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Investigation of the Protective Efficacy of Intratympanic Dexamethasone and Nimodipine on Cisplatin Ototoxicity in a Rat Model

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Objective: To investigate and compare the levels of efficacy of dexamethasone and nimodipine that are known for their neuroprotective properties on cisplatin ototoxicity in a rat model.
Methods: The study included 24 male Wistar Albino rats that generated distortion product otoacoustic emission (DPOAE) response. The rats were randomized into three groups. Group 1 (n=8) was taken as the Control Group and administered intraperitoneal cisplatin at a dose of 5 mg/kg on days 1, 3 and 5, adding to a cumulative dose of 15 mg/kg in total. Afterwards, intratympanic saline solution of 0.1-0.3 ml was administered on days 5, 10 and 15. In Group 2 (n=8) the same cisplatin protocol was used followed by intratympanic dexamethasone administered on days 5, 10 and 15 at a dose of 0.1-0.3 ml. In Group 3 (n=8) the same cisplatin protocol was used followed by intratympanic nimodipine administered on days 5, 10 and 15 at a dose of 0.1-0.3 mL. In all groups DPOAE was measured before (Day 1) and after (Day 5) cisplatin administration and after intratympanic treatment (Day 20). After the final measurement all rats were sacrificed and histopathologically examined. The study complied with the guidelines for the care and utilization of animals set forth by the Declaration of Helsinki.
Results: Cisplatin have caused hearing loss at all frequencies, with more significance at higher frequencies ($p<0.005$). In the group that received intratympanic nimodipine, improvement was identified in the mean emission levels at 4000, 6000 and 8000 Hz. The improvement at 8000 Hz was found statistically significant compared to the control group ($p<0.005$). In the group that received intratympanic dexamethasone, improvement was seen in the mean emission levels at 1500, 3000, 4000, 6000 and 8000 Hz. The improvement levels at 6000 Hz and 8000 Hz were found statistically significant compared to the control group ($p<0.005$). When the efficacy outcomes of intratympanic nimodipine and dexamethasone were compared, the improvement in the dexamethasone group at 8000 Hz was found significant. Comparison of all groups for degeneration and TUNEL staining showed that the control group which was given cisplatin + saline solution had the highest level of degeneration and apoptotic cells. It was concluded that dexamethasone was the best application in terms of degenerative changes as well as in reducing apoptotic cells.
Conclusion: Evaluation of DPOAE and histologic data showed that dexamethasone and nimodipine were autoprotective in rats which autotoxicity was induced by cisplatin. Our study is the first to demonstrate that nimodipine, both histologically and at high frequencies, has a significant healing effect, albeit less than dexamethasone. Accordingly, further experimental and clinical studies are needed on this subject.
Keywords: Ototoxicity, cisplatin, protective agent, nimodipine, dexamethasone

Reverse Nystagmus and its Effect on Prognosis in Posterior Canal Benign Paroxysmal Positional Vertigo

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Objective: To investigate the incidence of reverse nystagmus seen in seated position, which is the second step in the Dix-Hallpike maneuver, in posterior canal BPPV, and to explore its correlation with the canalith repositioning procedure (Epley maneuver).
Methods: Records of 5,651 patients who underwent the videonystagmography test in a tertiary hospital between October 2016 and March 2019 were examined. Video recordings of 321 patients with posterior canal BPPV were scrutinized and the data obtained were analyzed.
Results: Reverse nystagmus was observed in 85% of the posterior canal BPPV patients. The number of canalith repositioning maneuvers required for treatment in patients with reverse nystagmus (1.32±0.68) was found to be less than that required in patients without reverse nystagmus (1.81±0.98) ($p<0.001$). Reverse nystagmus was not associated with recurrence ($p=0.623$).
Conclusion: The absence of reverse nystagmus in seated position in the Dix-Hallpike test predicts that the therapeutic success of the maneuver in posterior canal BPPV will be low and repeated applications would be necessary to achieve successful outcome.
Keywords: Benign paroxysmal positional vertigo, posterior semicircular canal, Dix-Hallpike test, nystagmus, prognosis

Correlation between Olfactory Function and Acoustic Rhinometry and Eye Dryness Results in Patients with Primary Sjögren's Syndrome

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Objective: Primary Sjögren's Syndrome (pSS) is a chronic autoimmune connective tissue disease characterized by the lymphocytic infiltration of the exocrine glands, mainly of the salivary and lacrimal glands Olfactory dysfunction is a major symptom that impairs the life quality of patients. This study aimed to assess olfactory functions in patients with pSS and to analyze the results for a correlation with acoustic rhinometry and eye dryness.

Methods: Thirty-eight pSS patients and 20 healthy individuals were included in the study. Patient and control groups were evaluated by acoustic rhinometry, the Connecticut Chemosensory Clinical Research Center Test (CCCRC), and the VAS score. Dry eye findings were evaluated with the Schirmer's test and the tear breakup time (TBUT) test.
Results: Mean CCCRC score, as well as subjective olfactory detection, olfactory identification and olfactory detection threshold levels were significantly lower in the patient group ($p<0.001$). Acoustic rhinometry scores right VOL2 ($p=0.001$), right TVOL ($p=0.001$) and MCA2 ($p=0.004$) were found to be significantly low in the patient group. A positive correlation was identified among the Schirmer's test and the TBUT test and all olfactory function tests ($p<0.001$).
Conclusion: In the olfactory function tests of pSS patients, olfactory detection threshold, olfactory identification and mean CCCRC scores were found to be significantly low and these results were positively correlated with eye dryness. Basing on these results, it was concluded that the dryness caused by pSS in the nasal mucosa could impair the olfactory function by preventing scent molecules from coming into contact with the mucus, hence reaching the olfactory epithelium.
Keywords: Sjögren's syndrome, olfaction, acoustic rhinometryi dry eye syndrome

Evaluation of the Effects of Platelet-Rich Fibrin Prepared in Titanium Tube on Regeneration in Acute Damage of the Facial Nerve in Rabbits

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Objective: Damage of the facial nerve (FN) is a common outcome after a trauma and resulting functional problems have an adverse effect on the quality of life. Despite the various surgical techniques, it is difficult to completely correct the condition and additional treatment methods are needed to enhance recovery. This study aimed to investigate the efficacy of platelet-rich fibrin prepared in titanium tube (T-PRF) as an agent enhancing healing in full-thickness cut wounds of the facial nerve.
Methods: Twenty-seven New Zealand rabbits were used in the study. The rabbits were divided into three experimental groups, the Sham group (Group 1), the Suture group (Group 2), and the Suture + T-PRF group (Group 3), and the study was performed on the right facial nerves of rabbits. The number of subjects in the three groups were determined as 7-10-10 respectively; however, two subjects from each of Groups 1 and 2 died during the study and the experiment was completed with 5, 8 and 10 subjects. In the Sham group, the facial nerve trunk was dissected from the surrounding tissues and the skin was closed without further surgical intervention. In the Suture group, a full-thickness incision was made on the facial nerve trunk and the nerve endings were anastomosed with suture. In the Suture + T-PRF group, a full-thickness incision was made on the facial nerve trunk. After the nerve endings were anastomosed with suture, the T-PRF membrane was wrapped around the damaged area. Following the operation all subjects were weekly monitored for corneal reflex, vibrissae movement and lowered ear. Bilateral facial electromyography (fEMG) was performed before the operation and in the 1st, 3rd, 5th, 7th and 10th weeks after the operation, and tissues were harvested for histopathologic examination in the 10th week. Intra- and inter-group comparisons were performed.
Results: In functional evaluation, the results of the Sham group were consistently found significantly better than those of the Suture and Suture + T-PRF groups. Although improvement was seen in the corneal reflex of the Suture and Suture + T-PRF groups compared to the initial postoperative weeks, no significant differences were observed between the two groups in terms of corneal reflex in weekly follow-ups. In the Suture + T-PRF group, noticeable vibrissae movement was observed in the eighth week, one week earlier than the Suture group. While lowered ears recovered in the seventh week in the Suture group, this recovery was observed two weeks earlier, in the fifth week in the Suture + T-PRF group. In electrophysiologic evaluation, compound muscle action potential (CMAP) maximum amplitude levels and CMAP amplitude levels triggered by supra threshold stimuli were found significantly low in the Suture and Suture + T - PRF groups after the injury, however, recovered over time. In the Suture + T-PRF group, CMAP maximum amplitude levels were significantly lower compared both to their own preoperative levels and to those of the Sham group in all weeks. Nerve conduction rates did not significantly differ among the groups in the weeks before and after the injury. The nerve stimulation threshold required to trigger CMAP significantly increased after the surgery in the Suture + T-PRF group compared to their preoperative control levels. In the Suture + T-PRF group these levels regressed two weeks earlier than those of the Suture group, reaching levels comparable to the preoperative levels in the fifth week. In histopathologic examination, the Sham group had significantly better results than the two other groups. While less edema and vacuolization were observed in the Suture + T-PRF group compared to the Suture group, the difference was not statistically significant. Myelin sheath thickness did not significantly differ between these two groups.
Conclusion: In our study, T-PRF application partially accelerated functional recovery, but did not contribute to nerve conduction rates, CMAP maximum amplitude levels and CMAP amplitude levels triggered by supra threshold stimuli. It was observed, however, that it contributed to an earlier recovery in the supra threshold stimuli levels required to trigger CMAP. It was seen to tend to reduce edema and vacuolization, and no contribution to myelin sheath thickness. Further, longer-term follow-up studies should be carried out to better assess the effects of T-PRF on nerve rehabilitation.
Keywords: Facial nerve, facial paralysis, platelet-rich fibrin, nerve regeneration

Can the Proteoglycan Decorin Be a Promising New Agent for Facial Nerve Regeneration? An Experimental Study

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Objective: To investigate the effect of systemically administered decorin (DC) on facial nerve regeneration.
Methods: Thirty-two female albino Wistar rats underwent nerve axotomy and neurorrhaphy. The rats were separated into four groups: Control, Sham, DC alone, and bilateral facial nerve neurorrhaphy (B-FNN) + DC. Nerve transmission measurements were performed before and in the 1st, 3rd, 5th and 7th weeks after the operation. Amplitude and latency levels of compound muscle action potentials (CMAPs) were recorded. The harvested facial nerve sections were examined under a light microscope and by immunohistochemical staining. Nerve and axon diameters, number of axons in the nerve, H-score, Schwann cell proliferation, and myelin and axon degenerations were quantitatively recorded.
Results: In the postoperative third and fifth weeks, amplitude levels were significantly lower in the Sham group compared to the B-FNN + DC group ($p=0.05$). Compared to the Control group, nerve diameters were found to be significantly larger in the Sham, DC and B-FNN + DC groups ($p<0.05$). Compared to the Sham group, the number axons in the nerve, axon diameters and H-scores were significantly higher in the Control, DC and B-FNN + DC groups ($p<0.05$). Compared to the Sham group, Schwann cell proliferation, myelin degeneration and axon degeneration scores were significantly lower in the Control, DC and B-FNN + DC groups ($p<0.05$).
Conclusion: Electrophysiologic evaluation and histopathologic examination results demonstrate the potential benefits of decorin in facial nerve regeneration. In the light of these results, it is concluded that decorin can enhance facial nerve regeneration.
Keywords: Facial nerve, axotomy, neurorrhaphy, compound muscle action potential, nerve regeneration, decorin

Nickel Oxide Nano-Coated Pressure Equalization Tubes Reduce Biofilm Formation Associated with Otopathogenic Bacterial Strains

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Objective: Pressure equalization tubes (PETs) play a major role in the treatment of chronic otitis media with effusion (cOME), yet with some significant complications. These primarily include (i) development of otorrhea, (ii) tympanic membrane perforation, (iii) structural changes in the tympanic membrane (e.g., granulation formation, development of atrophy and myringosclerosis), (iv) early excretion, and (v) lumen occlusion. Today, it is known that the major cause of these complications seen in PETs is the development of bacterial biofilm on the material. The aim of this study was to investigate two different metal oxides (Nickel Oxide [NiO] and Zinc Oxide [ZnO]) that potentially minimize bacterial adhesion and thereby bacterial biofilm formation on the surface of the material, and produce nanoparticle-coated PET prototypes, and to comparatively analyze the microbiologic characteristics of the produced PETs along with the changes in biofilm formation.
Methods: Otopathogenic bacteria cultures that were procured for the study (*Staphylococcus aureus* XIX [ATCC®25923™], *Pseudomonas aeruginosa* [ATCC®19142™], *Moraxella catarrhalis* [ATCC®43617™], *Staphylococcus aureus* [ATCC®BAA-40™], *Staphylococcus aureus* [ATCC®33592™] and *Pseudomonas aeruginosa* GFP [ATCC®10145GFP™]) were revived. The antibacterial properties of metal oxide nanoparticles against otopathogenic bacteria were examined with the agar disk-diffusion method and the agar well diffusion method. Pressure equalization tubes were coated with metal oxide nanoparticles using a vacuum cushion system. In order to optimize biofilm formation on the pressure equalization tubes under in vitro conditions, first a method was defined for the count of bacteria in the inoculum, the incubation period and for removing the biofilm off the surface. This enabled the quantitative examination of biofilm formation. Further, PET surfaces were visualized with a scanning electron microscope (SEM) and a laser confocal scanning microscopy (LCSM). Finally, images from the LCSM were analyzed via the COMSTAT program, biofilm density on the inner surface of the PET was measured and comparative analyses were made.
Results: While the antibacterial properties of the metal oxide nanoparticles could not be determined with the agar disk-diffusion method, the agar well diffusion method has shown that NiO and ZnO have antibacterial properties against *Staphylococcus aureus* and *Pseudomonas aeruginosa*. Both of the metal oxide nanoparticles were demonstrated to successfully coat the PET surface. Biofilm was created on the 4th day after otopathogenic strains were used on the metal oxide nanoparticles coated PETs. Analysis of the quantitative measurements of the biofilm found a significant decrease, compared to the Control group, only in the number of live bacteria on the biofilm produced by the *Staphylococcus aureus* (ATCC®33592™). Further, analysis of the images from the LCSM demonstrated a significant decrease in the biomass of the biofilm on the NiO coated inner surface of the PET.

Conclusion: As a first in the literature, this study has successfully produced the prototypes of PETs coated with different metal oxide nanoparticles and examined in detail the microbiological characteristics and their roles in minimizing biofilm formation. The results of this pioneering and first-of-its-kind scientific study have demonstrated that NiO, with its antibacterial properties and particularly with its potential to reduce the amount of biofilm formation on both the inner and outer surface of PETs, can contribute to reducing complications caused by biofilm formation on PETs and comes forth as a promising coating material to be used in PET production.
Keywords: Pressure equalization tube, biofilm, otopathogenic bacteria, otitis media with effusion

Assessment of the Effects of Submucosal PRP Injection on Wound Healing Following Functional Endoscopic Sinus Surgery: An Experimental Study

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Objective: To explore the effects of platelet-rich plasma (PRP) injection on wound healing following endoscopic sinus surgery.
Methods: Twenty-four white New Zealand rabbits were separated into three groups of eight. Endonasal surgery was performed in all three groups. To mimic surgery, damage was endoscopically inflicted in the mucosa of the ventral conchae with a 3-mm punch forceps. After this procedure Group 1 (PRP group) was injected with submucosal PRP, Group 2 (saline group) was injected with submucosal saline. Group 3 (control group) did not receive any injections. Fourteen days after the surgical procedure the subjects were sacrificed and all mucosae of the three groups were histopathologically examined (for epithelial and subepithelial thickness, neutrophil, ciliary body and goblet cell counts, and collagen density), and measured for wet tissue hydroxyproline levels.
Results: Neutrophil and goblet cell counts, and collagen density were significantly lower in the PRP group compared to the control group. Ciliary and goblet cell counts, and collagen density were significantly lower in the PRP group compared to the Saline Group. In histopathologic analysis, no significant differences were observed between saline and control groups for any of the parameters. Measurement of hydroxyproline levels in wet tissue was statistically lower in the PRP group compared to the saline and the control groups.
Conclusion: Further to the positive effects of PRP shown in human and animal studies reported in the literature, our study also found PRP to have positive effects on healing in the nasal mucosa. Our study showed that PRP has anti-inflammatory and mucus softening effects on damaged nasal mucosa and is effective in reducing the formation of synechia by reducing collagen density. Also the results suggested that submucosal injection of PRP after endonasal surgery is an effective application for preserving nasal physiology.
Keywords: Endoscopic sinus surgery, platelet-rich plasma, wound healing, experimental study

Investigating the Effects of Cross-Linked Hyaluronic Acid on the Inner Ear in a Vestibular and Cochlear Toxicity Model

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Objective: Cross-linked hyaluronic acid polymers are among the molecules that are being increasingly used in similar fields. In our study we aimed to investigate the effects of the cross-linked hyaluronan molecule on the inner ear in a vestibulotoxicity and ototoxicity model that was experimentally created in rats using Gentamicin.
Methods: Thirty-two male Wistar rats weighing about 200-250 g were obtained from the Animal Experimentation and Research Laboratory of the Dokuz Eylül University. Twenty-eight rats were divided into four groups, including the Control Group. All animals were free to reach food and water in the course of the study. Multi-dose intratympanic injections were given to all rats (including the seven rats of control group) of the four groups for seven days. After the appropriate size speculum was placed in the external auditory canal, the drug was intratympanically injected so as to fill the tympanic cavity (approximately 0.06 mL) with a tuberculin syringe and 28-gauge needle (0.40x38 mm) under microscopic view provided by an operating microscope. Rats in Group 1 received 0.06 mL of physiological saline solution (PSS Group), rats in Group 2 received 0.06 ml of cross-linked hyaluronic acid, rats in Group 3 received 0.06 mL of gentamicin at a concentration of 13.33 mg/mL, and rats in Group 4 received a mixture of 0.03 mL gentamicin + 0.03 mL cross-linked hyaluronic acid at a concentration of 26.66 mg/mL intratympanically for seven days.
Results: Higher hearing thresholds were achieved at all frequencies in the Gentamicin Group compared to the PSS Group. In the Hyaluronic acid + Gentamicin Group, hearing thresholds were found better compared to the Gentamicin Group. On the other hand, while the Gentamicin Group had the highest exposure score in behavioral tests, the Hyaluronic Acid Group remained close to the score of the Control Group.

Conclusion: According to the results of our study, cross-linked hyaluronic acid may have anti-inflammatory, regeneration-enhancing, antioxidant properties. Although it does not have a toxic effect on the middle and inner ears, it may cause temporary conductive hearing loss due to its viscous structure. In the group which cross-linked hyaluronic acid was administered in combination with gentamicin, it was seen to reduce ototoxicity after the 7th day. Behavioral test battery examinations also showed a protective effect without a toxic effect on the cochlea and the vestibule. As shown in in vitro studies, there was no evidence to support a prolonged release function with the target agent in the combination group.
Keywords: Gentamicin, hyaluronic acid, ototoxicity, vestibulotoxicity

Comparison of Systemic and Intranasal BCG Treatment in Experimental Allergic Rhinitis-Induced Rats

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Objective: To investigate the efficacy of intranasally (topical) and systemically Bacillus Calmette-Guerin (BCG) in the treatment of allergic rhinitis in an allergic rhinitis model.
Methods: All rats included in the study were divided into six groups. Each group had seven animals. Group A, was the Control Group, Group B included allergic rhinitis-induced rats, Group C included topical BCG treated ones, Group D included systemic BCG treated ones, Group E consisted of rats with allergic rhinitis treated with intranasal BCG and Group F had rats with allergic rhinitis which treated with systemic BCG. Study groups B, E, F were administered intraperitoneal ovalbumin every other day for 14 days to induce allergic rhinitis. As of the 15th day, these ones were provoked with a daily dose of intranasal ovalbumin for 15 days. As of the 15th day, Group E was given intranasal BCG daily for two weeks, 1 hour after intranasal ovalbumin was administered. Group F was given a daily dose of systemic BCG for seven weeks starting two weeks before the allergy was induced. Blood samples were taken 24 hours after the end of the study and tested for ELISA, IL-4, IL-5 and IFN-γ. Also, nasal mucosae were harvested after the rats were sacrificed and stored for histopathologic examination.
Results: In the two groups in which rats were induced with allergic rhinitis and treated with systemic BCG or topical BCG, histopathologic evaluation scores (increase in goblet cells, increase in connective tissue, vascular congestion, vascular proliferation, inflammatory cell infiltration, eosinophil infiltration) were significantly decreased compared to the Allergy Group. No significant difference was identified between these two treatment groups in terms of their histopathologic evaluation scores ($p>0.05$). No significant differences were identified between the Allergy Group and the group treated with topical BCG or the group treated with systemic BCG with respect to serum IL- 4, IL-5 and IFN- γ ($p>0.05$).
Conclusion: The results of this study show that BCG reduces allergic inflammation at tissue level and may be an alternative treatment option for allergic rhinitis. Considering that allergic rhinitis is a disease affecting approximately 25-35% of the population, it is evident that further studies are needed on this subject.
Keywords: Allergic rhinitis, experimental study, ovalbumin, BCG

The Effect of N-Acetyl Cysteine on Biofilm Layer in an Experimental Chronic Otitis Media Model

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Objective: The aim of this study was to investigate the efficacy of n-acetyl cysteine on the biofilm layer and on the course of the disease in resistant chronic otitis media.
Methods: Thirty Wistar albino rats were used. Twenty-five rats were inoculated with 10x6 colonies with *Pseudomonas aeruginosa* strains through the tympanum. The inoculation was repeated one week later. Then the rats were observed without receiving any treatment. Meanwhile, two rats were lost due to malnutrition. The rats that were induced with chronic otitis media were separated into three groups. In Group 1 (n=18) the right ears of the rats were injected with 0.2% Ciprofloxacin + 0.1% Dexamethasone sodium phosphate + 0.5 mg/mL n-acetyl cysteine solution; in Group 2 (n=18) the left ears of the rats were locally injected with 0.2% Ciprofloxacin+0.1% Dexamethasone sodium phosphate solution. No treatment was applied to the inoculated ears of the rats in Group 3 (n=5, both ears). Group 4 (n= 5, both ears) was the control group with no inoculation or treatment. All rats in all groups were decapitated after a four-week follow-up, and histopathological and scanning electron microscope evaluations were performed.
Results: In all rats induced with chronic otitis media, *Pseudomonas aeruginosa* was identified in the swab cultures taken three weeks after the second inoculation from their external auditory canal. Scanning electron microscope revealed biofilm formation in all chronic otitis media induced groups.

No statistically significant differences were seen between Groups 1 and 2 in terms of suppuration levels, fibrosis, inner ear involvement, infection staging and biofilm formation (p>0.05). Suppuration, fibrosis and inner ear involvement were not observed in the control group.
Conclusion: The efficacy of n-acetyl cysteine on the biofilm layer in chronic otitis media is controversial due to insufficient number of studies. While no effects of n-acetyl cysteine were found on the biofilm in the histopathological and scanning electron microscopy results of this study, further studies with n-acetyl cysteine at different concentrations are needed on different types of experimental animals to arrive at a conclusion.
Keywords: Chronic otitis, biofilm, n-acetyl cysteine, experimental study

Protective Effect of Creatine in Amikacin Ototoxicity

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Objective: This study aimed to assess the protective effect of creatine monohydrate (CrMn) on amikacin ototoxicity using distortion product otoacoustic emission (DPOAE) and auditory brainstem response (ABR) in an experimental animal model.
Methods: Twenty healthy rats were separated into four even groups (Control Group, CrMn Group, Amikacin Group, and Amikacin + CrMn Group). The CrMn Group was administered CrMn (2 g/kg/day) once a day by gastrogavage for 21 days. The Amikacin Group was administered amikacin (600 mg/kg/day) by once-a-day intramuscular injections for 21 days, and the Amikacin + CrMn Group was administered amikacin (600 mg/kg/day) by once-a-day intramuscular injections plus CrMn (2 g/kg/day) once a day by gastrogavage for 21 days. The Control Group did not receive any treatment. DPOAE and ABR tests were performed in all rats on days 0, 7 and 21.
Results: On the 21st day ABR results showed a significant increase in the hearing thresholds of only the Amikacin Group (p>0.001). In the ABR assessment performed on the 21st day, hearing thresholds of the Amikacin + CrMn Group were significantly lower than those of the Amikacin Group (p<0.001). No significant difference was found between the hearing thresholds of the Control Group and the Amikacin + CrMn Group (p> 0.05). By the 21st day DPOAE levels of the Amikacin + CrMn Group were significantly increased compared to the 7th day. While there were no significant differences on the 7th day between the DPOAE levels of the Amikacin Group and the Amikacin + CrMn Group (p>0.05), on the 21st day the Amikacin + CrMn Group showed significantly higher levels than the Amikacin Group (p<0.001).
Conclusion: The results of this study show that a CrMn treatment applied for an adequate period and at sufficient doses will have protective effect against amikacin ototoxicity.
Keywords: Amikacin, ototoxicity, antioxidants, creatine monohydrate, otoacoustic emissions

Investigating the Effects of the Expression of Toll-Like Receptor 2, 3, 4 Genes on Tumor Invasion in Laryngeal Cancer

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Objective: The aim of this study was to investigate the expression of toll-like receptor 2,3,4 genes in larynx cancers, one of the cancers with no increase in survival rates despite the recent advancements, and to demonstrate their clinicopathologic correlation with the disease.
Methods: The study was retrospectively conducted on 50 patients who underwent an open total or partial laryngectomy procedure for squamous cell carcinoma of the larynx in the years 2016-2018. Toll-like receptor 2,3,4 expression levels were measured by real-time Polymerase Chain Reaction in the normal tissue and the tumor tissue samples of patients. Toll-like receptor gene expression levels were compared with the demographic (age, gender, alcohol and tobacco consumption), clinical and histopathologic characteristics of patients. Gene expressions were examined based on the cartilaginous, vascular, lymphatic and perineural invasion conditions of the tumors. Further, toll-like receptor expression levels were compared between the larynx tumor materials and the normal tissues of the same patients.
Results: The ages of the patients ranged from 34 to 84 with a mean of 60.56±9.67 years. Of the 50 patients 47 (94%) were male and 3 (6%) were female. Examination of the cases of the 50 patients found a 2^ΔΔCT level of 1 in normal tissue and 0.1±0.1 in tumor tissue for TLR-2; of 1 in normal tissue and 0 in tumor tissue for TLR-3; and of 1 in normal tissue and 1±1 in tumor tissue for TLR-4. There was reduced expression in tumor tissues compared to normal tissues for all three genes and the difference was statistically significant (p<0.001). No statistically significant correlations were found in terms of the clinicopathological characteristics of patients between the groups that showed unchanged or increased expression for TLR-2, TLR-3, TLR-4 and the group that showed decreased expression.
Conclusion: According to the data obtained in our study, TLR 2, 3, 4 expressions decrease in squamous cell cancers of the larynx. Targeting this gene in future studies can provide beneficial results in the diagnosis and treatment of the disease.
Keywords: Larynx cancer, toll-like receptors 2-3-4, squamous cell carcinoma, real-time polymerase chain reaction

Investigation of National Self-Citations in Otorhinolaryngology Publications and of the Attitudes of Turkish Otorhinolaryngologists

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Objective: This cross-sectional study investigated the level of national self-citations to nationally and internationally published otorhinolaryngology articles and the attitude of Turkish otorhinolaryngologists on national self-citation.
Methods: In the first phase of the study, issues of four Turkish otorhinolaryngology journals, and in the second phase of the study issues of otorhinolaryngology journals indexed by SCI were manually screened for citations by Turkish authors to articles from Turkey in the years 2015-2018. In the third phase, journals published by the national otorhinolaryngology associations of five selected countries were screened. These journals were screened for citations made by Turkish authors to articles from Turkey in the period from January 2015 through December 2018. In the fourth phase of the study, questionnaires of the survey that was conducted from December 2016 to January 2019 about the attitudes of Turkish otorhinolaryngologists on national self-citations were analyzed.
Results: The rate of citations by Turkish authors to articles by Turkish authors in national otorhinolaryngology journals in the specified years was 10-20%. While the mean rate of the citations in articles with Turkish authors to articles of Turkish authors in otorhinolaryngology journals indexed by SCI was 10.32%, this rate was 0.96% in Turkish national otorhinolaryngology journals. The mean rates of national self-citations in national journals from Japan, Brazil, Italy, India and Iran were 26.03%, 22.05%, 18.93%, 8.34% and 11.03%, respectively. The surveys conducted with Turkish otorhinolaryngologists in two different timeframes revealed a general unwillingness and a lack of effort to cite national otorhinolaryngology journals featuring Turkish authors.
Conclusion: This four-phase study demonstrated that Turkish otorhinolaryngologists are unbiased for national self-citation, and quite to the contrary, are far behind in citing national otorhinolaryngology journals. The most important reasons for the low rate of citations to national otorhinolaryngology journals came forth as the difficulty of screening the national otorhinolaryngology literature and lack of confidence in national publications.

Keywords: Citation analysis, bibliometrics, Turkey, otorhinolaryngology, publication

Place of Transcervical Ultrasound in the Diagnosis of Pediatric Obstructive Sleep Apnea

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Objective: Obstructive sleep apnea syndrome (OSAS) is a condition seen at a rate of 1 to 5% in the pediatric population, with increasing prevalence. It is often said to be due to the hypertrophy of the tonsils and the adenoids. In this study, we aimed to investigate the place of tonsil ultrasound as a noninvasive, easy-to-apply method in pediatric OSAS.
Methods: Patients who presented to our ENT clinic with complaints of sleeping with an open mouth, snoring, and restless night-time sleep and had identified hypertrophy of the tonsils (± of adenoids) and were planned for tonsillectomy (± adenoidectomy) were included in the study. One day before their operation, the OSAS screening questionnaire was completed and tonsil ultrasound was performed by the same radiologist. Polysomnography (PSG) was performed in patients who were able to cooperate. All patients then underwent tonsillectomy (± adenoidectomy) and postoperative tonsil volumes were calculated.
Results: A total of 47 patients, 31 (66%) male and 16 (34%) female, participated in the study. Their mean age was 7.23±3.09. The mean tonsil size measured by ultrasound imaging before the surgery was 3.49±1.65 cm^3. PSG was applied to 15 of the patients who were able to cooperate, and the mean PSG AHI score was reported as 6.98±10.3. The mean postoperative PSG AHI score of these patients was found as 0.95±0.58. We found a statistically significant correlation between the objective tonsil dimensions measured in tonsil ultrasound and both the PSG AHI scores and the questionnaire scores ($p<0.05$).
Conclusion: Basing on the results of our study, we believe that preoperative tonsil ultrasound may be useful in identifying the condition in children who are suspected of OSAS but are unable to cooperate for PSG, however, more comprehensive studies are needed.

Keywords: Obstructive sleep apnea syndrome, tonsil ultrasound, polysomnography, tonsillectomy, pediatric

Effects of Septorhinoplasty Techniques and Poly-p-dioxanone Plates on Maxillofacial Development: An Experimental Study

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Objective: Basing on the key role the septum plays in midfacial growth, this study explored the effects of the techniques that can be applied to the septum in pediatric septorhinoplasty and of poly-p-dioxanone (PDS) plate usage on maxillofacial development.

Methods: Thirty-three rabbits aged eight weeks were divided into five groups. The first group was taken as the control group and their growth was monitored without any intervention. In the remaining four groups septorhinoplasty was performed with different techniques. Volumes of the maxilla, the incisive bone, the mandible and maxillary sinus, length and width of the nasal bone were examined in 3D by tomography scanning at the beginning and at the end of the study and compared between the groups.

Results: The nasal bone was observed to be shorter in the group that had osteotomy and mucosal elevation ($p<0.05$). While cartilage resection and use of crushed cartilage did not affect midfacial growth, incisive bone volume was significantly reduced and malocclusion developed in the group which PDS plate and composite crushed cartilage was used. Limited cartilage resection by preserving the dorsal stratum and crushed cartilage use had no significant effects on maxillofacial development parameters ($p>0.05$).

Conclusion: Septal surgeries can be safely performed in the pediatric period with limited resections by observing the septodorsal cartilage. In our study, contrary to the reports in the literature, osteotomy and mucosa elevation were seen to adversely affect nasal bone growth ($p<0.05$). In the pediatric period, however, osteotomy is usually applied in patients presenting with extensive deviation after a nasal trauma, and if not treated, can lead to more serious deformities like short nasal bone, flattened nasal base, short columella, type ptosis. Therefore, osteotomy can be performed in order to prevent more serious deformities in pediatric period. Although positive results have been reported for PDS plate use in adults, in our study, it was observed to have negative effects on maxillofacial growth when used in developing noses. Invasive bone development significantly regressed and malocclusion developed. Compared to the other techniques used in our study, that the most statistically significant effect on maxillofacial development was seen in the PDS Plate Group suggests that the histological effects of PDS plate on developing noses should be further investigated. Moreover, whereas growth continues for 20-24 weeks in rabbits, maxillofacial development is a much longer process in humans. Therefore, clinical studies investigating the effects of PDS plate on developing noses are needed.

Keywords: Maxillofacial growth, septoplasty, pediatric, poly-p-dioxanone

Prevalence and Influence Factors of Otitis Media with Effusion among 4-7 Year-Old-Children in the Wide Geography from the Balkans to the Caspian Basin: A Multi-Center Study

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Objective: Otitis media with effusion (OME) is a very common multifactorial disease in childhood. Because its symptoms are insidious and therefore diagnosis is often delayed, OME causes conductive hearing loss and adversely affects academic performance. Despite all the

advancements, OME still remains a major health problem all over the world. Research on the prevalence of OME consist only of studies carried out in several different countries, in different seasons and focused on different etiologic factors. The aim of our study was to contribute to the literature with a study on the prevalence of OME in the 4-7 age group through a survey inquiring about the many associated factors along with otoscopic examination, tympanometric examination and acoustic reflex test and by also considering the possible influence of the altitude and the latitude of the study centers. The study was conducted in the same season in countries located on different geographical latitudes and at different altitudes.

Methods: The study was planned with the participation of centers from 18 cities in 16 countries spanning the Balkans and the Caspian Basin. The target age group was 4-7 years. After receiving the ethics committee approvals, children of the families who have filled-out and signed the informed consent form and completed the questionnaire were included in the study. The results of the survey, which included the possible factors deemed to be involved in the etiology of OME, were evaluated together with otoscopic examination, tympanometry and acoustic reflex results.

Results: Of the 18 planned centers, 10 received the legal permission and launched the study. In these 10 centers, a total of 4,768 children were evaluated together with their examination findings, and tympanometry and survey results. Although OME prevalence based on otoscopic examination varied among the centers, in overall, bilateral prevalence was 12%, unilateral was 10.36% and total was 20.08%.

When this overall prevalence, which is based only on the otoscopic diagnosis results, are analyzed together with the results of Type B tympanometry, overall prevalence decreased to 13.74%. And when the presence of negative acoustic reflex was also considered the overall prevalence was found 5.58%. Major factors that were found to have statistically significant effect on OME prevalence were identified as: mother's education at high school or a lower level (p=0.016), child's age of less than 7 years (p=0.006), history of one or more URTI incidences in the past one year (p=0.001), smoking father (p=0.011), stay-at-home or blue-collar-worker mother (p=0.013), vaccinations (p=0.002), history of allergies (p=0.001), presence of allergic symptom (p=0.019), and history of asthma (p=0.044).

Conclusion: This unique multi-center study that was conducted in a wide geography from the Balkans to the Caspian Basin has provided access to important information about the prevalence and factors affecting OME. Clinical examination and tympanometry may give different results. Therefore, all components should be considered for diagnosis. Focusing on the factors that increase the incidence of OME and addressing the preventable factors like smoking, education, combat with allergies may reduce the incidence of this public health issue.

Keywords: Otitis media with effusion, prevalence, associated factors, survey, otoscopy, tympanometry

Exploring the Ototoxicity Associated with the Tyrosine Kinase Inhibitor Imatinib: An Experimental Study

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Objective: Our study aimed to investigate whether imatinib has an ototoxic effect in rats using auditory brainstem response (ABR).

Methods: Twenty-four albino Wistar rats were separated into three groups as Group C (0.25 mL/kg/day; n=8) with distilled water application, Group I-30 (30 mg/kg/day; n=8) and Group I-50 (50 mg/kg/day; n=8) with imatinib mesylate dissolved in distilled water application. ABR tests were performed at baseline and on days 7, 14, and 21 to measure hearing threshold levels, latency, amplitude and interpeak latency levels. On days 0, 7, 14 and 21 wave-V was obtained in all rats at 4, 6 and 8 kHz frequencies with 10 dB stimulus.

Results: In intra-group analyses for mean wave-V latencies, differences were found among the levels measured with 8 kHz stimulus on the four days in Group I-50 ($p<0.05$). Intra-group analyses for mean wave-III latencies also showed differences between Group I-30 (4 kHz-50, 70 dB and 6 kHz-50 dB) and Group I-50 (4 kHz-50, 70 dB and 8 kHz-50, 70 dB) ($p<0.05$). Intra-group analysis for mean wave I-III interpeak latency showed differences in Group I-30 at 4 kHZ and 70 dB ($p<0.05$). Inter-group analysis for mean wave I-III interpeak latency presented significant differences among the groups on day 7 at 6kHz and 50 dB (p=0.044) and on day 14 at 8 kHz and 70 dB (p=0.036). Intra-group analysis for mean wave-I amplitude showed significant variations at 4 kHz (p=0.003) and 6 kHz (p=0.018) in Group I-50.

Conclusion: While our results showed prolonged latency and interpeak latency, changes in amplitude values, these differences found in inter-group and intra-group analyses do not suffice to say that imatinib has an ototoxic side effect. Therefore, we believe that further studies are needed to reach a definitive conclusion about the ototoxic effect of tyrosine kinase inhibitors.

Keywords: Auditory brainstem evoked responses, imatinib, hearing loss, ototoxicity, experimental study

Ultrasound Assessment of the Effectiveness of Deglutition Therapy in Pediatric Dysphagia Patients

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Objective: Dysphagia has an increasing incidence rate in the pediatric population. Various methods are used for diagnosing dysphagia. In this study we aimed to evaluate therapeutic efficacy of deglutition therapy with ultrasound imaging in the pediatric patients who have presented to our department with complaints of dysphagia.

Methods: Twenty-five pediatric dysphagia patients were included in the study. Deglutition rehabilitation was applied to all patients. Modified barium swallow study (MBSS) and ffunctional endoscopic swallow study (FESS) were performed. Results were analyzed with deglutition assessment scales. All patients underwent ultrasound examination in which tongue base cross-sectional area, submental muscle (digastric, mylohyoid, geniohyoid) cross-sectional thickness and hyoid elevation were examined. All examinations, assessment scales and US imaging were repeated following their therapies. The data were statistically compared.
Results: Pediatric EAT-10 (pEAT-10) scores were significantly decreased after the therapy ($p<0.001$). There was a significant improvement in the scale scores based on the patients' post-therapeutic examination findings ($p<0.001$ on all scales). In ultrasound examination of the patients, submental muscle thicknesses, tongue base cross-sectional areas and hyoid elevation levels were seen to have significantly increased after the therapy ($p<0.001$ in all measurements). Post-therapeutic comparison of the ultrasound examination results and the clinical scales showed that only the increase in the cross-sectional area of the tongue base was correlated with the decrease in PAS (penetration/aspiration scale) and pEAT-10 scores ($p<0.05$). Post-therapeutic ultrasound comparison of the submental muscle thickness and the increase in the cross-sectional area of the tongue base with the increase in the hyoid elevation level showed that the increase in digastric muscle thickness was correlated with the increase in the hyoid elevation level ($p=0.012$).
Conclusion: Ultrasound measurement is a suitable, efficient and reliable method for the diagnostic and post-therapeutic assessment of deglutition in the pediatric population. Given the disadvantages of other screening methods, ultrasound imaging is a preferable method for the evaluation of dysphagia.
Keywords: Deglutition disorders, rehabilitation, diagnosis, ultrasonography

Does the Microbiata in Otitis Media with Effusion Originate from the Adenoids?

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Objective: The aim of this study was to evaluate the content and the diversity of the tympanic effusion (TE) bacteriome and the adenoid specimens bacteriome in pediatric otitis media with effusion (OME) patients.
Methods: After receiving approval from the ethics committee, samples were collected from children with adenoid vegetation and OME. The new generation sequence analysis was performed. Seventeen adenoids and 42 tympanic effusion samples taken from 25 children with OME were evaluated. Microbiome analysis was performed with Ion 16S rRNA metagenomics kit.
Results: In total 22 different bacterial species were identified in the analyzed samples. Bacteriomes in the adenoid and TE samples showed differences in terms of prevalence and density. While the TE microbiome predominantly showed *Alloicoccus otitis* (44%), *Turicella otitidis* (6%), and *Staphylococcus auricularis* (3%), adenoid samples contained significantly higher levels of *Rothia mucilaginosa* (39%), *Rothia dentocariosa* (11%), *Staphylococcus aureus* (5%), *Veillonella rogosae* (2%), *Granulicatella elegans* (2%), *Granulicatella adiacens* (2%), *Eikenella corrodens* (1%) and *Prevotella nanceiensis* (1%).
Conclusion: Whereas *Alloicoccus otitis* was predominant in TE bacteriome, presence of other bacteria at lower levels suggests that OME could be a polymicrobial process. Despite the similarities, the significant difference in the density of some of the predominant species in the TE bacteriome and the adenoid bacteriome raises questions about the theory that OME in children is caused by adenoids.
Keywords: Microbiome, otitis media with effusion, adenoids, sequence analysis

Prevalence of High-risk Oropharyngeal Human Papillomavirus in Healthy Individuals

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Objective: This study aimed to evaluate the presence of oncogenic high-risk Human Papillomavirus (HR-HPV) in tonsil tissues with an in situ hybridization (ISH) technique and identify the prevalence of oropharyngeal HR-HPV in healthy individuals.
Methods: The study was planned as a retrospective cross-sectional study. Cases of adult patients who had undergone a tonsillectomy procedure in our hospital in the years 2014-2018 were retrospectively reviewed. Patients who had tonsillectomy due to malignancy were excluded from the study. Two-hundred-and-twenty patients who were randomly selected based on age and gender were included in the study. Tonsil tissues of the included cases were reexamined by the pathology department and the presence of HPV in tonsil tissues was investigated with the ISH technique using a HR-HPV probe.
Results: The prevalence of oropharyngeal HR-HPV was 6.8% (n=15) among the 220 patients included in the study, (154 [70%] were male; 66 [30%] were female with an age range from 17 to 66 years). Of the patients identified with HR-HPV, 13 (86.6%) were male and 2 (13.4%) were female and their mean age was 30.83±8.37 years. Prevalence rates were found 8.4% among male patients and 3% among female patients; while these rates were found 9.35% in patients aged less than 40 years and 2.46% in patients aged over 40 years.
Conclusion: In our study, the prevalence of oncogenic HR-HPV in our region was found as 6.8%. Further, prevalence rates were found higher in young people and in males. This study, to the best of our knowledge, is the first study conducted in Turkey to determine the prevalence of oropharyngeal HR-HPV, but multicenter epidemiologic studies with larger series are needed on this subject.
Keywords: Papillomaviridae, oropharynx, prevalence, in situ hybridization, tonsillectomy

Effects of Probiotics on Experimental Otitis Media with Effusion

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Objective: The aim of this study was to demonstrate the effect of probiotics in the treatment and prevention of experimental otitis media with effusion.
Methods: Twenty-four albino Wistar rats were used and randomized into four groups. Rats were injected with intratympanic histamine solution to create experimental otitis media with effusion. The presence of effusion was confirmed by otomicroscopic examination 24 hours after the injections. Group 1 (control group) did not receive any treatment. Group 2 (treatment group) received probiotics for seven days from the day effusion was identified, Group 3 (prophylaxis group) received probiotics for seven days prior to intratympanic histamine injection, Group 4 (prophylaxis + treatment group) received probiotics for seven days prior to intratympanic injection and for seven days from the day effusion was identified. All rats were sacrificed on the 8th day after effusion was identified. Tympanic membranes were examined under otomicroscopy to assess the levels of effusion. Histopathologic evaluation was performed for identifying the neutrophil leukocyte counts at 25 sites of the samples prepared from the submucosa of temporal bullae.
Results: In otomicroscopic evaluation, the rate of effusion recovery was found 10% in Group 1, 25% in Group 2, 50% in Group 3, and 100% in Group 4 ($p<0.013$). In the 25 sampled sites of the temporal bullae submucosa, mean neutrophil leukocyte counts were 86.8±24 in Group 1, 66.5±21 in Group 2, 66.2±16 in Group 3, and 26.3±6.5 in Group 4 ($p<0.001$).
Conclusion: Probiotics have positive effects on the prevention and treatment of otitis media with effusion. This effect may be associated with the anti-inflammatory properties of probiotics. Probiotics can be used as a nutritional supplement for complementary therapy in the at-risk age group for otitis media with effusion.
Keywords: Otitis media with effusion, treatment, probiotics, experimental study

Programmed Death-1 Ligand-1 (PD-L1) Expression and Clinicopathologic Correlation in Salivary Gland Tumors

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Objective: Studies on markers such as cytotoxic T-lymphocyte-associated protein 4 (CTLA-4), programmed cell death protein-1 (PD-1) and programmed death ligand-1 (PD-L1) that transmit negative signals to cells have gained importance. Immunotherapies using checkpoint inhibitors like Anti-PD-1 and anti-PD-L1 (Programmed death-1 and ligand-1) have changed the management standards and prognoses of the diseases including malignant melanoma, lung cancer, renal cancer, Hodgkin's lymphoma. Accordingly, we planned a prospective study to investigate PD-L1 expression in patients who were operated on in our clinic for salivary gland tumors.
Methods: Records of patients who were aged over 18 years and operated on and followed-up for a major or minor primary salivary gland tumor in our Ear Nose and Throat (ENT) and Head and Neck Surgery Clinic of the tertiary healthcare institution in the years from 2008 through 2018 were reviewed. Patients who had a second primary tumor, previously received chemotherapy or radiotherapy for another condition, were receiving immunosuppressive therapy or taking immunomodulatory medication were excluded. In total 80 patients, 70 with malignant pathology and 10 with benign pathology, were included in the study. The cases were grouped by diagnoses. The groups were evaluated in terms of age, gender, smoking, tumor localization, locoregional and distant metastasis (TNM) stage, type of surgery, histopathologic diagnosis, tumor staging, perineural invasion, lymphovascular invasion, need for adjuvant treatment, recurrence or metastasis development. PD-L1 expression was explored in both tumor cells and tumor-infiltrating mononuclear cells placed in formalin-fixed paraffin blocks.
Results: Of the 70 malignant primary salivary gland tumors included in our study, 17 (24.3%) stained positive for PD-L1. PD-L1 positivity was observed in 12 (85.7%) of the 14 high grade tumors, two (18.1%) of the 11 intermediate grade tumors, and three (10.7%) of the 28 low grade tumors ($p=0.004$). PD-L1 stained positive in 10 (76.9%) of the 13 patients with lymphovascular invasion ($p=0.02$). No significant relationship was identified between PD-L1 staining and gender, age, smoking, tumor size, histopathologic diagnosis, perineural invasion of tumor, nodal metastasis, distant metastasis, staging, recurrence and survival ($p>0.05$). Also, no significant relationship was identified between the PD-L1 expression in tumor-infiltrating mononuclear cells and gender, age, smoking, tumor size, histopathologic diagnosis, perineural or lymphovascular invasion (LVI) of tumor, nodal metastasis, distant metastasis, staging and recurrence ($p>0.05$). PD-L1 expression in tumor-infiltrating mononuclear cells was observed to be increased as PD-L1 expression increased in tumor cells ($p=0.000$).
Conclusion: In malignant salivary gland tumors, PD-L1 expression is associated with the staging of the tumor and the presence of LVI. Tumor-infiltrating mononuclear cell count was seen to be increased as PD-L1 expression increased. These results suggest that immunomodulation (PD-1/PD-L1 pathway inhibition) may be a treatment option for predicting the prognosis, reducing recurrence risk and increasing survival in selected patients with salivary gland cancer.
Keywords: Immunohistochemistry, immunotherapy, salivary gland neoplasms, B7-H1 Antigen

Exploring the Effects of Mesenchymal Stem Cell and Cholecalciferol on Regeneration in Facial Nerve Damage

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Objective: To evaluate the effects of adipose-derived mesenchymal stem cells (ADMSCs) and cholecalciferol (Vitamin D3, active form, calcitriol) on the regeneration of the facial nerve.

Methods: 32 Sprague-Dawley rats were used. Right facial nerves of the rats were dissected and the main truncus of the nerve was pressed for 60 seconds with a sensor-fitted device to create a crush injury in each rat. The rats were evenly separated into four groups: Group 1 (positive control group): Physiological saline solution was applied to the damaged site, and the left facial nerves of these rats were evaluated as the sham group (negative control group). Group 2: Oral cholecalciferol (3500 IU/kg/week) was administered for four weeks. Group 3: 1x106 ADMSC was applied to the site of injury. Group 4: 1x106 ADMSC was applied to the site of injury in combination with oral cholecalciferol (3500 IU/kg/week) administered for four weeks. Nerve regeneration: Functional evaluation was performed by monitoring eye blink reflex at weekly follow-ups and with EMG (nerve transmission study) after four weeks; and histologic evaluation was made at the end of the fourth week by analyzing the number of axons and the diameter of myelinated axons in the nerve section.

Results: In functional evaluation Group 3 and Group 4 were observed to show the fastest improvement ($p<0.05$). In EMG, compound muscle action potential (CMAP) amplitude was found significantly higher and CMAP latency was found significantly shorter in all experiment groups compared to the control group ($p<0.05$). In EMG, Groups 3 and 4 showed the most favorable results in terms of regeneration. In histologic evaluation, the most favorable axon morphometry and myelinization results were found in Group 4 ($p<0.05$). Groups 2 and 3 showed better results, but no statistically significant difference compared to the control group ($p>0.05$).

Conclusion: In experimental facial nerve crush injury, ADMSC application combined with cholecalciferol treatment will functionally, electrophysiologically and histologically increase nerve regeneration and remyelination.

Keywords: Mesenchymal stem cells, facial nerve, nerve regeneration, cholecalciferol