analysis showed significant age ($p<0.05$) and gender (Fisher's Exact test, $p<0.05$) differences between the two groups.

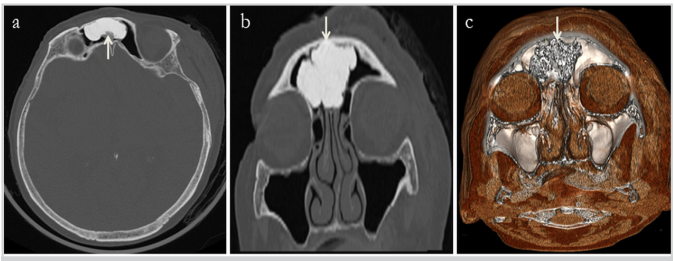


Figure 2. A giant osteoma (white arrows) in the right frontal sinus of an 89-year-old female patient. a) axial, b) coronal, c) volume-rendering CT images

CT: Computed tomography

Analysis of Paranasal Sinus Variations

Table 3 summarizes the anatomic variations in patients with unilateral PSOs. In these patients, agger nasi cell and frontal sinus hypoplasia were significantly more common in the paranasal sinuses with osteoma compared to the sinuses

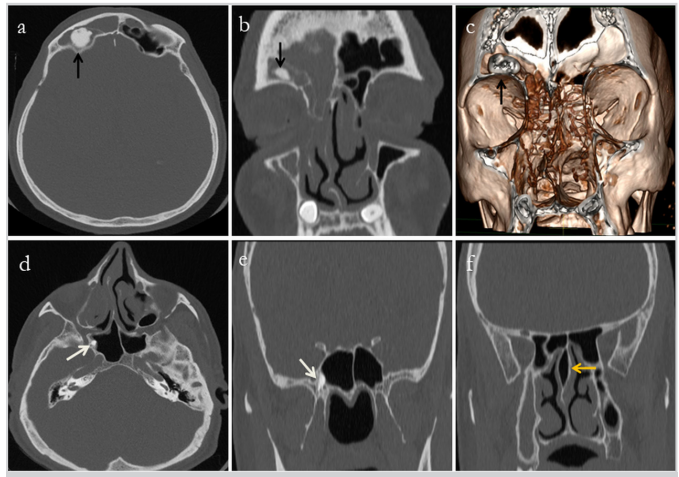


Figure 3. Osteoma in the right supraorbital ethmoid cell (black arrows) of a 49-year-old male patient. a, d) axial, b, e, f) coronal reformat, c) volume-rendering CT images. A second osteoma in the right sphenoid sinus (thin white arrows) and septum pneumatization (yellow arrow)

CT: Computed tomography

Table 2. Location of the paranasal sinus osteomas

	Localization of solitary osteoma, n (%) (152 patients)	Localization of multiple osteomas, n (%) (24 patients)	p*
Frontal sinus	74 (48.6)	28 (43.07)	
Left	37	17	>0.05
Right	37	11	
Anterior ethmoid sinus	57 (37.5)	23 (35.3)	
Left	25	11	>0.05
Right	32	12	
Posterior ethmoid sinus	15 (9.8)	5 (7.6)	
Left	9	3	>0.05
Right	6	2	
Sphenoid sinus	3 (1.9)	6 (9.2)	
Left	0	0	**<0.05**
Right	3	6	
Maxillary sinus	3 (1.9)	3 (4.6)	
Left	1	2	**<0.05**
Right	2	1	
Total	152	65	
Left	72	33	**>0.05**
Right	80	32	

n: Number

*Fisher's Exact test. P<0.05 value was regarded as significant. Significant differences between the groups are shown in bold

without osteoma. No significant differences were found for other anatomic variations.

Table 4 summarizes the comparison of the anatomic variations in patients with and without PSOs. In these patients, agger nasi cell and frontal sinus hypoplasia) were more frequent in the PSO patient group compared to the control group, while paradoxical MT, pneumatized uncinate process, agger nasi cell, Kuhn's type 2 cell and PPP were significantly more common in the control group than the PSO patient group.

Discussion

With the widespread use of CT in the evaluation of the paranasal sinuses, the detection and treatment approaches of PSOs have been further developed (1). Although the incidence of PSO is reported between 0.01% and 0.23% in earlier studies, this frequency varies from 1 to 3% in recent studies (1, 3, 5). This is associated with the advancements in imaging methods enabling to detect very-small size osteomas (12). In the presented study, PSO frequency was found 0.92%, a value close to the lower limits reported in the more recent studies. In most earlier studies, PSO detection was done with paranasal sinus CT scanning (3, 5, 7, 12). It was argued that the incidence of PSO in sinusitis was higher (3, 7). The patients evaluated in our study did not consist solely of individuals that were admitted for sinonasal symptoms. The fact that paranasal sinus CT examination is done more commonly for sinusitis evaluation could explain the lower frequency in the presented study compared to the previous studies in the literature . This finding could also be attributed to the difference in the patient populations, hence to the fact that we studied a quite large population.

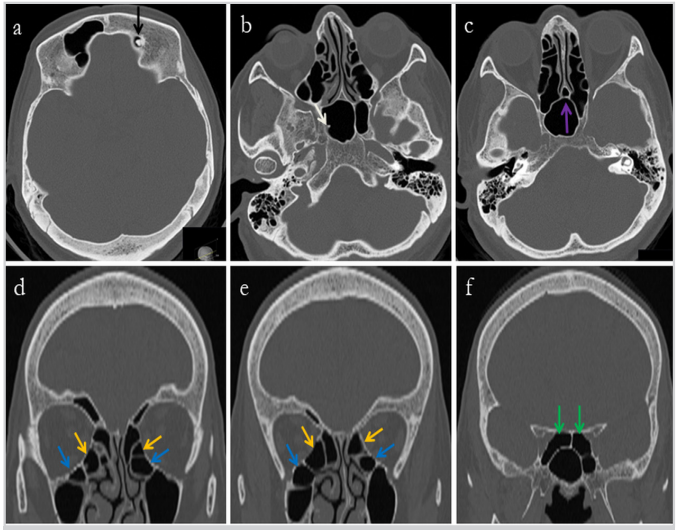


Figure 4. Osteoma in the left frontal sinus (black arrow), a second osteoma in the right sphenoidal sinus (white arrow) of a 64-year-old female patient. a, b, c) axial, d, e, f) coronal reformat CT images. Septum pneumatization (purple arrow), bilateral Haller's cells (yellow arrows), bilateral ethmomaxillary cells (blue arrows) and bilateral Onodi cells (green arrows) are shown

CT: Computed tomography

Unlike most previous studies, our study showed a female predominance (F:M=1.1:1) (1, 5, 13). Halawi et al. (12) attributed a higher incidence of PSOs detected by CT in females to the higher number of CT scans taken in women who presented with headache complaints. In our study, the mean age of the patients with PSO was 59.9 years, which was somewhat higher than the average ages in the previous studies reported in the literature (1, 5, 7). Erdogan et al. (3), having evaluated the osteoma frequencies on paranasal sinus CTs, reported a higher incidence rate in the third decade of life. The differences in the ages at which the PSOs were detected could be because our study especially included older patients whose brain CTs were taken for stroke symptoms.

Like in the other studies in the literature, the most common localization of PSOs were found to be the frontal sinuses (48.6%) also in our study (1, 5, 7, 12). PSOs were more common in the anterior ethmoid sinuses compared to the posterior ones. The pathogenesis of this frequent localization in the frontoethmoidal region is unclear. According to the embryological theory, osteomas in this region originate from the embryonal cartilaginous rest or the persistent embryonal periosteum (13). According to the traumatic theory, traumas to the frontoethmoidal region increase osteoblastic activity in this region (1). In our study, though few, some sphenoid and maxillary localizations were observed. An interesting finding in the present study was that, as in the patients with solitary osteomas, the most frequent localization was frontal and ethmoid sinus in 24 patients with multiple osteomas. However, in 24 patients with multiple osteomas, sphenoid and maxillary sinus localizations were found significantly more frequent than in the patients with solitary PSOs (Table 2). Multiple osteomas in the head can also be seen in Gardner's syndrome, a hereditary disease (9). In the presented study, the Gardner's syndrome was observed in one of the 24 patients with multiple PSOs.

The pathogenesis of osteomas has not been fully elucidated yet. According to the traumatic theory, traumas, especially those to the frontal region, trigger osteoblastic activity in the sinus walls. More frequent PSO incidence in men were attributed to trauma (14). Nevertheless, in the presented study, PSO frequency was higher in women. Buyuklu et al. (5) studied 243 patients with PSO and found no association between a history of trauma and the presence of osteomas. Besides, presence of osteomas in patients without a trauma history cannot be explained by traumatic pathogenesis (7). According to the infectious theory, on the other hand, chronic mucosal irritation observed in mucosal sinus diseases, such as sinusitis and nasal polyposis, increase osteoblastic activity and prepare the ground for PSO formation (7, 8).

Table 3. Distribution of anatomic variations based on the localization of unilateral osteomas (comparison of the anatomical variations of the side with the osteoma and the side without the osteoma)

Anatomic variation side / Anatomic variation	Left	Right	Bilateral	None	Left	Right	Bilateral	None	p
Septum deviation	17 (25.8)	22 (33.3)	-	27 (40.9)	19 (27.1)	12 (17.1)	-	39 (55.7)	0.077
Septal spur	6 (9.1)	5 (7.6)	-	55 (83.3)	5 (7.1)	3 (4.3)	-	62 (88.6)	0.640
Vertical concha bullosa	7 (10.6)	6 (9.1)	13 (19.7)	40 (60.6)	9 (12.9)	8 (11.4)	13 (18.6)	40 (57.1)	0.936
Bulbous concha bullosa	5 (7.6)	5 (7.6)	11 (16.7)	45 (68.2)	5 (7.1)	3 (4.3)	5 (7.1)	57 (81.4)	0.256
Superior concha bullosa	5 (7.6)	5 (7.6)	6 (9.1)	50 (75.8)	3 (4.3)	3 (4.3)	3 (4.3)	61 (87.1)	0.395
Paradoxical MT	0 (0)	2 (3)	1 (1.5)	63 (95.5)	1 (1.4)	1 (1.4)	1 (1.4)	68 (97.1)	0.38
Secondary MT	1 (1.5)	0 (0)	3 (4.5)	62 (93.9)	0 (0)	3 (4.3)	8 (11.4)	59 (84.3)	0.101
Pneumatized IT	-	-	-	66 (100)	-	-	-	70 (100)	-
Paradoxical IT	-	1 (1.5)	-	65 (98.5)	-	-	-	70 (100)	0.485
Twisted uncinate process	3 (4.5)	1 (1.5)	2 (3)	60 (90.9)	3 (4.3)	2 (2.9)	2 (2.9)	63 (90)	0.962
Atelectatic uncinate process	-	1 (1.5)	2 (3)	63 (95.5)	-	-	2 (3)	69 (98.6)	0.475
Pneumatized uncinate process	3 (4.5)	1 (1.5)	1 (1.5)	61 (92.4)	1 (1.4)	2 (2.9)	0 (0)	67 (95.7)	0.475
Accessory ostium	4 (6.1)	1 (1.5)	3 (4.5)	58 (87.9)	0 (0)	2 (2.9)	3 (4.3)	65 (92.9)	0.202
Lamina papyracea dehiscence	1 (1.5)	-	-	65 (98.5)	1 (1.4)	-	-	69 (98.6)	1
Agger nasi cell	5 (7.6)	0 (0)	30 (45.5)	31 (47)	3 (4.3)	2 (2.9)	14 (20)	51 (72.9)	**0.004**
Kuhn's type 1	10 (15.2)	8 (12.1)	5 (7.6)	43 (65.2)	2 (2.9)	4 (5.7)	1 (1.4)	4 (5.7)	**0.005**
Kuhn's type 2	1 (1.5)	3 (4.5)	-	62 (93.9)	3 (4.3)	1 (1.4)	-	66 (94.3)	0.366
Kuhn's type 3	6 (9.1)	3 (4.5)	-	57 (86.4)	4 (5.7)	2 (2.9)	-	64 (91.4)	0.641
Kuhn's type 4	2 (3)	0 (0)	-	64 (97)	1 (1.4)	2 (2.9)	-	67 (95.7)	0.319
SOEC	11 (16.7)	3 (4.5)	12 (18.2)	40 (60.6)	4 (5.7)	1 (1.4)	-	13 (18.6)	0.124
Frontal bullar cell	8 (12.1)	3 (4.5)	0 (0)	55 (83.3)	2 (2.9)	4 (5.7)	2 (2.9)	62 (88.6)	0.109
EMC	2 (3)	2 (3)	1 (1.5)	61 (92.4)	0 (0)	4 (5.7)	3 (4.3)	63 (90)	0.310
Haller's cell	5 (7.6)	2 (3)	5 (7.6)	54 (81.8)	5 (7.1)	2 (2.9)	2 (2.9)	61 (87.1)	0.66
Onodi cell	5 (7.6)	6 (9.1)	12 (18.2)	43 (65.2)	7 (10)	2 (2.9)	10 (14.3)	51 (72.9)	0.379
Maxillary sinus hypoplasia	0 (0)	2 (3)	8 (12.1)	56 (84.8)	1 (1.4)	1 (1.4)	4 (5.7)	64 (91.4)	0.379
Septated maxillary sinus	1 (1.5)	2 (3)	2 (3)	61 (92.4)	0 (0)	0 (0)	1 (1.4)	69 (98.6)	0.294
Frontal sinus aplasia	-	1 (1.5)	1 (1.5)	64 (97)	-	1 (1.4)	-	69 (98.6)	0.585
Frontal sinus hypoplasia	2 (3)	13 (19.7)	8 (12.1)	43 (65.2)	4 (5.7)	3 (4.3)	6 (8.6)	57 (81.4)	**0.029**
Frontal sinus hyperaeration	6 (9.1)	0 (0)	3 (4.5)	57 (86.4)	2 (2.9)	1 (1.4)	2 (2.9)	65 (92.9)	0.307
Pneumosinus dilatans	2 (3)	-	-	64 (97)	-	-	-	70 (100)	0.234
Sphenoid sinus agenesis	1 (1.5)	-	-	64 (97)	-	-	-	70 (100)	0.485
Sphenoid sinus hypoplasia	9 (13.6)	5 (7.6)	5 (7.6)	47 (71.2)	5 (7.1)	4 (5.7)	4 (5.7)	57 (81.4)	0.530
ACPP	6 (9.1)	9 (13.6)	5 (7.6)	46 (69.7)	6 (8.6)	7 (10)	6 (8.6)	51 (72.9)	0.923
PPP	3 (4.5)	4 (6.1)	4 (6.1)	55 (83.3)	2 (2.9)	3 (4.3)	4 (5.7)	61 (87.1)	0.911
GSWP	7 (10.6)	5 (7.6)	7 (10.6)	47 (71.2)	5 (7.1)	5 (7.1)	8 (11.4)	52 (74.3)	0.911

MT: Middle turbinate, IT: Inferior turbinate, SOEC: Supraorbital ethmoid cell, EMC: Ethmoidomaxillary cell, ACPP: Anterior clinoid process pneumatization, PPP: Pterygoid process pneumatization, GSWP: Greater sphenoid wing pneumatization

Significant differences between the groups are shown in bold. (Crista galli pneumatization, septum pneumatization and ISSC were not used here because they are unilateral pathologies.)

According to another hypothesis, osteoma obstructs the sinus ostium and triggers the mucosal pathology (15). Thus, it is difficult to distinguish the causality of the relationship between osteoma and mucosal pathologies such as sinusitis and nasal polyp. Halawi et al. (12) found that 30.8% of the patients with osteoma had sinusitis, 3.3% had nasal polyp and 5.3% had mucocele. Similarly, in our study most common radiopathological finding accompanying osteoma was sinusitis, while nasal polyps were less common.

Diagnosis of osteomas by X-ray radiography or CT is generally straightforward and they appear as radio-dense

Table 4. Comparison of the distribution of anatomic variations between the osteoma patient group (with a single osteoma) and the control group

		Osteoma; (n=136) (%)	Control; (n=200) (%)	p
Septum Deviation	Absent	66 (48.5)	89 (44.5)	0.467
	Present	70 (51.5)	111 (55.5)	
Septal spur	Absent	117 (86)	122 (61)	**<0.001**
	Present	19 (14)	78 (39)	
Septum pneumatization	Absent	126 (92.6)	193 (96.5)	0.184
	Present	10 (7.4)	7 (3.5)	
Vertical concha bullosa	Absent	80 (58.8)	95 (47.5)	**0.041**
	Present	56 (41.2)	105 (52.5)	
Bulbous concha bullosa	Absent	102 (75)	142 (71)	0.42
	Present	34 (25)	58 (29)	
Superior concha bullosa	Absent	111 (81.6)	179 (89.5)	0.057
	Present	25 (18.4)	21 (10.5)	
Paradoxical MT	Absent	131 (96.3)	165 (82.5)	**<0.001**
	Present	5 (3.7)	35 (17.5)	
Secondary MT	Absent	121 (89)	199 (99.5)	**<0.001**
	Present	15 (11)	1 (0.5)	
Pneumatized IT	Absent	136 (100)	197 (98.5)	0.275
	Present	0 (0)	3 (1.5)	
Paradoxical IT	Absent	135 (99.3)	196 (98)	0.652
	Present	1 (0.7)	4 (2)	
Twisted uncinate	Absent	123 (90.4)	196 (98)	**0.004**
	Present	13 (9.6)	4 (2)	
Atelectatic uncinate	Absent	132 (97.1)	196 (98)	0.719
	Present	4 (2.9)	4 (2)	
Pneumatized uncinate	Absent	128 (94.1)	168 (84)	**0.008**
	Present	8 (5.9)	32 (16)	
Accessory ostium	Absent	123 (90.4)	157 (78.5)	**0.006**
	Present	13 (9.6)	43 (21.5)	
Lamina papyracea dehiscence	Absent	134 (98.5)	199 (99.5)	0.568
	Present	2 (1.5)	1 (0.5)	
Agger nasi cell	Absent	82 (60.3)	50 (25)	**<0.001**
	Present	54 (39.7)	150 (75)	
Kuhn's type 1	Absent	106 (77.9)	161 (80.5)	0.569
	Present	30 (22.1)	39 (19.5)	
Kuhn's type 2	Absent	128 (94.1)	164 (82)	**0.001**
	Present	8 (5.9)	36 (18)	
Kuhn's type 3	Absent	121 (89)	170 (85)	0.376
	Present	15 (11)	30 (15)	
Kuhn's type 4	Absent	131 (96.3)	197 (98.5)	0.277
	Present	5 (3.7)	3 (1.5)	
SOEC	Absent	92 (67.6)	183 (91.5)	**<0.001**
	Present	44 (32.4)	17 (8.5)	
ISCC	Absent	123 (90.4)	197 (98.5)	**0.002**
	Present	13 (9.6)	3 (1.5)	

Table 4. continued

Crista galli pneumatization	Absent	127 (93.4)	191 (95.5)	0.549
	Present	9 (6.6)	9 (4.5)	
Frontal bullar cell	Absent	117 (86)	156 (78)	0.064
	Present	19 (14)	44 (22)	
EMC	Absent	124 (91.2)	195 (97.5)	**0.019**
	Present	12 (8.8)	5 (2.5)	
Haller's cell	Absent	115 (84.6)	192 (96)	**0.001**
	Present	21 (15.4)	8 (4)	
Onodi cell	Absent	94 (69.1)	149 (74.5)	0.279
	Present	42 (30.9)	51 (25.5)	
Maxillary sinus hypoplasia	Absent	120 (88.2)	186 (93)	0.191
	Present	16 (11.8)	14 (7)	
Septated maxillary sinus	Absent	130 (95.6)	194 (97)	0.556
	Present	6 (4.4)	6 (3)	
Frontal sinus aplasia	Absent	133 (97.8)	188 (94)	0.166
	Present	3 (2.2)	12 (6)	
Frontal sinus hypoplasia	Absent	100 (73.5)	167 (83.5)	**0.026**
	Present	36 (26.5)	33 (16.5)	
Frontal sinus hyperaeration	Absent	122 (89.7)	167 (83.5)	0.147
	Present	14 (10.3)	33 (16.5)	
Pneumosinus dilatans	Absent	134 (98.5)	197 (98.5)	1
	Present	2 (1.5)	3 (1.5)	
Sphenoid sinus agenesis	Absent	135 (99.3)	197 (98.5)	0.65
	Present	1 (0.7)	3 (1.5)	
Sphenoid sinus hypoplasia	Absent	104 (76.5)	172 (86)	**0.036**
	Present	32 (23.5)	28 (14)	
ACPP	Absent	97 (71.3)	143 (71.5)	0.972
	Present	39 (28.7)	57 (28.5)	
PPP	Absent	116 (85.3)	87 (43.5)	**<0.001**
	Present	20 (14.7)	113 (56.5)	
GSWP	Absent	99 (72.8)	157 (78.5)	0.228
	Present	37 (27.2)	43 (21.5)	

MT: Middle turbinate, IT: Inferior turbinate, SOEC: Supraorbital ethmoid cell, ISCC: Intersinus septal cell, EMC: Ethmoidomaxillary cell, ACPP: Anterior clinoid process pneumatization, PPP: Pterygoid process pneumatization, GSWP: Greater sphenoid wing pneumatization

Significant differences between the groups are shown in bold

masses. Contrast matter use is not necessary, and they are observed in CT as well-limited, homogeneous, and generally hyperdense masses of benign nature. These characteristic radiological features differentiate osteomas from other benign tumors such as fibrous dysplasia (5). CT is the gold standard for PSO. Magnetic resonance imaging is suggested in case of intracranial or intraorbital extension (16, 17). A great majority of osteomas are incidentally detected on CT. It was reported that they could manifest symptoms when they disrupt frontal sinus drainage. Osteomas could lead to symptoms such as loss of vision, exophthalmos, diplopia, pneumocephalus and intracranial mucocele depending upon their intraorbital and intracranial compression (18). None of the patients in the present study had intracranial or intraorbital complications due to compression of osteoma. However, one patient had headache symptoms because of impaired frontal sinus drainage. Osteoma was excised using endoscopic sinus surgery in this patient.

Evaluation of Anatomic Variations

Association of paranasal sinus anatomic variations with conditions such as nasal polyps, chronic sinusitis and

antrochoanal polyp were investigated previously in many studies. Bilge et al. (19) found that frequencies of conditions such as septal deviation, concha bullosa, agger nasi cell and frontal sinus hypoplasia were significantly higher in patients with nasal polyp detected by CT compared to control group. They suggested that some variations caused obstruction in the involved region of nasal cavity, resulting in nasal polyp formation (19). Başer et al. (20) investigated the association of antrochoanal polyp on CT with anatomic variations, and found that variations such as concha bullosa, agger nasi, hyperpneumatized ethmoid bulla and Haller's cells were significantly more frequent in the side where antrochoanal polyp was located compared to the side without polyp.

There are several studies that have addressed the effects of genetic and environmental factors on paranasal sinus anatomic variations. It was revealed that concha bullosa was more common in monozygotic twins than in dizygotic ones (11). Thus, the authors suggested that genetic factors play a role in the formation of paranasal sinus anatomic variations. In the present study, frequencies of some anatomic variations were found to be higher in patients with osteomas. For example, pneumatization of the vertical part of the MT was significantly less frequent in patients with osteoma compared to the control group ($p<0.05$). However, pneumatization of the bulbous part was not significantly different between the two groups. Another finding was that concha bullosa variations were not dominant on the side where osteoma was located. Janovic et al. (7) reported that concha bullosa was not associated with the presence of osteoma. Less frequent vertical concha bullosa in the osteoma group in the present study could be because of the possible compression of osteoma, which is generally observed in frontal recess region in MT. This finding implies that alongside genetic factors, neighboring pathologies could also affect anatomic variations.

It was argued that environmental factors contribute to septum deviation and to the formation of Haller's cell and supraorbital cell (11,21). Septum deviation has been suggested to arise from environmental causes, genetics, and trauma (22). Genetic and environmental factors also play roles in the formation of osteomas, as mentioned above. Therefore, we compared the presence of septum deviation in patients with and without osteoma, and the possible associations between the two conditions. Thus, we investigated the possibility that similar etiologies could lead to different conditions (osteoma and septum deviation) in the nasal cavity. In the presented study, no difference was found between the osteoma group and control group regarding the presence of septum deviation and the side of the osteoma localization. This finding suggests that the impact of environmental factors in septum deviation could be more prominent. Haller's cell and EMC frequencies were higher in the osteoma group compared to the control group in our study (Table 4). Our study also showed that these two variations were not affected by the side where the osteoma was located (Table 3). Janovic et al. (7) also reported a higher incidence of Haller's cell in patients with osteoma. Chaiyasate et al. (11) claiming that presence of Haller's cell was more common in monozygotic twins compared to dizygotic twins, pointed to the contribution of genetic factors in the formation of this variation.

The uncinate process can have variations such as pneumatization and twisting. Pneumatization can disrupt sinus drainage and cause mucosal pathologies (23). Pneumatization frequency in the uncinate process was reported as 1%–9%, while twisted uncinate process frequency was reported as 3%–19% (24). Moreover, it was revealed that the twisted variation of the uncinate process was associated with the ethmoid sinusitis. However, there are no studies that have investigated the association of this variation with osteoma. In our study, the frequency of pneumatized uncinate processes was 11.9%, while the frequency of twisted uncinate processes was 4.4%. The frequency of twisted uncinate processes was higher, whereas the frequency of pneumatized uncinate processes was significantly lower in the osteoma patient group compared to the controls (Table 4). These variations were not associated with the side where osteoma was located (Table 3).

Kuhn (25) evaluated frontoethmoidal cells by separating them into four classes. This classification includes agger nasi cells, ISSC, the frontal bullar cell and SOEC. In the present study, agger nasi cell was significantly lower in the osteoma patient group than the control group. However, SOEC and ISSC were significantly more common in the osteoma group, while the frequency of Kuhn's type 2 was significantly higher in the control group (Table 4). Given that, in osteoma patient group, agger nasi cell and Kuhn's type 2 cell cases were less frequent, whereas variations closer to the frontal sinus ostium, such as SOEC and ISSC, were more common, and the frequency of frontal sinus osteomas was higher, osteomas appeared to have an association with these variations. As mentioned above, the embryological theory of PSO pathogenesis mentions that the higher incidence of PSOs in the frontal sinus and the frontal recess could be due to genetic factors. Frontal sinus localization was reported as 75.3% by Buyuklu et al. (5) and 59.3% by Larrea-Oyarbide et al. (13). Similarly, the frontal sinus (48.6%) and the anterior ethmoid sinuses (37.5%), i.e., the frontonasal region, was the most common localization of PSOs in the present study. Janovic et al. (7), on the other hand, reported the PSO incidence with frontal sinus localization as 68.3% and observed that crista galli pneumatization in the frontonasal region was significantly higher in patients with PSO. Similarly, the significantly higher incidence of variations, such as SOEC and ISSC, in the frontonasal region in the patients with PSO compared to the ones without PSO in our study, could indicate the possible effects of genetic factors. As mentioned

above, this finding could be due to genetic causes, as well as environmental factors such as the compression effect of osteoma.

Frontal sinus hypoplasia and aplasia frequencies were reported to be in the range of 11.9%–40% (26). Maxillary sinus hypoplasia is less frequently observed, with a maximum reported incidence rate of 10.4% (27). Frontal and maxillary sinus hypoplasia are frequently observed in cystic fibrosis (28). To the best of our knowledge, however, there are no studies that have evaluated maxillary and frontal sinus pneumatization in patients with osteoma. In our study maxillary sinus hypoplasia was found to be higher in patients with PSO. Besides, frontal sinus hypoplasia was significantly more frequent in osteoma patients compared to the control group. Another interesting finding was that frontal sinus dysplasia was less frequent on the side where the osteoma was located (Table 3). In addition, sphenoid sinus hypoplasia was significantly more common in the osteoma patient group (Table 4). In accordance with this, PPP was less frequent in the PSO patient group compared to the control group ($p<0.001$). The incidence rates of ACPP and GSWP were similar in both groups. Lower frequency of sinus pneumatization in patients with PSO suggests that the patients with lower sinus pneumatization could tend to develop osteoma.

In the present study, associations between some characteristics of osteomas with anatomic variations were evaluated in a large patient group. To the best of our knowledge, there are no studies in the literature that have evaluated the associations between PSOs and such a wide range of anatomic variations as we did in the present study. Our results showed that some anatomic variations were more frequent in patients with osteomas. Especially vertical concha bullosa, secondary MT, twisted uncinate process, SOEC, ISSC, EMC, Haller's cell, frontal sinus hypoplasia and sphenoid sinus hypoplasia were more common in patients with PSO, while paradoxical MT, pneumatized uncinate process, agger nasi cell, Kuhn's type 2 and PPP were more common in patients without PSO.

Our study had some limitations. First, since this was a retrospective study, the clinical findings associated with osteomas could not be comprehensively analyzed. This is because as well as the patients with a paranasal sinus CT, the study also included the patients whose CTs were taken for stroke and similar intracranial reasons. It was difficult to distinguish whether their headache was associated with osteoma. Another limitation of the study was the presence of statistical difference between the study and control groups in terms of age and gender.

Conclusion

Our results suggest that patients with osteoma presented with a higher frequency of anatomic variations of the paranasal sinuses compared to patients without osteoma. PSO was associated with concha bullosa, secondary MT and some other anatomic variations. These associations could be due to genetic as well as environmental factors. Future studies on this area could better reveal these associations.

Ethics Committee Approval: Approval was granted by the Ethics Committee of Gaziosmanpaşa University (approval no: 20-KAEK-109, date:21/05/2020).

Informed Consent: Informed consent was obtained from all individual participants included in the study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Conception: C.A., M.B., E.G., Design: C.A., M.B., E.G., Data Collection and/or Processing: C.A., M.B., E.G., Analysis and/or Interpretation: C.A., M.B., E.G., Literature Review: C.A., M.B., E.G., Writing: C.A., M.B., E.G.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

Main Points

- Genetic or environmental factors are among the possible factors affecting PSO formation.
- Patients with paranasal sinus osteoma have a higher rate of paranasal sinus variations than patients without paranasal osteoma.
- The paranasal sinus osteoma was associated with vertical concha bullosa, secondary middle turbinate, twisted uncinate process, supraorbital ethmoid cell, intersinus septal cell, ethmoidomaxillary cell, Haller's cell, frontal sinus hypoplasia and sphenoid sinus hypoplasia, all of which showed significantly higher prevalence in the osteoma group compared to the control group.

References

1. Earwaker J. Paranasal sinus osteomas: a review of 46 cases. Skeletal Radiol 1993; 22: 417-23. [Crossref]
2. Childrey JH. Osteoma of the sinuses, the frontal and the sphenoid bone. Arch Otolaryngol 1939: 30: 63-72. [Crossref]

3. Erdogan N, Demir U, Songu M, Ozenler NK, Uluç E, Dirim B. A prospective study of paranasal sinus osteomas in 1,889 cases: changing patterns of localization. Laryngoscope 2009; 119:2355-9. [Crossref]
4. Cokkeser Y, Bayarogullari H, Kahraman SS. Our experience with the surgical management of paranasal sinus osteomas. Eur Arch Otorhinolaryngol 2013; 270: 123-8. [Crossref]
5. Buyuklu F, Akdogan MV, Ozer C, Cakmak O. Growth characteristics and clinical manifestations of the paranasal sinus osteomas. Otolaryngol Head Neck Surg 2011; 145: 319-23. [Crossref]
6. Atallah N, Jay MM. Osteomas of the paranasal sinuses. J Laryngol Otol 1981; 95: 291-304. [Crossref]
7. Janovic A, Antic S, Rakocevic Z, Djuric M. Paranasal sinus osteoma: is there any association with anatomical variations? Rhinology 2013; 51: 54-60. [Crossref]
8. Dell'Aversana Orabona G, Salzano G, Iaconetta G, Piombino P, Ponzo L, Santella A et al. Facial osteomas: fourteen cases and a review of literature. Eur Rev Med Pharmacol Sci 2015; 19: 1796-802. [Crossref]
9. Kamel SG, Kau CH, Wong ME, Kennedy JW, English JD. The role of cone beam CT in the evaluation and management of a family with Gardner's syndrome. J Craniomaxillofac Surg 2009; 37: 461-8. [Crossref]
10. Spaeth J, Krügelstein U, Schlöndorff G. The paranasal sinuses in CT-imaging: development from birth to age 25. Int J Pediatr Otorhinolaryngol 1997; 39: 25-40. [Crossref]
11. Chaiyasate S, Baron I, Clement P. Analysis of paranasal sinus development and anatomical variations: a CT genetic study in twins. Clin Otolaryngol 2007; 32: 93-7. [Crossref]
12. Halawi AM, Maley JE, Robinson RA. Swenson C, Graham SM. Craniofacial osteoma: clinical presentation and patterns of growth. Am J Rhinol Allergy 2013; 27: 128-33. [Crossref]
13. Larrea-Oyarbide N, Valmaseda-Castellón E, Berini-Aytés L, Gay-Escoda C. Osteomas of the craniofacial region: review of 106 cases. J Oral Pathol Med 2008; 37: 38-42. [Crossref]
14. Appalanarasayya K, Murthy AS, Viswanath CK, Devi OB. Osteoma involving the orbit: case report and review of literature. Int Surg 1970; 54: 449-53. [Crossref]
15. Mansour AM, Salti H, Uwaydat S, Dakroub R, Bashshour Z. Ethmoid sinus osteoma presenting as epiphora and orbital cellulitis: case report and literature review. Surv Ophthalmol 1999; 43: 413-26. [Crossref]
16. Chahed H, Hachicha H, Bachraoui R, Marrakchi J, Mediouni A, Zainine R et al. Paranasal sinus osteomas: diagnosis and treatment. Rev Stomatol Chir Maxillofac Chir Orale 2016; 117:306-10. [Crossref]
17. Exley RP, Markey A, Rutherford S, Bhalla RK. Rare giant frontal sinus osteoma mimicking fibrous dysplasia. J Laryngol Otol 2015; 129: 283-7. [Crossref]
18. Turan Ş, Kaya E, Pınarbaşlı MÖ, Çaklı H. The analysis of patients operated for frontal sinus osteomas. Turk Arch Otorhinolaryngol 2015; 53: 144-9. [Crossref]
19. Bilge T, Akpinar M, Mahmutoğlu AS, Uçak I, Uslu Coşkun B. Anatomic variations in paranasal sinuses of patients with sinonasal polyposis: radiological evaluation. J Craniofac Surg 2016; 27: 1336-9. [Crossref]
20. Başer E, Sarıoğlu O, Arslan İB, Çukurova İ. The effect of anatomic variations and maxillary sinus volume in antrochoanal polyp formation. Eur Arch Otorhinolaryngol 2020; 277: 1067-72. [Crossref]
21. Grymer LF, Bosch C. The nasal septum and the development of the midface. A longitudinal study of a pair of monozygotic twins. Rhinology 1997; 35: 6-10. [Crossref]
22. Neskey D, Eloy JA, Casiano RR. Nasal, septal, and turbinate anatomy and embryology. Otolaryngol Clin North Am 2009; 42: 193-205. [Crossref]
23. Dasar U, Gokce E. Evaluation of variations in sinonasal region with computed tomography. World J Radiol 2016; 8: 98-108. [Crossref]
24. Fadda GL, Rosso S, Aversa S, Petrelli A, Ondolo C, Succo G. Multiparametric statistical correlations between paranasal sinus anatomic variations and chronic rhinosinusitis. Acta Otorhinolaryngol Ital 2012; 32: 244-51. [Crossref]
25. Kuhn FA. Chronic frontal sinusitis: the endoscopic frontal recess approach. Oper Tech Otolaryngol Head Neck Surg 1996; 7: 222-9. [Crossref]
26. Guerram A, Le Minor JM, Renger S, Bierry G. Brief communication: the size of the human frontal sinuses in adults presenting complete persistence of the metopic suture. Am J Phys Anthropol 2014; 154: 621-7. [Crossref]
27. Bolger WE, Woodruff WW Jr, Morehead J, Parsons DS. Maxillary sinus hypoplasia: classification and description of associated uncinate process hypoplasia. Otolaryngol Head Neck Surg 1990; 103: 759-65. [Crossref]
28. Eggesbø HB, Søvik S, Dølvik S, Eiklid K, Kolmannskog F. CT characterization of developmental variations of the paranasal sinuses in cystic fibrosis. Acta Radiol 2001; 42: 482-93. [Crossref]

Non-Traumatic Laryngeal Fractures: A Systematic Review

Systematic Review

Noor Khalid[1], Muhammad Bilal[2], Muhammad Umer[3]

[1]Department of Otorhinolaryngology, Rawalpindi Medical University, Rawalpindi, Pakistan
[2]Department of Otorhinolaryngology, Foundation University Medical College, Islamabad, Pakistan
[3]Department of Otorhinolaryngology, Army Medical College, Rawalpindi, Pakistan

Abstract

Non-traumatic laryngeal fractures are an extremely uncommon presentation, and the diagnosis can be missed. Recognizing these fractures is important to appropriately direct management because most have a good prognosis and result in complete recovery. This article aimed to review the characteristics of all documented cases of non-traumatic fractures of the larynx. We sought to address questions related to the etiology, clinical presentation, and diagnostic assessment of this condition and provide recommendations about the management of these fractures. Electronic databases, mainly PubMed and Google Scholar, were searched for relevant literature with no language or time restrictions. Since 1950, 15 cases of non-traumatic laryngeal fractures have been documented in the medical literature. Out of these, thyroid cartilage fractures have been described in 14 patients, while only one instance demonstrated a fracture in the cricoid cartilage. Patients were managed conservatively using voice rest and observation with complete recovery in all cases. All patients who present with odynophagia, hoarseness, and tenderness over the thyroid cartilage after an episode of severe coughing or sneezing, should be evaluated for a thyroid cartilage fracture using laryngoscopy and computed tomography scan. Management of the airway should be the primary priority in any laryngeal injury, and further management performed after the airway is stable.

Keywords: Larynx, spontaneous fractures, thyroid cartilage, management, computed tomography, systematic review

ORCID ID of the authors:
NK: 0000-0003-4928-8749
MB: 0000-0003-1314-1315
MU: 0000-0001-5165-7844

Cite this article as: *: Khalid N, Bilal M, Umer M. Non-Traumatic Laryngeal Fractures: A Systematic Review. Turk Arch Otorhinolaryngol 2021*

Corresponding Author:
Noor Khalid; nbks1024@gmail.com

Received Date: 21.10.2020
Accepted Date: 27.12.2020

DOI: 10.4274/tao.2020.6093

Introduction

Non-traumatic fractures of the larynx remain a less understood phenomenon in the medical literature. Since the first case of a spontaneous thyroid cartilage fracture documented in 1950, our knowledge regarding the etiology and the pathophysiology of these fractures has not substantially improved (1). There are yet no established guidelines for the management of these cases. Fractures of the laryngeal cartilages without a prior history of trauma are a rarely encountered entity; however, it is vital to be able to recognize this pattern of injury, as most of these fractures have an excellent prognosis without the need for surgical intervention.

This systematic review summarizes and critically analyzes the available literature, which includes 15 cases documented from 1950 through 2020 (1–14).

Methods

Review Protocol

The protocol of our review follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocol (The PRISMA Statement) guidelines (15). The protocol was previously not registered.

Search Strategy and Study Selection

We conducted a systematic literature review using Harzing's Publish or Perish software (16). Two authors (M.B. and M.U.) independently searched PubMed Central and Google Scholar databases for relevant articles up to October 2020. Other resources used were Cureus and ResearchGate. A broad core search term "laryngeal fracture" was used. Articles dealing with traumatic fractures and those irrelevant to our study were excluded. We included case reports or case series documenting non-traumatic laryngeal fractures, with no language or time restrictions. The references of the included articles were also used to identify additional cases. We screened all case reports manually for duplication and relevance, and any uncertainty encountered during the process was resolved by mutual consensus.

Quality Assessment of Included Case Reports

We assessed the quality of the included case reports by comparison with the 2013 Case Report guidelines (CARE checklist) (17) and the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Case Reports (18). An evaluation form was used to score each article against the checklist items. Each positive item on the form conferred a score of one. In this manner, the articles were scored out of 28 for the CARE checklist, and 8 for the JBI checklist. To minimize bias, two reviewers independently assessed each case report, and the mean of the two scores was then calculated.

Data Retrieval and Analysis

After thorough research and screening, 14 articles that documented 15 cases were selected for review. Data retrieved from case reports included the title of study, name(s) of the author(s), year of publication, age and sex of patients, fracture type, etiology, precipitating event, comorbid conditions, signs and symptoms, investigations, and management plan. Data were then recorded in Microsoft Excel 2016 (Microsoft Corporation, Redmond, Washington, USA) and analyzed.

Results

The initial PubMed search for "Laryngeal Fracture" revealed 828 results, while a Google Scholar search revealed 920 results. Three articles were identified from additional sources. After removing duplicates and excluding irrelevant studies, 14 articles were selected for analysis. The PRISMA flowchart for the literature review process is shown in Figure 1.

Until now, 15 cases of spontaneous laryngeal fractures have been documented, 14 of which reported thyroid fractures, while one study reported a fracture of the cricoid cartilage. For the sake of simplicity in analysis, all fractures were assigned a grade using the Schaefer Fuhrman's classification of laryngeal injuries (19). Mildly displaced fractures were classified as grade II alongside nondisplaced fractures. Table 1 provides a summary of the characteristics of all included case reports.

The included cases were further analyzed based on their presentations and management, as shown in Table 2. Only the detailed characteristics of thyroid fractures (1-13) were analyzed, and the case that demonstrated cricoid cartilage fracture (14) was excluded from the analysis. We did so because no other cases of spontaneous cricoid cartilage fractures have been reported in the literature, and hence, we did not have any study to compare it.

Pathophysiology

Non-traumatic fractures of the larynx occur when the pressure inside the laryngotracheal complex rises in the presence of a closed glottis. This phenomenon occurs during coughing and swallowing, and results in a substantial force being exerted on the cartilages of the larynx. Amongst the documented cases, sneezing was the most common cause of thyroid fractures (n=9, 64.3%), followed by coughing (n=3, 21.4%) and swallowing (n=2, 14.2%). Sneezing on a closed airway increases the pressure by 38 times, which results in a higher risk (3). The precipitating event of the only reported non-traumatic cricoid fracture was unclear (14).

Patient Characteristics

Fractures of the thyroid cartilage made up 93.3% (n=14) of all non-traumatic laryngeal fractures. These fractures occurred exclusively in males (n=14, 100%) with the mean age of patients being 40 years old (range: 29-61). Most patients (n=9, 64.3%) were otherwise perfectly healthy, with no known comorbid conditions. Of the remaining, the most common comorbid condition was smoking, which was observed in three patients (n=3, 21.4%). Other reported conditions include gastrointestinal reflux disease (GERD), asthma, type 1 diabetes mellitus (DM), hypertension, and obstructive sleep apnea, all of which had a frequency of one.

Only one case report reported the ethnicity of the patient to be African-American (12). The rest of the studies do not give any information regarding the patient's ethnic background.

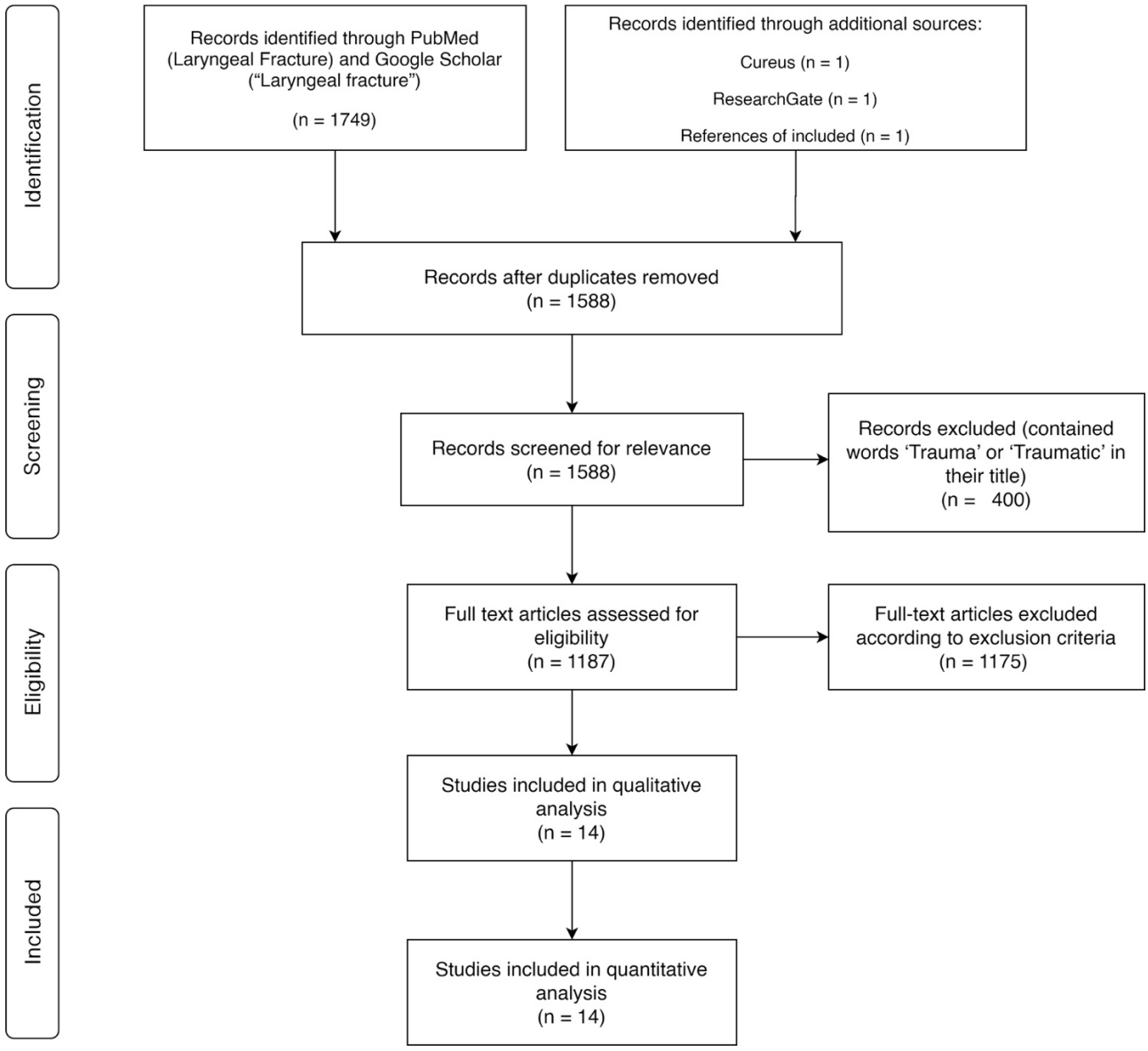


Figure 1. PRISMA Diagram of the literature retrieval process
n: Number

Other patient characteristics, including occupation and geographical residence, were not reported for any case.

On the other hand, there has only been one case of a cricoid fracture documented, and the patient was a 69-year-old female with significant comorbidity. She had a prolonged history of DM and was on dialysis due to end-stage renal disease. Her ethnicity and occupation were not reported (14).

Fracture Characteristics

Almost all thyroid fractures occurred in the anterior part of the thyroid cartilage. Most fractures occurred in the paramedian plane (n=10, 83.3%). Soft tissue infection with the fracture was present only in two (14.3%) cases (8, 11). Most fractures belonged to Shaefer grade II (n=12, 85.7%) with slight or no displacement of the fracture segments. Only one case reported significant displacement of the fracture fragments, which was due to compression by an anterior neck abscess (11). The case with the cricoid cartilage fracture demonstrated a posterior lamina fracture with airway compromise but no soft tissue infection (14).

Clinical Presentation

The main presenting complaints included odynophagia (n=12, 85.7%), hoarseness (n=13, 92.9%) and tenderness to palpation over the thyroid cartilage (n=9, 64.3%).

Table 1. Characteristics of the included studies demonstrating non-traumatic fractures of the larynx (n=15)

#	Year of Publication	Author(s)	Fracture	Schaefer grade	Precipitating factor	Age	Sex	Comorbid or associated conditions	Symptoms and signs	Endoscopic examination of laryngeal inlet	CT findings	Management	Follow-up showing resolution
1	1950	Quinlan (1)	Thyroid	II	Sneezing	44	M	None	O, H, P, S, T, vertical non-displaced paramedian # felt	supraglottic ED, ER normal VCM	Not available	Ant. neck strapping, VR, liquid diet	7 d
2	2007	Martínez et al. (2)	Thyroid	II	Sneezing	41	M	None	O, H, P, T, C	ED, HM (Rt.) normal VCM	Ant. midline TC #, non-displaced, SC air	VR, IV abx, IV steroids, liquid diet, gastric protection	7 d
3	2011	Faden et al. (3)	Thyroid	II	Sneezing on closed airway	38	M	None	HP, H, P, C	subglottic ED normal VCM	Vertical TC #, non-displaced, SC air	VR, steroids, PPI, abx, painkillers, face mask	7 d
4	2012	Alexander and Toynton (4)	Thyroid	II	Coughing	29	M	None	O, D, H, HP, T, C	ED, HM (Lt.)	Midline TC #, slightly displaced, SC air	VR, NBM, NGT	7 d
5	2013	Fenig et al. (5)	Thyroid	II	Coughing	47	M	URI	O, D, H, T, S, P	ED, normal VCM	Ant. TC #, slightly displaced, phlegmon, SC air	IV steroids, abx, liquid diet	7 d
6	2016	Forner et al. (6)	Thyroid	I	Sneezing	33	M	Smoking	O, H, P, HP	HM (Rt.), normal VCM	SC air, no identifiable # line	Observation, Voice therapy	30 d
7	2017	Reuther and Weissbrod (7)	Thyroid	II	Sneezing	34.5[a]	M	None	O, H, P, S, T	HM (Lt.), normal VCM	Paramedian vertical TC #, non-displaced	VR, steroids	14 d
8	2017	Santamaría et al. (8)	Thyroid	II	Sneezing	36	M	None	O, H, T	HM (Lt.), normal VCM	Parasagittal Lt. TC #, non-displaced	VR, steroids	21 d
9	2017	Santamaría et al. (8)	Thyroid	II	Swallowing on bending over	32	M	None	O, D, H, T	supraglottic ED, normal VCM	Parasagittal Lt. TC #, non-displaced	VR, NSAIDs	10 d
10	2018	Matrka and Li (9)	Thyroid	II	Sneezing	35	M	None	O, H, P, T	ED, ER, hemorrhage, normal VCM	Vertical Rt. TC #, non-displaced, SC air, reactive LNs	Conservative[b]	60 d
11	2019	Salguero et al. (10)	Thyroid	II	Coughing	48	M	GERD, asthma	S, C	Not available	Ant. # of TC, mildly displaced, SC air	Conservative[b], observation	Lost to follow-up
12	2020	Balai et al. (11)	Thyroid	III	Swallowing	61	M	T1DM, smoking	O, H, D, S,	Supraglottic ED, saliva pooling	Rt. vertical # of TC, post. displacement by ant. neck abscess	VR, IV steroids, abx, liquid diet, I&D for abscess	30 d
13	2020	Byrne et al. (12)	Thyroid	II	Sneezing (stifled sneeze)	47	M	OSA, HTN, smoking	O, H, T	Not available	Ant. # of TC, non-displaced, subglottic edema	Observation, pain control	10 d
14	2020	Ateş et al. (13)	Thyroid	II	Sneezing	34	M	None	O, H, C, discomfort	ED, HM (Rt.), normal VCM	Paramedian # of TC, non-displaced, SC air	VR, IV abx, steroids	7 d
15	2019	Matsuo et al. (14)	Cricoid	III	Unclear	69	F	T2DM, ESRD	Intermittent dyspnea	Subglottic narrowing, normal VCM	CC # with airway narrowing	oral intubation, tracheostomy	---

M: Male, F: Female, d: Day(s), URI: Upper respiratory tract infection, GERD: Gastroesophageal reflux disease, T1DM: Type 1 diabetes mellitus, T2DM: Type 2 diabetes mellitus, OSA: Obstructive sleep apnea, HTN: Hypertension, ESRD: End-stage renal disease, O: Odynophagia, D: Dysphagia, H: Hoarseness, P: Pain, S: Swelling of the neck, T: Tenderness, C: Crepitus, HP: Hemoptysis, HM: Hematoma, Lt: Left, Rt: Right, ED: Edema, ER: Erythema, VCM: Vocal cord motion, TC: Thyroid cartilage, CC: Cricoid cartilage, CT: Computed tomography scan, SC: Subcutaneous, #: Fracture, Ant: Anterior, Post: Posterior, VR: Voice rest, IV: Intravenous, PPI: Proton pump inhibitor, Abx: Antibiotics, NBM: Nil by mouth, NGT: Nasogastric intubation, NSAIDs: Non-steroidal anti-inflammatory drugs, I&D: Incision and drainage, n: Number

[a]The original case report mentioned the patient to be in his 30s. After author consensus, median age of 34.5 years was chosen for analysis.

[b]No other detail about the management protocol was available

Table 2. Analysis of selected characteristics of non-traumatic thyroid fractures (n=14)

Characteristic	**Mean**	**Median**	**Range**
Age	39.9	37	29-61
Follow-up showing resolution (days)	16	8.5	7-60
Characteristics	No. of cases	Total	Percent (%)
Demographics			
Male	14	14	100.0
Female	0	14	0.0
Comorbid or associated conditions			
None	9	14	64.3
Smoking	3	14	21.4
Type 1 diabetes mellitus	1	14	7.1
Hypertension	1	14	7.1
Asthma	1	14	7.1
GERD	1	14	7.1
OSA	1	14	7.1
URI	1	14	7.1
Precipitating event			
Sneezing (includes closed airway sneeze and stifled sneeze)	9	14	64.3
Coughing	3	14	21.4
Swallowing	2	14	14.2
Signs and symptoms			
Odynophagia	12	14	85.7
Hoarseness/Dysphonia	13	14	92.9
Dysphagia	4	14	28.6
Neck Pain	7	14	50.0
Neck Swelling	5	14	35.7
Hemoptysis	3	14	21.4
Tenderness to palpation	9	14	64.3
Crepitus	5	14	35.7
Triad of odynophagia, dysphonia, dysphagia	4	14	28.6
Triad of odynophagia, dysphonia, tenderness	9	14	64.3
Endoscopic examination			
Performed	12	14	85.7
Edema	9	12	75.0
Erythema	2	12	16.7
Hematoma	6	12	50.0
Hemorrhage	1	12	83.3
Normal vocal cord movements	12	12	100.0
CT Scan findings			
CT performed	13	14	92.9
Fracture observed	12	13	92.3
Subcutaneous emphysema	8	13	61.5
Fracture characteristics			
Anterior	13	14	92.9
Midline	2	12	16.7

Table 2 contiuned

Paramedian	10	12	83.3
Non-displaced	10	14	71.4
Slightly displaced	3	14	21.4
Significantly displaced	1	14	7.1
Schaefer Grade I	1	14	7.1
Schaefer Grade II	12	14	85.7
Schaefer Grade III	1	14	7.1
Associated soft tissue infection (as visualized on CT)	2	14	14.3
Phlegmon	1	14	7.1
Anterior neck abscess	1	14	7.1
Management			
Surgical Fixation	0	14	0.0
Conservative	14	14	100.0
Voice rest	9	14	64.3
Steroids	7	14	50.0
NSAIDs	1	14	7.1
Antibiotics	5	14	35.7
Gastric protection/PPIs	2	14	14.3
No details	2	14	14.3

GERD: Gastroesophageal reflux disease, OSA: Obstructive sleep apnea, URI: Upper respiratory tract infection, CT: Computed-tomography, NSAIDs: Non-steroidal anti-inflammatory drugs, PPI: Proton pump inhibitor

Fenig et al. (5) suggested that the triad of odynophagia, hoarseness, and dysphagia after an episode of coughing or sneezing should raise the suspicion of thyroid fracture. However, analysis of the included cases showed that this triad was documented only in four cases (28.6%). Alternatively, the triad of odynophagia, dysphonia, and tenderness was present in nine of 14 cases (64.3%). Crepitus was present only in five cases (35.7%) although it is a strong indicator of laryngeal injury. The only reported symptom of a non-traumatic cricoid fracture was intermittent dyspnea (14). Further cases need to be documented for more information regarding the presentation of these fractures.

Assessment and Diagnosis

The two primary investigations in the diagnosis of this condition are the examination of the larynx by endoscopy and computed tomography (CT). Of all reported cases, 85.7% patients underwent endoscopic examination via flexible nasendoscopy, laryngoscopy, or bronchoscopy. The most frequently encountered findings were edema over the laryngeal inlet or in the subglottic region (n=9, 75%) and hematoma over the ipsilateral vocal cord (n=6, 50%). All cases showed normal vocal cord movement (n=10, 100%). This investigation is important for its value in the assessment of the airway status and in ruling out other (and more common) causes of hoarseness including laryngitis, benign vocal cord lesions, and vocal cord paralysis.

CT is the most significant diagnostic investigation. A CT scan of the neck outlined the fracture in almost all of the cases. All cases underwent CT imaging except the case reported in 1950 (1), which can be attributed to the nonavailability of CT scans during that period. For that patient, the diagnosis was made by physical examination, which showed a fracture line and slight mobility of fracture segments. A plain radiograph performed was not diagnostic (1). Similar principles were used for the diagnosis of cricoid fracture. Laryngoscopy and bronchoscopy were performed, followed by CT scan which revealed the fracture (14).

Management

All patients who had thyroid fractures were managed conservatively (n=14, 100%) with complete recovery after a median follow-up time of 8.5 days. No fracture required surgical fixation or compromised the airway to warrant a tracheostomy. The management protocol was not stated in detail for most case reports; however, most patients were managed using voice rest (n=9, 64.3%) and observation.

Analysis of the cases shows that steroids were administered in seven cases (n=7, 50%) whereas one case reported the use of nonsteroidal anti-inflammatory drugs (NSAIDs), resulting in a similar outcome (8). Alexander and Toynton (4) suggested that antibiotics should be used only in cases where there is mucosal injury. Of all included cases, five cases

received antibiotics (35.7%), however the precise antibiotic used and the details of its administration were lacking. Many reports have also mentioned use of soft and liquid diet in the treatment regime (1, 2, 5, 11). Based on observations from the documented cases, the main principles for managing non-traumatic thyroid cartilage fractures are summarized in Figure 2.

Alternatively, the cricoid fracture compromised the airway causing intermittent dyspnea, so a tracheostomy was performed (14). Ideally, the fracture should have been surgically repaired; however, the patient was not fit for surgery. The patient was managed conservatively by airway preservation and observation.

Discussion

This article is the first comprehensive review summarizing the characteristics of laryngeal fractures that occur without a prior history of trauma. While most of these fractures occur in middle-aged men, their presentation and examination findings vary from patient to patient. After diagnosis by CT and laryngoscopy, these fractures can be successfully managed conservatively.

The pathophysiology of these fractures has been described in detail by many case reports (3, 5, 9) and is satisfactorily explained by the biomechanics of coughing and sneezing (20, 21). Increased intraluminal pressure during these reflex processes has been described as the causative event, however, it is still unclear as to why certain individuals are more susceptible to this injury than the others. Quinlan (1) suggested the possibility of a congenital defect in the cartilage which predisposes to these fractures, while a few authors have suggested that inflammatory or neoplastic processes result in pathological fractures (11). Most authors, however, believe defects in ossification and mineralization of the thyroid cartilage to be the primary culprit (4, 7). This hypothesis is favored because the ossification process differs between the two sexes; and therefore, it may explain the predominance of laryngeal fractures in men (22-24).

A problem with this etiological hypothesis is that it does not explain why the only documented case of a cricoid fracture involved a female patient (14). Cricoid cartilage is thicker and stronger than the thyroid cartilage, and it ossifies later (25, 26). The case involved a 69-year-old lady with a posterior cricoid fracture. Since the patient did not recall any precipitating event and no other similar case has been reported in the literature, it is possible that her fracture occurred secondary to blunt trauma to the neck, which the patient did not recall at the time of presentation. This is a common phenomenon in older adults, and studies show that many elderly patients do not remember injuries well (27). Besides, abuse is often not reported by elderly patients (28). Additional cases need to be documented before any conclusions can be drawn regarding cricoid fractures.

Most non-traumatic fractures of the larynx belonged to Schaefer grade II. The Schaefer classification of traumatic laryngeal fractures and the management plan for each fracture type is summarized in Table 3. Faden et al. (3) highlighted that the management of grade II traumatic injuries often requires a tracheostomy (19). On the other hand, non-traumatic grade II injuries were all managed conservatively without the need of a tracheostomy. This difference in treatment has been attributed to the mechanism of injury, and it further emphasizes that the mechanism of injury must be considered during its management. Additionally, traumatic laryngeal injuries are often associated with other injuries, while non-traumatic fractures are almost always an isolated

Table 3. Schaefer Fuhrman's Classification of traumatic laryngeal injuries and suggested management according to injury grade

Injury grade	Description of injury	Suggested management
Grade I	Minor endolaryngeal hematoma without detectable fracture or airway compromise	Conservative (voice rest +/- antibiotics, steroids)
Grade II	Edema, hematoma, minor mucosal disruption without exposed cartilage, or nondisplaced fractures of larynx. Variable degree of airway compromise	Group I management + airway stabilization via tracheostomy/intubation, panendoscopy with endoscopic relocation
Grade III	Massive edema, large mucosal tears, exposed cartilage, vocal cord immobility, displaced laryngeal fractures. Significant airway compromise	Open surgical repair +/- tracheostomy
Grade IV	Grade III + severe mucosal injuries, disruption of the anterior larynx, unstable fractures, two or more fractures lines. Significant airway compromise/impending airway obstruction	Tracheostomy, panendoscopy, open surgical repair with stenting
Grade V	Complete laryngotracheal separation. Severe airway obstruction	Tracheostomy, open exploration with reconstruction, restoration, or resection

Source: Data from Omakobia et al. (19) and Moonsamy et al. (33)

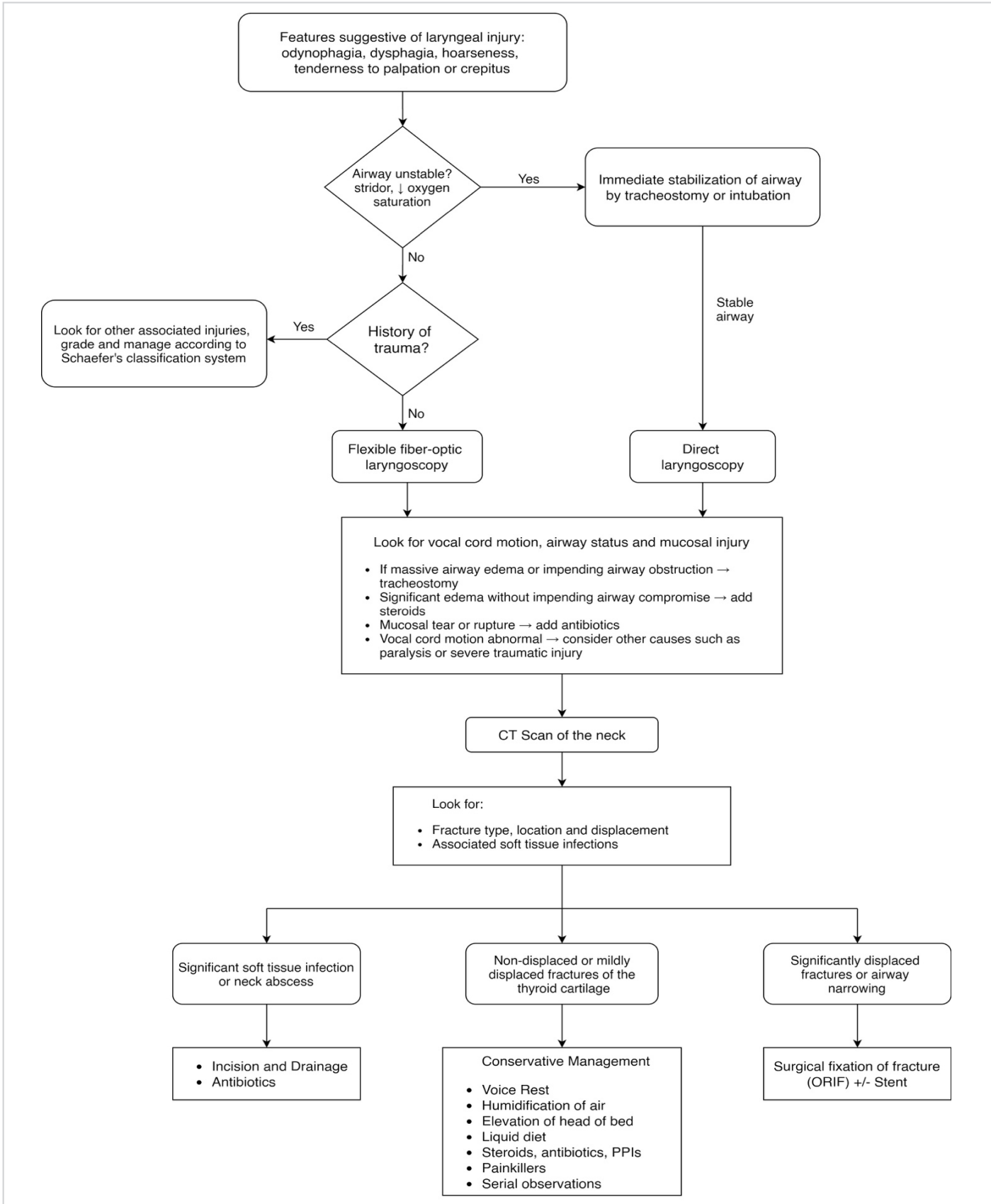


Figure 2. Algorithm summarizing the management principles of all included cases of thyroid fractures

CT: Computed tomography, ORIF: Open reduction and internal fixation, PPI: Proton pump inhibitor

phenomenon and hence can be managed successfully with a less aggressive approach (29). A separate classification system should thus be developed for the grading and management of non-traumatic laryngeal fractures.

A controversy exists over the use of steroids in laryngeal trauma. Traditionally, steroids have been administered to all patients with edema of the larynx and were believed to relieve laryngeal edema and its exacerbation after intubation and bronchoscopy (30). However, recent guidelines on the use of steroids in these injuries are unclear (31-33). Fifty percent of the reviewed cases mentioned steroids to be a part of their treatment regimen. For the other half, steroids were either not administered or their use was not documented. Of note, all patients reported similar outcomes, i.e., complete recovery. In the absence of established guidelines, a reasonable approach would be to use steroids in cases with significant airway edema only. Further studies are needed before any objective recommendations can be made.

In addition, there are no clear principles about the use of antibiotics in these patients. Based on observations from the reviewed cases and recommendation by Alexander and Toynton (4), antibiotics should be administered only if there is associated soft tissue infection or if laryngeal mucosa is injured. We identified two cases where antibiotics were administered without any of these indications (3, 5). It is possible that antibiotics were added to the treatment regimen as a "general practice," keeping in view the universal tendency of doctors and hospitals to overuse these drugs (34, 35). However, since two cases of spontaneous laryngeal fractures did have an associated infection necessitating their use, it is unclear whether antibiotics should be administered as routine prophylaxis to prevent infection or not. Further research is required to answer this question.

An important observation made during the quality assessment of the case reports was the fact that no case report completely conformed to the principles stated in quality assessment guidelines. This finding is similar to the overall low quality of published case reports as highlighted by many studies (36, 37).

Out of 15 cases of non-traumatic laryngeal fractures reported, 14 cases did not report the ethnicity or racial origin of the patient. Many medical conditions have specific ethnicity patterns, so this information should not be regarded as insignificant (38, 39). Furthermore, most case reports do not provide sufficient detail about their treatment regimen, mentioning it only as "conservative." Details regarding the dosage and administration of drugs have been excluded. All future authors need to be thorough in their documentation since no treatment guidelines exist for this condition, and case reports are the only available source of evidence.

This review has several limitations. Primarily, there is a lack of documented cases, with extensive literature review revealing only 15 instances of such fractures. Second, as described above, the included case reports are lacking in important information regarding patient characteristics and management protocol, and hence no concrete recommendations can be made. Third, case reports are the lowest level of evidence, and further studies are needed before evidence-based guidelines can be constructed for clinicians to be able to manage this condition effectively (40). This review is the first attempt to organize all the published knowledge about this entity, and we hope that it will pave way for further research on this topic.

Conclusion

Non-traumatic fractures of the larynx are rare clinical entities. Although important information regarding the presentation and management of these fractures can be obtained by reviewing cases documented in the literature, areas of further research remain. All such cases encountered in clinical practice must be documented in the form of high-quality case reports for evidence-based guidelines to be constructed.

Acknowledgement

The authors are thankful to Daneyal Arshad from Rawalpindi Medical University for his guidance and support.

Peer-review: Externally peer-reviewed.

Conflict of Interest: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Authorship Contributions

Conception: N.K., Design: N.K., M.B., Materials: M.U., Data Collection and/or Processing: N.K., M.B., M.U., Analysis and/or Interpretation: N.K., M.B., Literature Review: M.B., M.U., Writing: N.K., M.B., M.U., Critical Review: N.K., M.U.

Main Points

- Fractures of the larynx can occur without a history of trauma and have been reported in the past after sneezing or coughing.
- These patients present with symptoms of odynophagia and hoarseness. Neck palpation may indicate tenderness and crepitus.
- The diagnosis is made on CT scan and endoscopic examination. Fractures occur mostly in the anterior part and are non-displaced or mildly displaced.
- Patients are managed conservatively. The decision to administer steroids or antibiotics should be based on the patient's clinical status and the physician's preference.

References

1. Quinlan PT. Fracture of thyroid cartilage during a sneezing attack. Br Med J 1950; 1: 1052. [Crossref]
2. Martínez AB, Juara ÁM, Moya JJ. Fracture of thyroid cartilage after a sneezing episode. Acta Otorrinolaringol (English Edition) 2007; 58: 73-4. [Crossref]
3. Faden DL, Elackatuu A, Platt M. The "closed-airway sneeze": an unusual cause of laryngeal fracture. Otolaryngol Head Neck Surg 2011; 145: 515-6. [Crossref]
4. Alexander VR, Toynton S. Spontaneous fracture of the larynx after coughing. Otolaryngol Head Neck Surg 2012; 147: 801-2. [Crossref]
5. Fenig M, Strasberg S, Cohen JC, Almadi R, Gold M. Laryngeal fracture after coughing. Am J Emerg Med 2013; 31: 1421.e1-3. [Crossref]
6. Forner D, Phillips T, Brown T. Laryngeal injury and subcutaneous emphysema caused by an episode of sneezing: a rare case treated with observation alone. J Laryngol Voice 2016; 6: 21-4. [Crossref]
7. Reuther MS, Weissbrod PA. Voice change, odynophagia, and neck pain following a sneeze. JAMA Otolaryngol Head Neck Surg 2017; 143: 89-90. [Crossref]
8. Santamaría A, Alarcón R, Sepúlveda I, Fredes F. Nontraumatic laryngeal fractures: report of two cases and review of the literature. Case Rep Otolaryngol 2017; 2017: 2153521. [Crossref]
9. Matrka L, Li M. Laryngeal fracture following violent sneeze: management and biomechanical analysis. OTO Open 2018; 2: 2473974X18757741. [Crossref]
10. Salguero B, Stoever J, Rose K. More than a tickle in the throat: a case of cough-induced laryngeal fracture. Chest 2019; 156: A1394. [Crossref]
11. Balai E, Bhamra N, Gupta KK, Jolly K, Barraclough J. A case of laryngeal fracture precipitated by swallowing. Cureus 2020; 12: e10303. [Crossref]
12. Byrne B, Tillman R, Johansson M. Laryngeal fracture after a stifled sneeze: a case report. J Emerg Med 2020; 58: e97-8. [Crossref]
13. Ateş MS, Turhal G, Aysel A, Durusoy D, Öztürk K. A case with thyroid cartilage fracture after sneezing. Turk Arch Otorhinolaryngol 2020; 58: 197-9. [Crossref]
14. Matsuo Y, Yamada T, Hiraoka E. Unique presentation of cricoid cartilage fracture causing intermittent dyspnea without preceding trauma. Nagoya J Med Sci 2019; 81: 687-91. [Crossref]
15. Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Syst Rev 2015; 4: 1. [Crossref]
16. Harzing AW. Publish or Perish. 2007. Available from: URL: https://harzing.com/resources/publish-or-perish [Crossref]
17. Riley DS, Barber MS, Kienle GS, Aronson JK, von Schoen-Angerer T, Tugwell P, et al. CARE guidelines for case reports: explanation and elaboration document. J Clin Epidemiol 2017; 89: 218-35. [Crossref]
18. Joanna Briggs Institute. Critical Appraisal tools for use in JBI Systematic Reviews. 2017. Available from: URL: https://joannabriggs.org/critical-appraisal-tools [Crossref]
19. Omakobia E, Micallef A. Approach to the patient with external laryngeal trauma: the Schaefer classification. Otolaryngol (Sunnyvale) 2016; 6: 2. [Crossref]
20. Dickey BF. What it takes for a cough to expel mucus from the airway. Proc Natl Acad Sci U S A 2018; 115: 12340-2. [Crossref]
21. Setzen S, Platt M. The dangers of sneezing: a review of injuries. Am J Rhinol Allergy 2019; 33: 331-7. [Crossref]
22. Yildiz AE, Sahap SK, Elhan AH, Fitoz S. Sonographic evaluation of the endochondral ossification process of the thyroid cartilage in children. J Clin Ultrasound 2018; 46: 89-95. [Crossref]
23. Mupparapu M, Vuppalapati A. Ossification of laryngeal cartilages on lateral cephalometric radiographs. Angle Orthod 2005; 75: 196-201. [Crossref]
24. Claassen H, Werner J. Gender-specific distribution of glycosaminoglycans during cartilage mineralization of human thyroid cartilage. J Anat 2004; 205: 371-80. [Crossref]
25. Junior SA, Rocha PR, Liquidato BM, Marques SR, Arráez-Aybar LA, de Moraes LO. Arch of cricoid cartilage anatomical variation: morphological and radiological aspects. Surg Radiol Anat 2019; 41: 539-42. [Crossref]
26. Pascual-Font A, Sanudo J. Laryngeal cartilages. Tubbs RS, Shoja MM, Loukas M, editors. Bergman's Comprehensive Encyclopedia of Human Anatomic Variation. Wiley Online Books; 2016.p.1209-11.
27. Hoffman GJ, Ha J, Alexander NB, Langa KM, Tinetti M, Min LC. Underreporting of fall injuries of older adults: implications for wellness visit fall risk screening. J Am Geriatr Soc 2018; 66: 1195-200. [Crossref]
28. Pereira C, Fertleman M. Elder abuse: a common problem, commonly missed in trauma and orthopaedics. Eur Geriatr Med 2019; 10: 839-41. [Crossref]
29. Jalisi S, Zoccoli M. Management of laryngeal fractures—a 10-year experience. J Voice 2011; 25: 473-9. [Crossref]
30. Hawkins DB, Crockett DM, Shum TK. Corticosteroids in airway management. Otolaryngol Head Neck Surg 1983; 91: 593-6. [Crossref]
31. Shaikh S, Verma H, Yadav N, Jauhari M, Bullangowda J. Applications of steroid in clinical practice: a review. ISRN Anesthesiol 2012; 2012: 985495. [Crossref]
32. Medscape. Laryngeal Fractures Treatment & Management. Available from: URL: https://emedicine.medscape.com/article/865277-treatment (Accessed: September 20, 2020). [Crossref]

33. Moonsamy P, Sachdeva UM, Morse CR. Management of laryngotracheal trauma. Ann Cardiothorac Surg. 2018; 7: 210-6. [Crossref]

34. Morgan DJ, Dhruva SS, Coon ER, Wright SM, Korenstein D. 2019 update on medical overuse: a review. JAMA Intern Med 2019; 179: 1568-74. [Crossref]

35. Camcioglu Y, Okur DS, Aksaray N, Darendeliler F, Hasanoglu E. Factors affecting physicians' perception of the overuse of antibiotics. Med Mal Infect 2020; 50: 652-7. [Crossref]

36. Dragnev NC, Wong SL. Do we CARE about the quality of case reports? A systematic assessment. J Surg Res 2018; 231: 428-33. [Crossref]

37. Agha RA, Fowler AJ, Lee SY, Gundogan B, Whitehurst K, Sagoo HK, et al. Systematic review of the methodological and reporting quality of case series in surgery. Brit J Surg 2016; 103: 1253-8. [Crossref]

38. Burchard EG, Ziv E, Coyle N, Gomez SL, Tang H, Karter AJ, et al. The importance of race and ethnic background in biomedical research and clinical practice. N Engl J Med 2003; 348: 1170-5. [Crossref]

39. Kanis JA, Cooper C, Dawson-Hughes B, Harvey NC, Johansson H, Lorentzon M, et al. FRAX and ethnicity. Osteoporos Int 2020; 31: 2063-7. [Crossref]

40. Murad MH, Asi N, Alsawas M, Alahdab F. New evidence pyramid. BMJ Evid Based Med 2016; 21: 125-7. [Crossref]

The Presentation and Management of Facial Artery Pseudoaneurysm: A Review of the Literature

Case Report

Suparna Roy, Neha Jain

Department of Otorhinolaryngology, Chacha Nehru Bal Chikitsalaya Hospital, Delhi, India

Abstract

Pseudoaneurysm is a rare vascular complication of trauma, causing an incomplete tear of the vessel wall. We present a clinical case report arising from the distal branch of facial artery in an infant. Facial artery pseudoaneurysm is a rare complication of facial trauma and can easily be misdiagnosed especially in the paediatric age group. Prompt investigation and diagnosis with timely and apt intervention is the key to the successful management of facial artery pseudoaneurysm.

Keywords: Facial artery, pseudoaneurysm, post traumatic, arteriography, false aneurysm, infant

ORCID ID of the authors:
SR: 0000-0003-0731-489X;
NJ: 0000-0001-5478-4101.

Cite this article as: *: Roy S, Jain N. The Presentation and Management of Facial Artery Pseudoaneurysm: A Case Report. Turk Arch Otorhinolaryngol 2021*

Corresponding Author:
Neha Jain; nehaajmera84@gmail.com

Received Date: 08.08.2020
Accepted Date: 07.12.2020

DOI: 10.4274/tao.2020.5594

Introduction

Pseudoaneurysm is a rare vascular complication of trauma, causing an incomplete tear of the vessel wall (1). The common presentation is a painless pulsatile swelling usually associated with a palpable thrill and an audible bruit (2). The preferred imaging modalities to clinch the diagnosis of such lesions are computed tomography (CT), arteriography, and ultrasonography (USG). Treatment options include compression, surgical resection, ligation of the involved vessel without resection, selective arteriography with embolization and intralesional sclerotherapy (3).

We present a case of facial artery pseudoaneurysm along with its clinical, radiological findings and management. To our knowledge, this is the first reported surgically managed case of distal facial artery pseudoaneurysm in an infant.

Case Presentation

A one-year-old girl presented with a right cheek mass that had been growing for three weeks. She had fallen from her bed one month ago. Clinical examination revealed a 3x2.5 cm, oval, ill-defined, reddish-purplish colored mass involving the right cheek and extending from the medial canthus to the right malar region, causing facial disfigurement (Figure 1). On palpation the mass was tense, firm, non-tender and pulsatile. Keeping differentials of A-V malformation and pseudoaneurysm in mind, color Doppler USG and CT scan were performed.

Color Doppler USG revealed a well-defined vascular cystic lesion in the right cheek highly suggestive of a pseudoaneurysm. CT images were suggestive of a large vascular mass; however, the exact origin of the lesion could not be confirmed (Figure 2). The child was taken up for surgical excision under general anaesthesia. The mass was dissected in toto and was found to be arising from the distal branch of the facial artery (Figures 3, 4). A standard pressure dressing was applied for 48 hours. The postoperative period was uneventful, and the child recovered well. Histopathological examination confirmed the diagnosis of pseudoaneurysm.

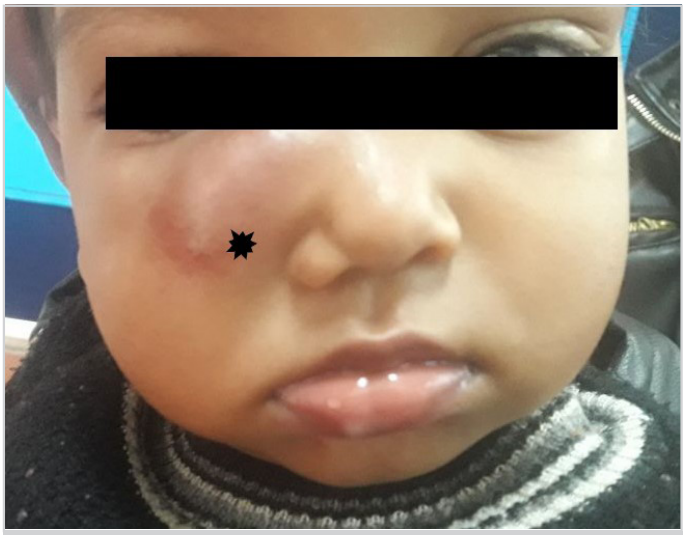


Figure 1. Right cheek swelling 3.0x2.5 cm (multi-point star)

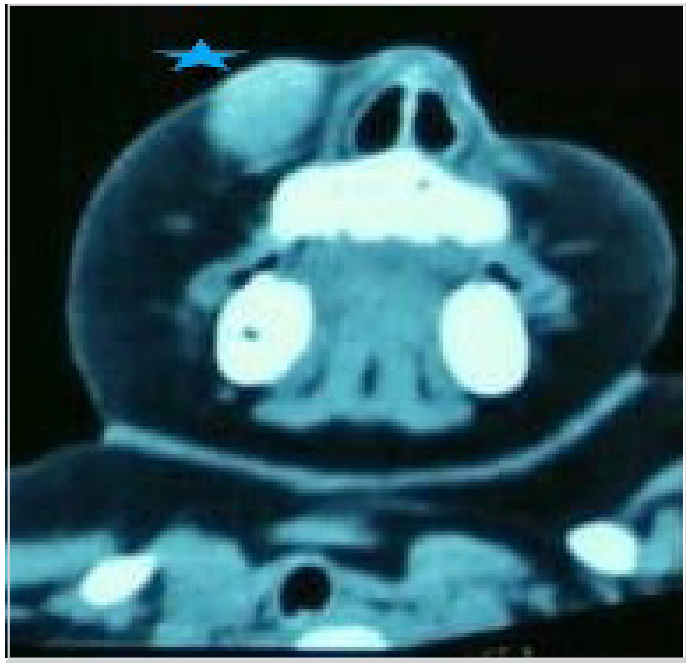


Figure 2. Contrast enhanced CT imaging showed an enhancing well-defined ovoid mass (5-point star) on the right side of the face with no bony erosion

CT: Computed tomography

Discussion

Aneurysms are classified as true, false, or dissecting. True aneurysm is a dilation of all the three layers of the intact vessel wall (1). False aneurysm or pseudoaneurysm occurs when blood leaks through an injured blood vessel into the surrounding tissues with a persistent communication or connection between them (1, 2).

Incomplete tear of the involved vessel wall causes blood to flow into the surrounding tissue resulting in tamponade and clot formation (1). Hemorrhage persists until the pressure in the periarterial zone equals the mean arterial pressure (4). Ultimately, the hematoma organizes. The perivascular connective tissue forms an endothelial lined sac leading up to the pseudointima (4). Eventually, the hematoma liquefies. The result is a communication between the artery and the aneurysmal sac, forming a pulsating mass. The persistent arterial pressure results in gradual expansion of the false aneurysm. The final outcome is further growth or rupture of the pseudoaneurysm. Thus, the time between the trauma and the clinical presentation of the pseudoaneurysm varies from days to years (1).

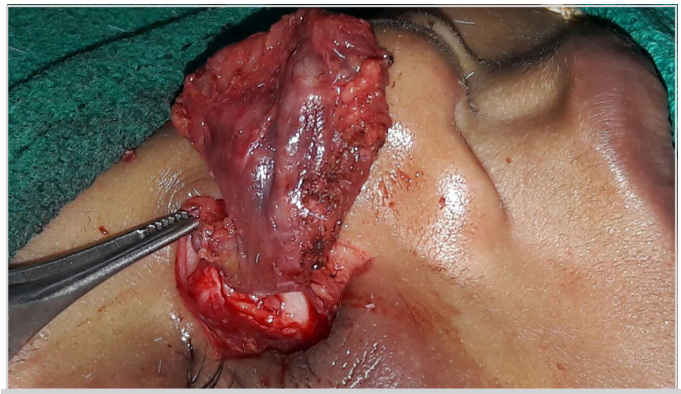


Figure 3. Vascular mass arising from distal branch of right facial artery was excised in toto

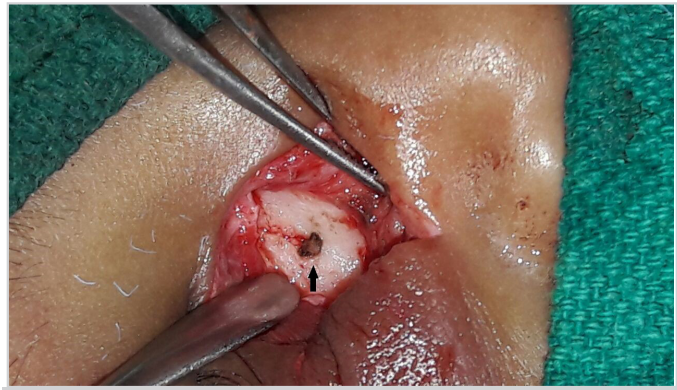


Figure 4. Distal branch of facial artery was ligated and secured (black arrow)

Facial artery pseudoaneurysms are rare because of the small diameter of the facial artery and its deep and protected location (4). Trauma, exposure to radiation, infection, undernutrition and malignancy are the risk factors for the formation of a pseudoaneurysm (1, 4). The classical presentation is a painful pulsatile swelling usually associated with a palpable thrill, an audible bruit or unexplained neurological deficit (1). On rare occasions, they present as a non-pulsatile mass due to thrombin formation or deep-seated location (5). Sometimes, pseudoaneurysm may rupture and cause hemorrhage (1).

The diagnostic tool of choice is arteriography (2). Arteriography outlines the feeding vessels and localizes the exact anatomic site of bleeding (6). Differentials to be kept in mind include lipoma, cyst, simple hematoma, abscess, A-V fistula, inflamed lymph node and neuroma (7). The final diagnosis of pseudoaneurysm is made by histopathological examination (1).

Non-invasive treatment modalities include compression and observation, but this modality is time consuming (1). Invasive treatment modalities include surgical resection, ligation of the feeding vessel, selective arteriography with embolization and percutaneous injection (3).

Classically, treatment of pseudoaneurysm has always been open surgical exploration with vessel ligation, but with the recent advancements in minimally invasive surgery, endovascular approach has become more popular. Endovascular management entails treatment aimed only at the aneurysm or the entire vessel from which the pseudoaneurysm arises (8).

Percutaneous embolization is performed by direct injection of thrombin under ultrasound guidance. This transforms the pseudoaneurysm into hematoma, which then resorbs in due course of time (9). Using the Seldinger technique, diagnostic arteriogram and therapeutic embolization can be performed in the same setting. This procedure is more selective with minimal risk of neural injury and scarring (10). For embolization, the different materials used are micro-coils, gel foam, polyvinyl alcohol particles, n-butyl cyanoacrylate glue, detachable balloons (2).

In the present case, mass was the result of a blunt trauma. Considering the superficial location of the mass, and the limited facilities for endovascular surgery in our center, surgical excision and ligation of the feeding vessels were planned. Outcome was good and no recurrence was reported in the 18-month follow-up period. The involvement of the distal facial artery makes this case all the more interesting and unique.

We recommend keeping pseudoaneurysm as a differential diagnosis in palpable pulsatile swellings of the head and neck. And an algorithm based on site (proximal/distal/superficial/deep), presentation, availability of facilities and clinical expertise should be formulated and considered for management of this uncommon entity. Although arteriography with embolization is the preferred method, surgical resection is also a safe and effective method for the treatment of head and neck pseudoaneurysms. An open procedure can be considered in cases of superficial swellings, failure of endovascular approach, or as in our case, non-availability of endovascular surgery resources.

Conclusion

Facial artery pseudoaneurysm is a rare complication of facial trauma. Prompt investigation and diagnosis with timely and apt intervention is the key to the successful management of facial artery pseudoaneurysm. Surgical resection is a safe and effective treatment method and can be considered in cases of superficial swellings, failure of endovascular approach, or as in our case, non-availability of endovascular surgery resources.

Informed Consent: Informed consent was obtained from the parents of the patient.

Peer-review: Externally peer-reviewed.

Conflict of Interest: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Authorship Contributions

Conception: N.J., Design: N.J., Supervision: N.J., Materials: S.R., Data Collection and/or Processing: S.R., N.J., Analysis and/or Interpretation: S.R., N.J., Literature Review: S.R., N.J., Writing: N.J., Critical Review: S.R., N.J.

References

1. Shetty NK, Shandilya R, Pawar S, Gadre PK, Gadre K, Singh D. Management of late post-traumatic facial artery pseudoaneurysmal cyst: review of literature. J Maxillofac Oral Surg 2015; 14: 201-5. [Crossref]
2. Conner WC 3rd, Rohrich RJ, Pollock RA. Traumatic aneurysms of the face and temple: a patient report and literature review, 1644 to 1998. Ann Plast Surg 1998; 41: 321-6. [Crossref]
3. Payami A, Montazen AH. Surgical treatment of facial artery pseudoaneurysm following blunt trauma: report of a case. J Oral Maxillofac Surg 2017; 75: 362.e1-e5. [Crossref]
4. Madani M, Venznedaroglu E, Pazoki A, Danesh J, Matson SL. Pseudoaneurysm of the facial artery as a late complication of bilateral sagittal split osteotomy and facial trauma. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2010; 110: 579-84. [Crossref]

5. Choi HJ, Kim JH, Lee YM, Lee JH. Pseudoaneurysm of the facial artery after the injection of local anesthetics. J Craniofac Surg 2012; 23: 419-21. [Crossref]

6. Rogers SN, Patel M, Beirne JC, Nixon TE. Traumatic aneurysm of the maxillary artery: the role of interventional radiology. A report of two cases. Int J Oral Maxillofac Surg 1995; 24: 336-9. [Crossref]

7. Evans CC, Larson MJ, Eichhorn PJ, Taylor RS. Traumatic pseudoaneurysm of the superficial temporal artery: two cases and review of the literature. J Am Acad Dermatol 2003; 49: 286-8. [Crossref]

8. Day AT, Genther DJ, Hui F, Mydlarz WK, Griffith G, Desai SC. Successful facial artery pseudoaneurysm coiling and pedicle preservation following free tissue transfer. Am J Otolaryngol 2017; 38: 103-7. [Crossref]

9. Zachariades N, Rallis G, Papademetriou G, Papakosta V, Spanomichos G, Souelem M. Embolization for the treatment of pseudoaneurysm and transection of facial vessels. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2001; 92: 491-4. [Crossref]

10. Hassan F, Younes A, Rifai M. Endovascular embolization of post-tonsillectomy pseudoaneurysm: a single-center case series. Cardiovasc Intervent Radiol 2019; 42: 528-33. [Crossref]

Foreign Body in the Eustachian Tube: A Challenging Diagnosis and Management

Case Report

Catarina Rato, Gustavo Lopes, Delfim Duarte, Nuno Oliveira

Department of Otorhinolaryngology & Head and Neck Surgery, Hospital Pedro Hispano, Matosinhos, Portugal

Abstract

Foreign bodies in the external ear are very common. The same cannot be said about foreign bodies in the Eustachian tube (ET). We report the case of a 63-year-old woman with a history of painless left side otorrhea and hearing loss. She reported a left ear surgery when she was 30-year-old but she did not know the diagnosis that was made at that time neither the kind of surgery performed. Otoscopic examination revealed an inferior perforation of the eardrum. Audiologic evaluation demonstrated a unilateral, moderate-severe mixed hearing loss. Computed tomography scan showed, in left ear, a soft tissue density filling the middle ear cavity and a foreign body in ET. The patient underwent middle ear exploration which required endoscopic assistance to visualize and remove the foreign body. It appeared to be a stapes prothesis of Robinson type. The displacement of a stapes prosthesis to the ET has not been reported in the literature. Surgeries in this region are challenging. This case highlights the importance of the integration of endoscopy into otologic surgery.

Keywords: Eustachian tube, foreign body, stapes surgery, endoscopy, middle ear, otosclerosis

ORCID ID of the authors:
C.R. 0000-0002-0454-5759;
G.L. 0000-0003-2954-0281;
D.D. 0000-0002-2160-1599;
N.O. 0000-0002-1726-5991.

Cite this article as: *: Rato C, Lopes G, Duarte D, Oliveira N. Foreign Body in the Eustachian Tube: A Challenging Diagnosis and Management. Turk Arch Otorhinolaryngol 2021*

Corresponding Author:
Catarina Rato; catarina.rato@hotmail.com

Received Date: 05.10.2020
Accepted Date: 17.11.2020

DOI: 10.4274/tao.2020.6058

Introduction

The Eustachian tube (ET) connects the middle ear to the nasopharynx (1). Its functions include ventilation, clearance and protection (1). Middle ear diseases may be due, at least in part, to failure or inadequacy of ET function (2). Sometimes the causes for this dysfunction are relatively easy to assess by history and physical examination (2). On the other hand, rare causes, such as ET obstruction by a foreign body, are only identifiable after imaging of temporal bone (3). Minimal working space and compromised visual field make surgeries in the region of the ET challenging (3).

Case Presentation

A 63-year-old woman presented with a history of painless left side otorrhea and hearing loss. She reported a left ear surgery when she was 30-year-old but she did not know the diagnosis that was made at that time neither the kind of surgery performed. At the age of 50 years old, the patient noticed an increasing hearing loss on the left side and ipsilateral

intermittent otorrhea. Otoscopic examination revealed an inferior perforation of the eardrum with granulation tissue at the edges and inflamed middle ear mucosa. The opposite ear was normal.

Pure tone audiometry demonstrated a moderate to severe left mixed hearing loss, with a 30 dB air-bone gap (Figure 1).

Computed tomography (CT) showed, in left ear, the presence of fluid and mucus in the mastoid air cells and a soft tissue density material occupying partially the middle ear cavity encasing the auditory ossicles without visible stapes. It also reported an incidental metallic foreign body with an intensity of 3,000 HU located at 3.5 mm from the ET opening in the middle ear and measuring 3.2x3.0 mm in size (Figure 2). In the right ear, there was also some fluid and mucus in the mastoid air cells but without any bone changes or associated ossicular chain abnormalities.

The diagnosis of foreign body in the ET associated with a chronic otitis media was made and surgical treatment was discussed with the patient, who consented a retroauricular exploratory tympanotomy.

First, with microscopic approach, the tympanomeatal flap was elevated and the middle ear was explored. Absence of the stapes and eroded incus were observed. After many unsuccessful attempts with microscope, it was only possible to see the foreign body in the ET thanks to the use of a 4 mm 30º endoscope (Figure 3A and 3B). The ET is not easily accessible with routine otological instruments. Removal of the foreign body was possible with the help of a fine curved pick (Figure 3C, 3D and 3E). It seemed to be a stapes prothesis of Robinson type made of metal wire and fluoroplastic (Figure 3F). The ET was found patent. A cartilage and perichondrium graft was used for tympanic membrane reconstruction.

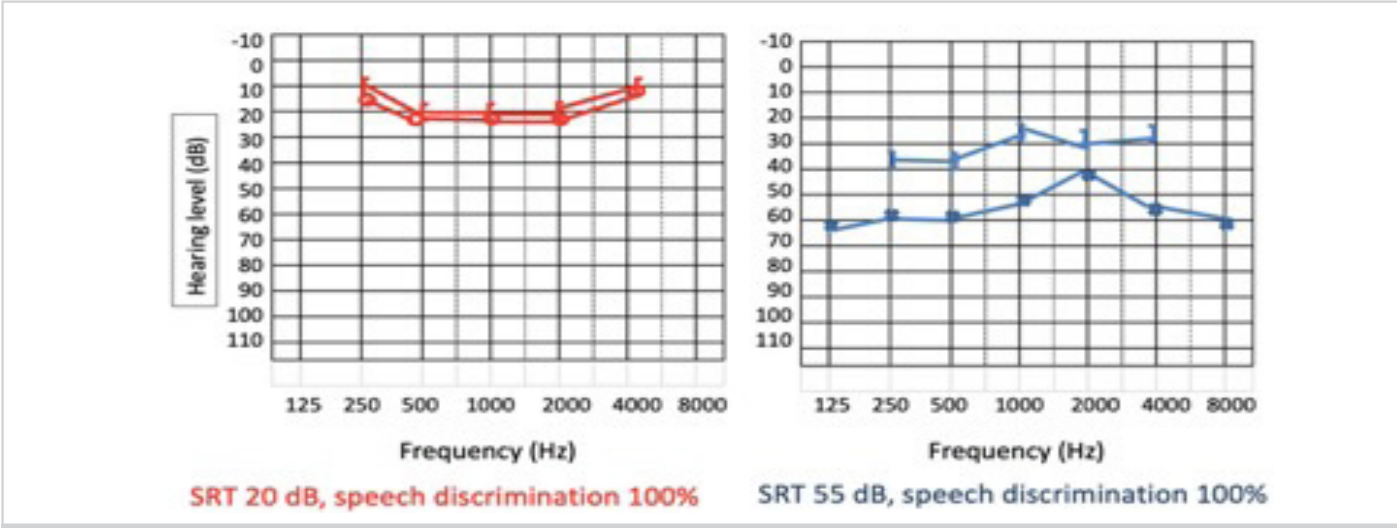


Figure 1. Audiogram before surgery
SRT: Speech reception threshold

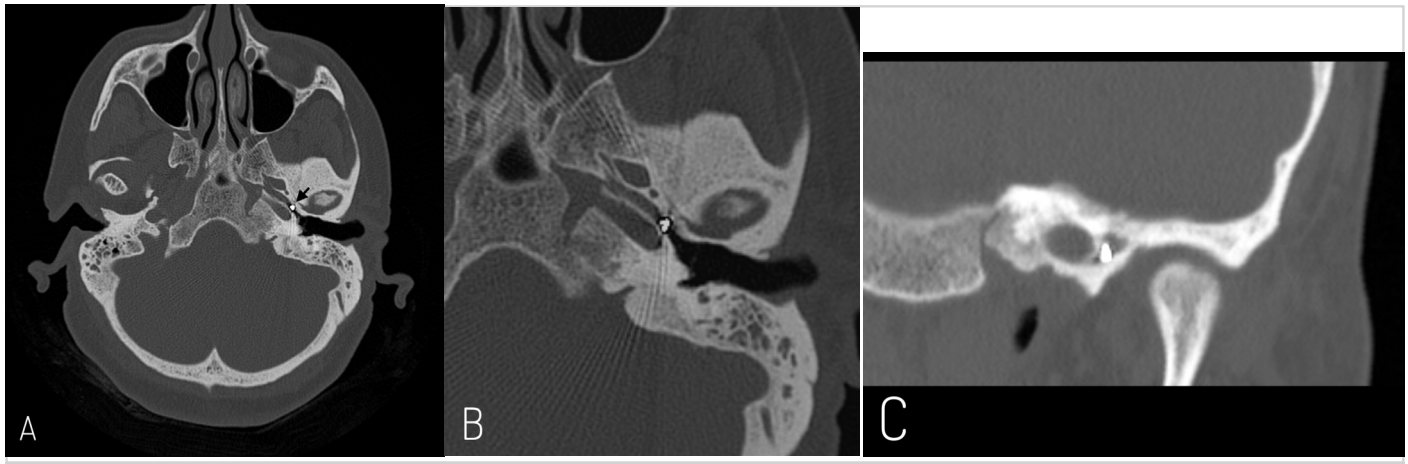


Figure 2. Computed tomography scan, temporal bones. Axial section (A) showing a foreign body in left Eustachian tube (arrow). Magnified axial (B) and coronal (C) sections demonstrating the proximity to the carotid artery

The patient recovered well with resolution of chronic otitis media. After one year of follow-up, the tympanic membrane is intact and preoperative hearing level is stable. The options for management of hearing loss, revision stapes surgery or conventional hearing aids were considered with the patient. However, to this date, she deferred any further surgical intervention.

Discussion

This case illustrates several interesting dilemmas. The similarity between the removed foreign body and a Robinson stapes prosthesis suggests that the surgery that patient underwent when she was 30-year-old was a stapes surgery. Probably, the displacement of the prothesis, followed by medial migration and obstruction of the ET, led to the development of chronic otitis media. However, there is no way to confirm the sequence of these events.

One of the most frequent complication of stapes surgery is the partial or total displacement of the prothesis (4). This finding has been correlated with erosion or fracture of incus long process (4). Nevertheless, in this case, it is also difficult to confirm if the incus erosion happened first or if was a consequence of chronic otitis media.

There are reports of stapes protheses extruded into the external ear canal (5). However, in this patient, there seems to have been a medial migration. Perhaps this can be explained by the clearance function of the ET. To our knowledge, this is the first report of a stapes prothesis dislocation to ET.

Another interesting aspect revolves around the difficulties of surgeries in ET region. Although endoscopic assistance was not initially planned, it was essential to visualize and remove the foreign body. Traditionally, with microscope approach, the presence of a foreign body in the ET require an extra dissection to increase the working space and vision (3, 6). Endoscopic ear surgery, with its wide field of view, permits to preserve the normal anatomy as much as possible and to complete more tasks transcanal (7), which may be, in the future, the preferred initial approach in similar cases.

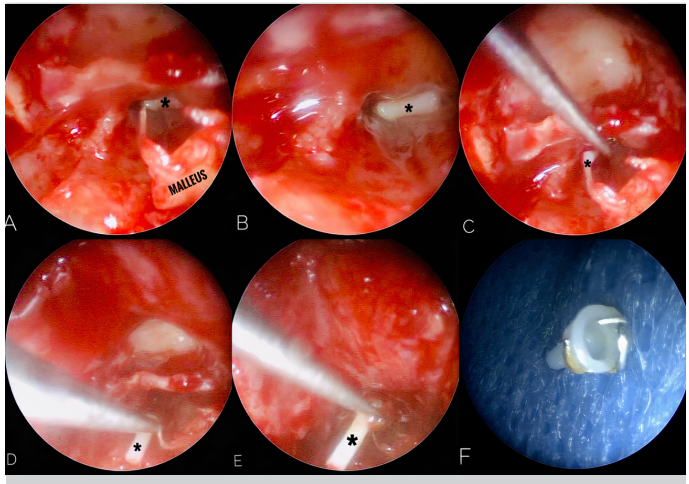


Figure 3. Intraoperative endoscopic findings. Only with endoscopic assistance was possible to see the foreign body (asterisk) (A and B). A fine curved pick was introduced into the left Eustachian tube orifice (C) and the foreign body was mobilized (C and D) and removed (E). It seemed to be a stapes prothesis of Robinson type made of metal wire and fluroplastic (F)

There have been reports of foreign bodies in the ET causing erosion of the carotid canal (8). The surgeon must keep in mind that the internal carotid artery lurks closely behind the bony wall (1). Although it might be easier to see the foreign body with the help of the endoscope, it can be difficult to manipulate with conventional instruments. Already available angled endoscopic ear instruments might be useful (3). There are many cases in which the foreign body tends to become displaced deeper (3). In cases where it is not possible to remove the foreign body, Parelkar et al. (6) propose to leave it and fashion a graft which would ventilate the middle ear.

Despite the concern regarding the possibility of a scar in ET being itself also a cause for its dysfunction, in this case, the repair of tympanic membrane was attempted with success. The replacement of stapes prothesis was not performed at the same surgical time to reduce the bacterial content of middle ear before opening the vestibule.

Conclusion

Foreign bodies can be one of the causes of ET dysfunction. Performing a CT scan may aid not only in surgical approach but also reveal unexpected and diagnostic findings. We report a very rare case of a stapes prothesis as an ET foreign body. Endoscopic, minimally invasive, and atraumatic techniques are recommended in surgeries in ET region.

Informed Consent: Informed consent was obtained from the patient.

Peer-review: Externally peer-reviewed.

Conflict of Interest: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Authorship Contributions

Conception: C.R., Design: CR, Supervision: G.L., D.D., N.O., Writing: C.R., Critical Review: N.O.

References

1. Luers JC, Hüttenbrink KB. Surgical anatomy and pathology of the middle ear. J Anat 2016; 228: 338-53. [Crossref]

2. Ars B, Dirckx J. Eustachian tube function. Otolaryngol Clin North Am 2016; 49: 1121-33. [Crossref]
3. Igarashi K, Matsumoto Y, Kakigi A. Acupressure bead in the Eustachian tube. J Acupunct Meridian Stud 2015; 8: 200-2. [Crossref]
4. Puxeddu R, Ledda GP, Pelagatti CL, Salis G, Agus G, Puxeddu P. Revision stapes surgery for recurrent transmissional hearing loss after stapedectomy and stapedotomy for otosclerosis. Acta Otorhinolaryngol Ital 2005; 25: 347-52. [Crossref]
5. Wilkinson EP, House JW. Extruding stapes prosthesis. Ear Nose Throat J 2009; 88: 718. [Crossref]
6. Parelkar K, Shere D, Wallic A, Dave V, Rao K. Impacted incus foreign body in the Eustachian tube. Iran J Otorhinolaryngol 2019; 31: 123-6. [Crossref]
7. Pollak N. Endoscopic and minimally-invasive ear surgery: A path to better outcomes. World J Otorhinolaryngol Head Neck Surg 2017; 3: 129-35. [Crossref]
8. Ribeiro FD. Foreign body in the Eustachian tube-case presentation and technique used for removal. Braz J Otorhinolaryngol 2008; 74: 137-42. [Crossref]

Congenital Mucocele of the Nasal Dorsum: A Case Report

Case Report

Seçil Bahar Dal, Ömer Faruk Ünal

Department of Otorhinolaryngology, Vehbi Koç Foundation American Hospital, İstanbul, Turkey

Abstract

Congenital nasal dorsum cysts are very rare lesions. Its differential diagnosis lies between gliomas, dermoid cysts and encephaloceles. We present a case of solitary congenital external nasal cyst with no intranasal fistulous tract connection in a newborn. Histopathologic analysis of the mass demonstrated findings consistent with an external mucocele. Total excision with external open approach provided the cure with good cosmetic outcome. This is the first report presenting an external mucocele in a newborn in the literature. External mucoceles should be kept in mind in the differential diagnosis of congenital nasal dorsum masses.

Keywords: Nasal dorsum, mucocele, congenital, cyst, newborn, pediatric otorhinolaryngology

ORCID ID of the authors:

S.B.D. 0000-0003-3005-3595;
Ö.F.Ü. 0000-0001-5692-2475.

Cite this article as: *Bahar Dal S, Ünal ÖF. Congenital Mucocele of the Nasal Dorsum: A Case Report. Turk Arch Otorhinolaryngol 2021; 59(1): 84-7.*

Corresponding Author:
Seçil Bahar Dal; drsecilbahar@gmail.com

Received Date: 21.12.2020
Accepted Date: 01.02.2021

DOI: 10.4274/tao.2021.6209

Introduction

Congenital nasal dorsal masses are rare, but mostly well-known pathologies. Differential diagnosis of these nasal lesions includes nasal dermoid cysts, gliomas and encephaloceles (1).

In this article we report the case of a newborn with a congenital external mucocele located on the tip of the nose. To the best of our knowledge, such a malformation in a newborn has not been described in the literature to date.

Case Presentation

A one-month-old male baby was observed to have a lesion on his nose at birth. The 2x2 cm, cystic and round shaped mass was located on the tip of the nose (Figure 1).

Magnetic resonance imaging (MRI) showed a well-circumscribed, T2 hyperintense, homogeneous cystic mass on the tip of the nose with no evidence of any fistulous tract into the cranial or nasal cavity (Figure 2).

Direct open approach with an alar rim incision was used to remove the cyst. The

cyst was just under the skin without any connection to the cartilages of the nasal dorsum (Figure 3). We did not observe any connection between the cyst and the nasal cavity during the operation.

Histopathologic examination revealed an external mucocele composed mainly of ciliated epithelium and regions of focal pseudostratified columnar epithelium without lymphoid tissue, seromucous gland, goblet cell, or crypt. Pressure atrophy caused by fluid accumulation was observed in the epithelial lining of the cyst (Figure 4 A,B).

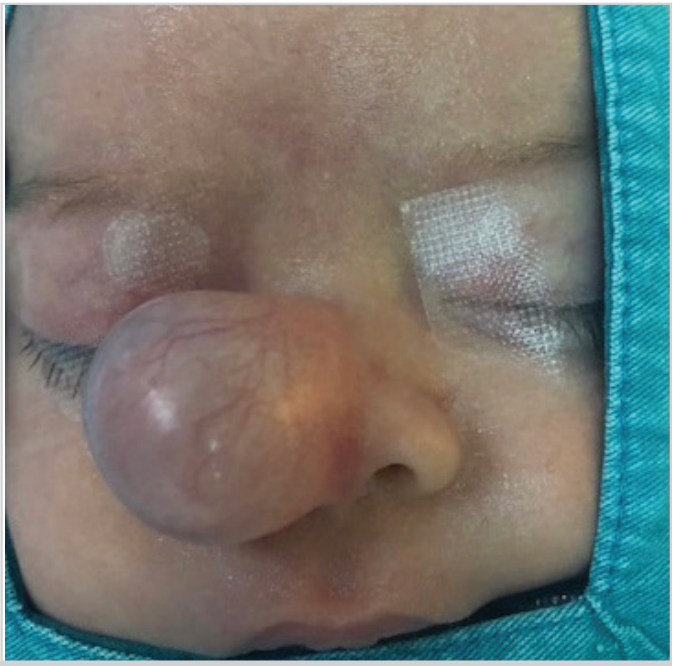


Figure 1. Preoperative view of the patient

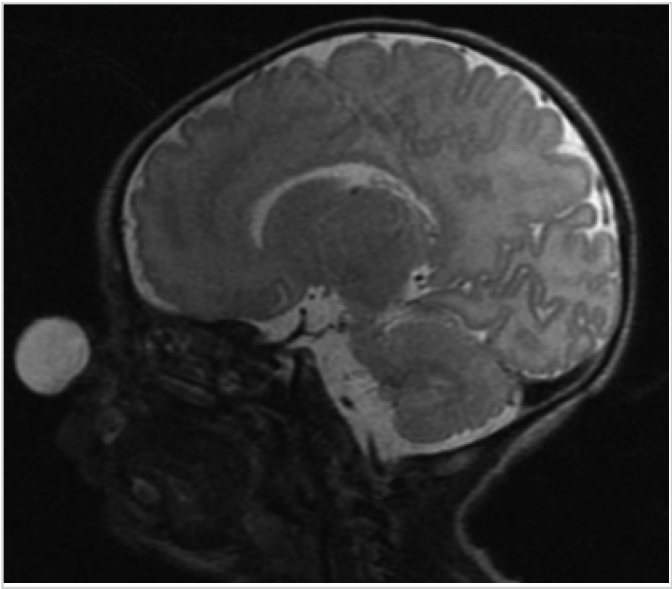


Figure 2. Sagittal T2 MRI view of the lesion
MRI: Magnetic resonance imaging

The tip of the nose was packed for two days after the operation. There was no complication during or after the operation. The patient's appearance one month after the

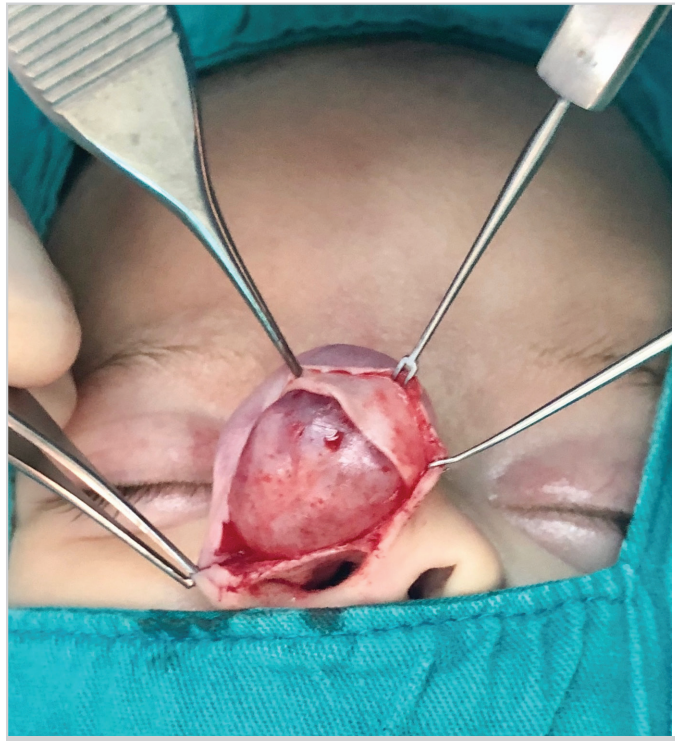


Figure 3. Intraoperative view of the nasal dorsal mass, showing the mucous cyst being dissected from the overlying skin

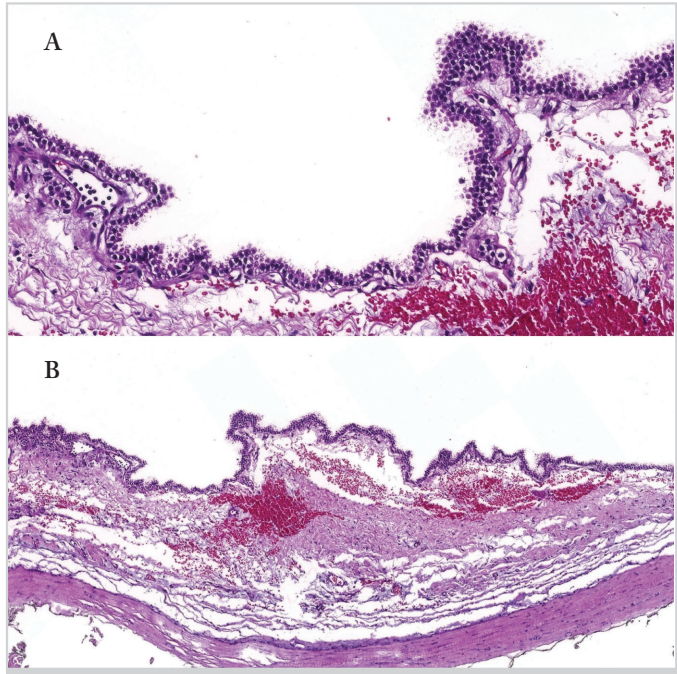


Figure 4 A, B. Histopathologic examination revealed an external mucocele, lined mainly with ciliated epithelium and the regions of focal pseudostratified columnar epithelium (Figure A x72 magnification with 3DHISTECH Case Viewer and Figure B x20 magnification with 3DHISTECH Case Viewer)

operation is shown in Figure 5. We did not observe any recurrence in a six-month follow-up period.

Informed consent was taken from the father of the patient for publication.

Discussion

Mucus retention cysts, benign skin adnexal tumors, cholesterol granulomas, dermoid and epidermoid cysts and encephalocele are included in the differential diagnosis of a nasal mucocele (2-4).

After detailed histopathological examination, presented case was diagnosed as an external mucocele. Histopathologically, the most similar lesions to our case are the cyst formations following rhinoplasty. The sites of these cysts vary from the glabellar region to the tip of the nose and the paranasal sinuses. Herniation of the mucosa, interposition or inoculation of the nasal mucosa are supposed to be the most accepted explanations of this entity (3, 5).

Similarly, in our case, proliferation of the cells in an ectopic mucous membrane island seems to be an acceptable theory of etiology. Occlusion of sebaceous glands, as reported by Rettinger and Steininger (6), can also lead to such mucous cysts.

Figure 5. Postoperative first month view of the patient

Comprehensive physical examination is important for diagnosis. Also, preoperative imaging of nasal congenital lesions is an essential tool to confirm the diagnosis. It is important to bear in mind intracranial extension of intranasal masses. Understanding the extent of the lesion with MRI will help to tailor the surgical approach, hence completely excise the lesion and prevent recurrences. In this type of lesions, it is also important to remove the cyst and the fistulous pathway in the same session to avoid possible infectious complications (1,7).

Given the risks of exposure to radiation, computed tomography scanning is not always necessary for diagnosis in young children, as in our case, when MRI findings provide adequate preoperative information. In patients with uncertain MRI findings or when further bone anatomy evaluation is needed, computed tomography scan can also be performed (7). MRI findings were consistent with intraoperative findings and we did not observe any fistulous tract extensions of the cystic mass in the presented case.

The treatment of choice is complete excision with intact capsule. For similar nasal masses, open or closed rhinoplasty approach, endoscopic excision or direct excision with external skin incision can be preferred (3, 7). Considering the location of the cyst we preferred a direct external open approach, which provided a wide exposure allowing a safe surgical excision and a relatively good aesthetic result.

Acknowledgements

The authors gratefully acknowledge Prof. Önder Peker, PhD (Department of Pathology, American Hospital, İstanbul) for his detailed histopathologic examination.

Informed Consent: Informed consent was taken from the parents of the patient for publication.

Peer-review: Externally peer-reviewed.

Conflict of Interest: The authors declare no conflicts of interest.

Financial Disclosure: There was no financial support.

Authorship Contributions: Conception: S.B.D., Ö.F.Ü., Design: S.B.D., Ö.F.Ü., Supervision: S.B.D., Ö.F.Ü., Funding: S.B.D., Materials: S.B.D., Data Collection and/or Processing: S.B.D., Analysis and/or Interpretation: S.B.D., Literature Review: S.B.D., Writing: S.B.D., Critical Review: S.B.D., Ö.F.Ü.

Main Points

- Nasal dorsum cyst in a newborn is a rare lesion.
- Nasal dermoid and epidermoid cysts, gliomas, encephaloceles, benign skin adnexal tumor and cholesterol granulomas are well-known lesions in differential diagnosis.
- In patients with congenital nasal masses preoperative radiologic examination is crucial for differential diagnosis and for determining the extension of the lesion and the appropriate surgical planning.
- External mucoceles of the nasal dorsum are cyst formations that have been reported following rhinoplasty. However, external mucocele formations in the nasal dorsum can also occur as congenital lesions.

References

1. Vora N, Kalagiri R, Guillory B, Shetty A, Raju VN, Powitzky RK, et al. Congenital midline nasal anomalies. Proc (Bayl Univ Med Cent) 2017; 30: 459-60. [Crossref]
2. Dionyssopoulos A, Nikolis A, Papaconstantinou A, Kakas P, Miliaras D, Kekes G. Mucous cysts of the nose: a postrhinoplasty complication? A long-term follow-up. Ann Plast Surg 2010; 64: 381-4. [Crossref]
3. Romo T 3rd, Rizk SS, Suh GD. Mucous cyst formation after rhinoplasty. Arch Facial Plast Surg 1999; 1: 208-11. [Crossref]
4. Topdag M, Iseri M, Sari F, Erdogan S, Keskin IG. Paranasal sinus mucoceles: our clinical experiments. Int J Clin Exp Med 2015; 8: 18518-22. [Crossref]
5. Pausch NC, Bertolini J, Hemprich A, Hierl T. Inclusion mucous cysts of the nose: a late complication septorhinoplasty in two cleft lip patients. Cleft Palate Craniofac J 2010; 47: 668-72. [Crossref]
6. Rettinger G, Steininger H. Lipogranulomas as complications of septorhinoplasty. Arch Otolaryngol Head Neck Surg 1997; 123: 809-14. [Crossref]
7. Herrington H, Adil E, Moritz E, Robson C, Perez-Atayde A, Proctor M, et al. Update on current evaluation and management of pediatric nasal dermoid. Laryngoscope 2016; 126: 2151-60. [Crossref]