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Investigation of the Effects of the Timing of Decompression and Topical Mitomycin-C Application on Nerve Regeneration in a Rat Model of Bell's Palsy

Original Investigation

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Abstract

Objective: The timing of facial nerve (FN) decompression (FND) for Bell's palsy is controversial. Intraneural fibrosis is one of the factors affecting post-traumatic nerve regeneration. This study aimed to investigate the effects of decompression timing and antifibrotic agent topical mitomycin-C (MMC) on nerve regeneration in rats in which a Bell's palsy model was created.

Methods: Bell's paralysis model was created by ligating the subjects' FN trunk. A total of 25 subjects were divided into five groups of five each. Group 1 was not decompressed. The FN was decompressed after one week in Groups 2,3 and after three weeks in Groups 4,5. Topical MMC was applied after decompression on the nerves of the rats in Groups 3,5. Clinical, electrophysiological and histopathological evaluations were performed at three weeks after compression in Group 1 and after decompression in the other groups.

Results: The median total clinical score in Group 1 was statistically significantly lower than the other groups (p=0.001). There were no statistically significant differences between Groups 2-5 (p>0.05). The mean left (operated)/right (undamaged) amplitude values of the subjects in Group 1 were statistically lower (p=0.006), while no statistically significant differences were found among Group 2-5 (p>0.05). It was observed that while axonal degeneration, macrovacuolization and myelin morphology disruption was more severe in subjects in Group 1 (adjusted p<0.05), there were no statistically significant differences between Group 2-5 (p>0.05).

Conclusion: FND can be effective in patients with total paralysis, even when performed in the late stages after allowing a period of recovery. Also, topical MMC applications aiming to reduce intraneural fibrosis have no effect on nerve regeneration.

Keywords: Bell palsy, facial nerve, animal experimentation, rats, surgical decompression

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Introduction

A possible treatment option for patients with Bell's palsy, facial nerve (FN) decompression (FND) intends to expand the facial canal to relieve pressure on the constricted FN. The question of when and for which patients to use this treatment option, which is highly complex and may lead to complications such as cerebrospinal fluid (CSF) leak, hearing loss and FN injury, is controversial in a condition like Bell's palsy that is associated with a high potential for recovery (1-3). The widespread opinion is that surgery is beneficial in patients with complete paralysis and poor prognosis (4-6). In terms of timing, while some authors recommend an early FND (in the first two weeks), others argue that it is possible to wait for the improvement of the paralysis and patients may benefit from surgery at later stages (7-9).

As well as factors such as age, comorbidities, duration and severity of trauma, tissue malperfusion and infection, perineural and endoneurial fibrosis can also negatively affect nerve regeneration after a peripheral nerve injury such as Bell's palsy (10). A chemotherapeutic agent, mitomycin-C (MMC) is relatively easily accessible and applied topically in ophthalmology, neurosurgery, orthopedics and otorhinolaryngology to prevent fibrosis-granulation (11).

It is quite difficult to recommend an optimal timing of FND due to reasons such as small patient sample sizes in studies, the lack of doubleblind randomized trials, and the different approaches of surgeons carrying out the surgical interventions. To develop an opinion on the matter, a rat model of Bell's palsy was created to observe the effects of decompression procedures carried out at different times on nerve repair. The effects of topical MMC application in reducing perineural and endoneurial fibrosis, which are among factors that may inhibit nerve regeneration, were also investigated.

Methods

Subjects

The study was conducted at Bezmialem Vakıf University Animal Laboratory with the approval of the same laboratory ethics committee (approval no: 2020/151, date: 26.10.2020). Twenty-five male Wistar rats weighing 300±50 g, aged 8-12 weeks, kept under standard conditions of a 12-14-hour light/dark photoperiod, 45-50% humidity and a temperature of 22+/-2 °C were included in the study. We confirmed that all subjects had normal motor function of the FN, symmetrical whisker (vibrissae) movements and a blinking reflex in response to air inflation. The subjects were provided with a standard diet with mechanisms allowing free access to water and food.

Surgical Technique and Groups

Standard Surgical Procedure Performed on All Rats

The induction of anesthesia, all surgical procedures and euthanasia at the end of the study were performed on all rats by the same surgeon. Induction of anesthesia was achieved through intraperitoneal injections of 80 mg/kg of ketamine hydrochloride and 25 mg/kg xylazine hydrochloride. 2.0x magnifying loupes were used in all surgical procedures and rats were operated on the left side. An approximately 1-cm horizontal incision was made under the auricle, parallel to the mandible. The superior parotid gland was elevated to expose the main trunk of the FN (Figure 1). The diameter of the nerve was measured using a Castroviejo caliper, and the nerve was ligated with a 5-0 nylon suture to decrease the diameter by 50%. (compression) (Figure 2). The skin was sutured with a 4-0 nylon suture. Rats were then randomized into five groups.

Mitomycin-C Application

The nerve was dried using a 1x1 cm sterile gauze swab attached to a rod and another swab with 0.4 mg/mL of MMC was used to apply MMC to this area for five minutes, after which the area was dried once again (MMC application). The dosage of 0.4 mg/mL was determined in reference to a study investigating the potential for toxicity in the local application of MMC, which found that the application of MMC at more than 0.5 mg/mL could induce neurotoxicity and that MMC should therefore be used at doses lower than 0.5 mg/mL (6).

Surgical Procedures Performed on Subgroups

Group 1 (Control Group: C, n=5): Electromyography (EMG) measurements and clinical scoring assessments were performed three weeks after compression, along with

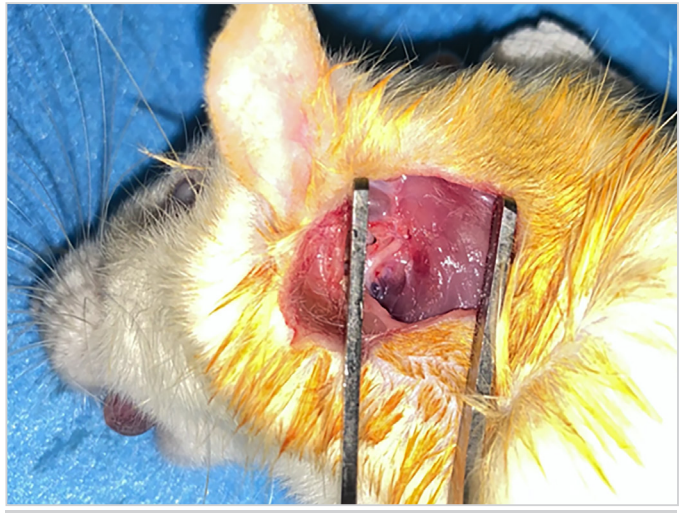

Figure 1. Exposed facial nerve trunk

histopathological examinations of samples following the termination of subjects.

Group 2 (Early Decompression Group: ED, n=5): One week after compression the ligated FN trunk was located using the same method and the 5-0 nylon suture was removed (decompression). EMG measurements and clinical scoring assessments were performed three weeks after the decompression procedure (week 4), along with histopathological examinations of samples following the termination of subjects.

Group 3 (Early Decompression and MMC Group: ED+MMC, n=5): The decompression procedure was performed one week after compression and then MMC application was performed. EMG measurements and clinical scoring assessments were performed three weeks later (week 4), along with histopathological examinations of samples following the termination of subjects.

Group 4 (Late Decompression Group: LD, n=5): The decompression procedure was performed three weeks after compression. EMG measurements and clinical scoring assessments were performed three weeks later (week 6), along with histopathological examinations of samples following the termination of subjects.

Group 5 (Late Decompression+MMC Group: LD+MMC, n=5): The decompression procedure and MMC application were performed three weeks after compression. EMG measurements and clinical scoring assessments were performed three weeks later (week 6), along with histopathological examinations of samples following the termination of subjects.

Assessment Methods

Clinical, electrophysiological and histopathological assessments were performed in week 3 from the start of the study for Group 1 (C), week 4 for Group 2 (ED) and Group 3 (ED+MMC), and on week 6 for Group 4 (LD) and Group 5 (LD+MMC). Electrophysiological assessments were therefore conducted in the third week after compression in the control group and on the third week after decompression in the other groups.

Clinical Assessment

Clinical assessments were performed according to the scoring system defined by de Faria et al. (7), looking at vibrissa and eye movements in response to air inflation on the animal face. In this scoring system, vibrissa movements and the blinking reflex are evaluated separately and added to each other to obtain the total clinical score (minimum-maximum: 2-10) (Table 1).

Electrophysiological Assessment

We used the Natus Keypoint EMG software (Keypoint net v3.23, Denmark) for electrophysiological assessment and braided pairs of 13 mm length and 0.4 mm diameter subdermal needle electrodes for recording. The electrodes were attached to the orbicular oris muscle. A single subdermal needle electrode of 13 mm length and 0.4 mm diameter was used as a ground electrode, which was placed subcutaneously along the zygomatic bone. The FN was stimulated using braided pairs of 13 mm length and 0.4 mm diameter subdermal needle electrodes placed subcutaneously where the nerve exits the temporal bone posteroinferior to the auricle. Stimulation was achieved with square wave pulses of 60 µs duration at a strength that would maximally stimulate the FN without extending beyond it (1.5-8

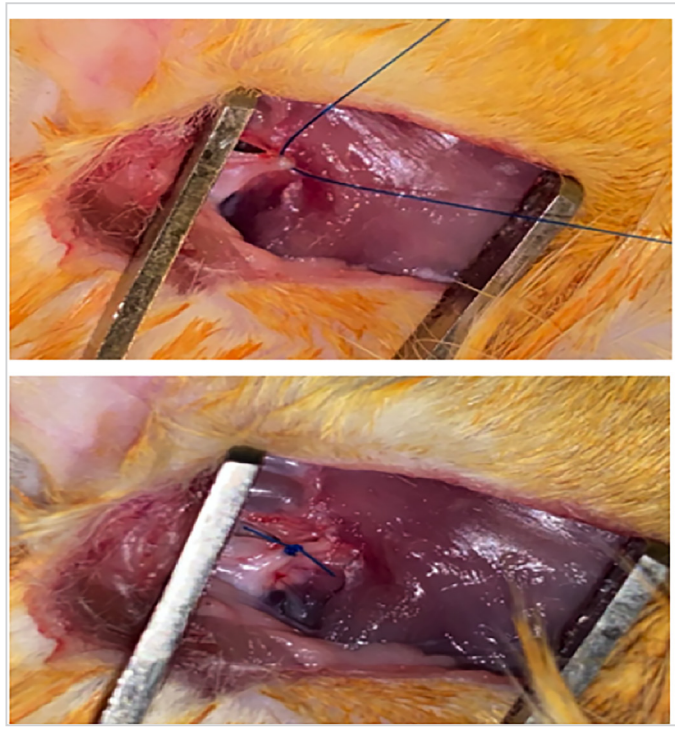

Figure 2. Ligature of the facial nerve with a 5-0 nylon suture (compression)

Table 1. Scale to evaluate facial paralysis in rats developed by de Faria et al. (7)

Score	Whisker movement	Eye movement
1	No movement (posterior position)	No movement (no contraction)
2	Light tremor (posterior position)	No movement (contraction present)
3	Greater tremor (posterior position)	50% (percentile) eye closure
4	Normal movement (posterior position)	75% (percentile) eye closure
5	Normal movement (anterior position)	Full eye closure

mA). At least three pulses were delivered to each side–left (operated) and right (unaffected)–of every rat. Of motor responses recorded, those with an initial negative deflection and shortest latency were selected for consideration and the base to peak amplitude and latency of said motor response was recorded (Figure 3).

Histopathological Assessment

Following euthanasia, an incision was made to the anteroinferior region of the auricle in the rats, and the buccal branch, one of the distal branches of the FN, was exposed to its distal limits (Figure 4). A 10-mm portion of the nerve was resected and split into two parts of 5-mm each to then be fixed with an alcohol-formalin-acetic acid (AFA) fixative. Material fixed with glutaraldehyde was embedded into Epon and semithin sections of 0.5 µm were cut using an ultramicrotome (Leica Microsystems GmbH, Vienna, Austria) and then stained with thionin. Material fixed with AFA was embedded in paraffin blocks using routine paraffin tissue processing methods. Five µm paraffin sections were cut using a rotary microtome, which were then stained with hematoxylin-eosin and the Masson and Gomori trichrome. These tissues were later examined under a light microscope (4 lm; Leica RM 2145 microtome, Leica Microsystems, Wetzlar, Germany) at 100x, 200x and 400x magnifications to assess axonal degeneration, macrovacuolization and myelin morphology. Assessments were based on a grading system modified from similar publications in the literature on this topic (8). Macrovacuolization and axonal degeneration was graded in three categories as mild (1), moderate (2) and severe (3). Myelin morphology was classified as 1 (mild morphological damage) if <25% of axons presented with myelin damage in the largest nerve fiber in the section, 2 (moderate morphological damage) if 25-50% of these axons presented with myelin damage, and 3 (severe morphological damage) if over 50% of these axons presented with myelin damage (Figure 5). The physician performing the histopathological examination was blinded to the groups.

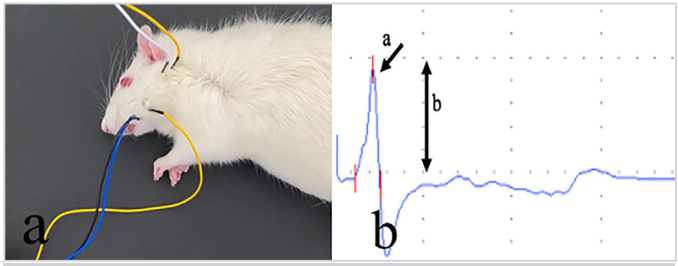

Figure 3. a) EMG performed on subjects, **b)** EMG data sample (**a:** Latency, **b:** Base to peak amplitude)
EMG: Electromyography

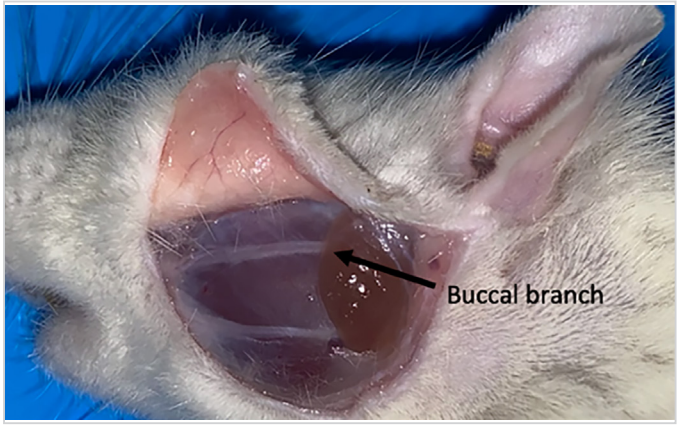

Figure 4. Facial nerve buccal branch

Statistical Analysis

G*Power (University of Düsseldorf, Düsseldorf, Germany) was used to conduct a power analysis. Differences between groups in electrophysiological studies conducted by Wang et al. (9) was considered for the power analysis. Expected effect size was set at 1, and the required sample size was calculated as a total of 25 with 5 in each group using a one-way ANOVA test comparing the five groups with an alpha error limit of 0.05 and beta error limit of 0.95.

The Shapiro-Wilk test and a normal Q-Q plot were conducted for statistical and visual evaluation. Differences among more than two independent groups of normally distributed variables were tested using one-way ANOVA, while non-normally distributed variables were compared with the Kruskal-Wallis H test. The Bonferroni correction was applied as in post-hoc pairwise comparisons, and the adjusted p-value <0.05 was defined as statistical significance.

The chi-square test of independence was used to compare categorical variables between groups, and Fisher's exact test was used in cases where more than 25% of cells had expected counts below five.

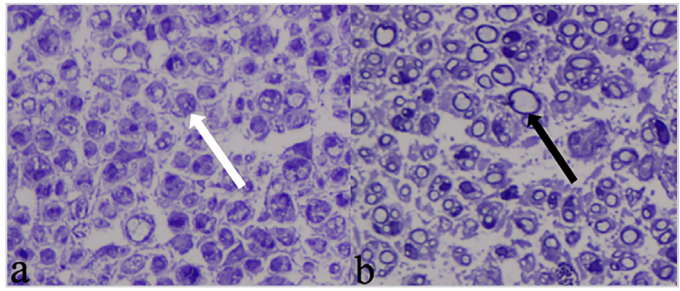

Figure 5. a) Assessment of a semithin section of the left facial nerve of subject no 4 in Group 1 (C), presenting severe macrovacuolization, moderate axonal degeneration and severely damaged myelin morphology (thionin 400x); white arrow: axon with damaged myelin sheath **b)** Assessment of a semithin section of the left facial nerve of subject no 3 in Group 3 (ED+MMC), presenting mild macrovacuolization, moderate axonal degeneration and mildly damaged myelin morphology (thionin 400x); black arrow: axon with normal myelin sheath

IBM SPSS v26.0 (IBM Corp., Armonk, NY, USA) was used for data analysis. Results were considered statistically significant at $p<0.05$.

Results

General Results and Observations

In controls performed in the 4th week after the start of the study (two days after decompression), one of the subjects in Group 4 (LD) presented with an open abdominal wound possibly due to cannibalism. Following debridement after anesthesia, the wound was irrigated with cefazolin diluted by half with saline, after which primary skin closure was performed. The subject was monitored in isolation from other subjects. In the absence of problems such as wound-site infection and lack of appetite in follow-ups, the subject was terminated six weeks after the start of the study as planned. No complications were observed in the other 24 subjects in the study.

Clinical assessments were performed on all subjects in the first week of the study. All subjects experiencing a surgical intervention to compress the FN presented with an absence of vibrissa movements and no blinking reflex in response to air inflation confirming the onset of total facial paralysis.

Clinical Results

Vibrissa movements, eye movements and total clinical scores were evaluated separately by groups.

A statistically significant difference was observed between the groups in terms of median eye movement, vibrissa movement and total clinical score (p-values 0.004, 0.017 and 0.001, respectively). Analyzing the median values of eye movements and total clinical scores in pairwise comparisons, scores of subjects in Group 1 (C) were found to be statistically significantly low (adjusted $p<0.05$), while no statistically significant differences were observed among the median values of the other groups ($p>0.05$) (Table 2). In terms of vibrissa movements, statistically significant differences were found between Group 1 (C) and Group 2 (ED) (adjusted $p=0.036$), and Group 1 (C) and Group 3 (ED+MMC) (adjusted $p=0.036$). No statistically significant differences were observed in comparisons of other combinations, potentially due to small sample size ($p>0.05$).

Electrophysiological Results

Amplitude values on the left (operated) and right (unaffected) sides of each group were averaged to perform a statistical comparison of groups based on mean values. A statistically significant difference was found between groups in terms of left/right amplitudes ($p=0.006$). On post-hoc analysis, left/right amplitude values of subjects in Group 1 (C) were found to be statistically significantly lower than the other groups ($p=0.006$), while no statistically significant differences were found among the other groups ($p>0.05$) (Table 3).

Latency values were, on the other hand, evaluated in terms of latency differences between the left and the right sides, and no statistically significant differences were found [$F(4,18)=2.238, p=0.105$] (Table 4). We observed that latency values presented varying results in some of the previous animal studies in the literature as well. This inconsistency in latency values is believed to be a result of the relatively short course of the FN in rats, creating a shorter interelectrode distance between the stimulating and recording electrodes in EMG testing (10).

Histopathological Results

For every group, macrovacuolization and axonal degeneration was classified as mild/moderate or severe and myelin morphology as mildly/moderately damaged or severely

Table 2. Median values of clinical assessment scores

Group	Whisker movement	Eye movement	Total score
1	1 (1-1)	1 (1-1.5)	2 (2-2.5)
2	2 (2-3)	2 (2-2.5)	5 (4-5)
3	2 (2-3)	2 (2-2)	4 (4-5)
4	2 (1.5-3)	2 (2-2)	4 (3.5-5)
5	2 (2-2.75)	2 (2-2)	4 (4-4.75)
p-value	**0.017***	**0.004***	**0.001***

Data expressed as median (1st to 3rd quartile), *Denotes statistical significance ($p<0.05$)

Table 3. Left/right amplitudes mean values

Group	Left/Right amplitude#	Left/Right amplitude difference from Group 1+	p-value
1	0.05+0.05		
2	0.20+0.09	0.15 (0.02-0.29)	0.019**
3	0.22+0.06	0.17 (0.03-0.31)	0.008**
4	0.20+0.10	0.15 (0.02-0.29)	0.020**
5	0.17+0.09	0.16 (0.01-0.30)	0.028**
p-value	**0.006***		

#: Data are presented as mean+standard deviation, +: The differences between the means of the other groups and Group 1 are provided (with 95% confidence intervals), *: Represents statistical significance in multiple analysis, **: Represents statistical significance in pairwise comparisons (p-values have been adjusted)

Table 4. Left-right (L-R) latency differences mean values

Group	L-R latency difference
1	1.52+0.53
2	0.88+0.34
3	1.07+0.31
4	0.80+0.63
5	0.58+0.55
p-value	**0.105**

Data are presented as mean+standard deviation

damaged to perform a statistical analysis. Statistically significant differences were found between groups in terms of axonal degeneration, macrovacuolization and myelin morphology (p-values: 0.001, 0.021, and 0.001, respectively). In pairwise comparisons it was observed that while axonal degeneration was more severe in subjects in Group 1 (C) (adjusted p<0.05), there were no statistically significant differences between the other groups (adjusted p>0.05). Again, while macrovacuolization and myelin morphology disruption was found to be more severe in subjects in Group 1 (C), no differences were observed between the other groups. However, in post-hoc analyses of the data on macrovacuolization, no differences were observed between any of the groups in pairwise group comparisons, most probably due to the small sample size (adjusted p>0.05). Post-hoc analyses of data on myelin morphology showed statistically significant differences only between Group 1 (C) and Group 2 (ED) (adjusted p=0.008) and between Group 1 (C) and Group 3 (ED+MMC) (adjusted p=0.004), while no significant differences were observed between the other groups, again possibly due to small sample size (adjusted p>0.05) (Table 5).

To briefly summarize the findings, no differences were found in terms of recovery between the early and late decompression groups based on clinical evaluations of eye movements and total clinical scores; electrophysiological evaluations of amplitudes; histopathological evaluations of macrovacuolization, myelin morphology disruption and axonal degeneration.

Discussion

Our study found that subjects undergoing decompression showed significantly better FN regeneration than those who did not. No differences in nerve regeneration were observed between rats decompressed in week 1 and those decompressed in week 3. These findings can be interpreted as favoring the view that FND proves beneficial even when performed at later stages. However, it should not be forgotten that in cases of FN paralysis showing no improvement for over 12 months, decompression will not be of use due to the onset of muscle atrophy and fibrosis caused by denervation (11). Topical MMC application following decompression was, on the other hand, seen to have no impact on nerve regeneration in our study.

The question of when and for which patients the surgical procedure known as FND is indicated in the treatment of Bell's palsy is a long-standing topic of discussion and research (2). It is known that nerve ischemia is reduced, and axonal regeneration increases after surgery (3). FND is considered a relatively infrequent and complicated surgical procedure. A survey conducted in 2011 found that only 22% of the members of the American Neurotology Society performed more than five FND procedures through the middle fossa approach in a period of ten years while only 4% did more than 10. The procedure involves serious complication risks including hearing loss, CSF leak, meningitis and FN injury (2). For this reason, it is quite difficult for physicians and patients alike to decide to move forward with it in a condition such as Bell's palsy that most often resolves on its own without sequelae. Although there are publications demonstrating that FND is a useful treatment as well as those that do not, the ones evidencing its benefits are in majority. Moreover, in most studies investigating the effects of FND, it was observed that only the mastoid segment of the FN was decompressed (3,11). Since the labyrinthine segment of the nerve is the main site of pathology in Bell's palsy, surgical intervention is found to be useful when performed through the middle cranial fossa or with a transmastoid approach to include the geniculate ganglion and the area lateral to the labyrinthine segment (3). Patients with complete paralysis and a more than 90% reduction in amplitudes in comparison to the unaffected side in electroneurography are considered candidates for surgery (2,3).

Since recovery in Bell's palsy can take up to six to nine months in certain cases although it most often occurs within three weeks, the main point of dispute with regards to FND is the timing of the surgery. In the literature on the subject, surgical interventions performed within two weeks of the onset of paralysis are considered early and those performed after two weeks are considered late. While some authors argue that surgery must be performed early on, others hold that the decision to operate or not must depend on the level of spontaneous recovery after a certain period of wait (3).

Table 5. Assessment of myelin morphology and the severity of macrovacuolization and axonal degeneration

Group	Macrovacuolization		Axonal degeneration		Myelin morphology	
	Mild/moderate	Severe	Mild/moderate	Severe	Mildly/moderately damaged	Severely damaged
1	2 (40%)	3 (60%)	1 (20%)	4 (80%)	0 (0%)	5 (100%)
2	5 (100%)	0 (0%)	4 (80%)	1 (20%)	5 (100%)	0 (0%)
3	5 (100%)	0 (0%)	4 (80%)	1 (20%)	5 (100%)	0 (0%)
4	5 (100%)	0 (0%)	4 (100%)	0 (0%)	3 (75%)	1 (25%)
5	5 (100%)	0 (0%)	3 (75%)	1 (25%)	3 (75%)	1 (25%)
p-value	**0.021***		**0.001***		**0.001***	

Data are presented as numbers (percentages), *: Denotes statistical significance

The hypothesis put forward by authors advocating early surgical decompression is that Wallerian degeneration occurring three to five days after nerve injury could negatively affect recovery, causing irreversible damage (3). The hypothesis put forward by authors advocating delaying surgical decompression in Bell's palsy to allow for spontaneous nerve recovery and using it only in the absence of recovery is based on the observation that recovery could be prolonged to six to nine months in certain cases. The fact that some cases where FND was performed in the early stage could potentially have healed without surgical intervention may create a serious harm-benefit conundrum. Just as there is a general bias and publications towards the greater benefits of early FND, findings are also present in studies that late FND could prove beneficial (2-4). It is quite hard to recommend an optimal timing of FND based on the existing studies and findings given their small patient sample sizes, the lack of double-blind randomized trials, and the different approaches of surgeons carrying out the surgical interventions.

To study the mechanism of this disease, it is necessary to conduct relevant animal experiments, among which the most important task is to create an animal model with the same pathogenesis as human diseases. There are prior studies where rat and mice models of Bell's palsy were developed through an ear inoculation of the herpes simplex virus into the middle ear, cold stimulation and clamp injury (12-14). Although the precise pathophysiology of Bell's palsy has not yet been elucidated, the existing understanding is that the nerve swells due to edema caused by viral infection or other reasons to then become compressed within the confines of the fallopian tube (3,15). Fisch and Esslen (16) reported that compression was most likely to occur at the junction of the meatal and labyrinthine segments, naming this area the meatal foramen. While the diameter of the fallopian tube ranges from 1.02 to 1.53 mm, it is reduced to almost half of this width—i.e., 0.68 mm—at this junction. That nerve compression with edema takes place right at this point has been verified by subsequent clinical observations and electrophysiological assessments (16). In our study, the FN trunk was explored and ligated to decrease the diameter by 50% for the purpose of creating similar compression, hence developing a Bell's palsy model. In literature, a facial paralysis model was created with clamp injury by Heckmann et al. (15), but this model was not created with suture ligation as we did. Thus, the nerve was left under pressure for a certain period and decompression surgery was imitated by opening it for different periods of time.

It is known that in Bell's palsy the FN becomes ischemic because of sustained pressure due to the swelling inside the fallopian tube (3,16). Cases that do not recover most probably involve damage to the endoneurium and epineurium as well. Intraneural fibrosis occurring after injuries of the third and fourth degrees according to the Sunderland classification, involving damage to the endoneurium and perineurium, is believed to negatively impact axonal regeneration (17).

Chemotherapeutic MMC is normally an agent that selectively induces fibroblast apoptosis and reduces fibrosis and scar formation. Due to these effects, it is used in ophthalmology, neurosurgery, orthopedics and otorhinolaryngology to prevent fibrosis-granulation (6). The effects of topical MMC on nerve regeneration were also investigated in our study, based on the assumption that it may have positive effects by reducing intraneural fibrosis.

Our study is the first to both develop a rat model of Bell's palsy with a long period of sustained compression and investigate the effects of decompression timing and topical MMC application on nerve regeneration. In our study, no significant difference was found between the late decompression group and the early decompression group when sufficient time was allowed for recovery. From this perspective, our study supports the publications that late decompression may also be beneficial.

One of the strengths of our study is that it involves clinical, electrophysiological as well as histopathological assessments for evaluating nerve regeneration. Our study is, however, limited by the fact that we were unable to examine with an electron microscope and that compression was achieved in a small area using a suture rather than over an entire segment. Another limitation of our study is the small number of subjects, as it leads to instability in some results.

Conclusion

Our findings support the hypothesis that decompression has value in patients with total paralysis even when performed at later stages after waiting for recovery for a certain period. It is also possible to deduce that topical MMC applications aiming to reduce intraneural fibrosis have no effect on nerve regeneration. Multicenter clinical trials are necessary both to further develop our first-time rat model of Bell's palsy and to gain a better understanding of the clinical effects of decompression timing.

Ethics

Ethics Approval: The study was conducted at Bezmialem Vakıf University Animal Laboratory with the approval of the same laboratory ethics committee (approval no: 2020/151, date: 26.10.2020).

Informed Consent: Animal experiment.

Footnotes

Authorship Contributions

Surgical and Medical Practices: B.Ç., H.K., S.S., C.Ş., K.S.O., B.P., Concept: B.Ç., E.K.O., N.G.Ş.İ., G.Ü.,

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Main Points

- A possible treatment option for patients with Bell's palsy is facial nerve decompression.
- There is no consensus on the timing of decompression in Bell's palsy.
- A rat model of Bell's palsy was created to observe the effects of decompression procedures carried out at different times on nerve repair.
- Our findings support the hypothesis that decompression has value in patients with total paralysis even when performed at later stages after waiting for recovery for a certain period.

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