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Review article

APPLICATION OF DIFFERENT TECHNIQUES IN FACIAL NERVE RECONSTRUCTION ON EXPERIMENTAL MODELS

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The facial nerve is the main motor nerve that activates the mimic musculature of the face. Nerve tree injuries lead to paralysis of the same half of the face. In addition to functional damage in the form of difficulty in chewing, speaking and closing the eyes, paresis is the cause of pronounced emotional and social problems in patients.

The etiology of facial nerve damage is diverse, including trauma, neurological, infectious, metabolic, vascular, neoplastic processes, as well as idiopathic and iatrogenic. Of special importance to us are iatrogenic injuries of the transcranial part of the facial nerve, which most often occur as part of surgical interventions in the area of the parotid lodge, where the nerve itself branches into its final branches that innervate facial muscles. A high degree of iatrogenic damage over 40% requires the timely application of adequate techniques and materials for the purpose of neuroregeneration.

Considering the delicacy of the function of the facial nerve and the consequences of its damage, previous methods described in some studies, used in the regeneration process are based on the summarized results of experimental studies on different animal models. A prerequisite for the success of an experimental study is certainly the anatomical compatibility of experimental animals and humans.

Based on the analyzed research, in the last decade rats were used the most, which can be linked to acceptable maintenance costs. Nevertheless, rabbits represent an ideal experimental model due to their anatomical and functional similarities with humans, in which it is possible to successfully simulate paralysis of the facial nerve and monitor the recovery of mimic musculature using the method of movement visualization and electromyography.

Keywords: nerve injury, facial nerve, experimental models, surgical repair

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INTRODUCTION

Injuries to the facial nerve lead to loss of motor, sensory and autonomic function, depending on which nerve fibers are damaged. [1] They are relatively common with a milder or more severe form of damage resulting in paresis or paralysis of facial muscles. [2] Depending on the severity of the trauma, the functional consequences can vary from mild to severe forms (Sunderland's classification) [3].

The mechanism of injury is classified based on mechanical causes of injury as: laceration, traction, contusion, compression, ischemia, electrical, thermal and radiation injuries, gunshot, injection and iatrogenic injuries. The highest percentage of iatrogenic complications is described after surgical treatment of parotid salivary gland tumors. Salivary gland tumors account for 3-10% [4] of all head and neck tumors, with the most common location in the parotid salivary gland area being 36.6-83% [5]. Most of these tumors have benign characteristics and are treated exclusively by surgery. One of the most described complications during surgical interventions is paresis of the facial nerve, which accounts for 30-65% [6], while permanent damage - paralysis occurs in 3-6% of cases [7].

Due to compression and stretching during surgical interventions in the parotid box, neuropraxia and axonotmesis usually occur, which results in facial nerve dysfunction, which has a reversible character. If there was a section of the nerve, which rarely happens on the right side (most often it happens during radical parotidectomy with the sacrifice of the facial nerve as part of the treatment of malignant tumors), then the damage is permanent and that is neurotmesis. Immediately after nerve injury, there is a breakdown of myelin with proximal retrograde degeneration characteristic of the facial nerve (Wallerian degeneration). By the end of the third week, Schwann cells proliferate within the basal membrane of the distal tip of the axon, and if there is a defect, they bridge it with numerous cellular strips (Bungner strips). Three weeks after the injury, both the neuron and the distal part of the frozen axon are capable of regeneration. Metabolites necessary for axon regeneration are provided not only by the nerve cell but also by the environment of the damaged nerve [8]. This information calls into question the expediency of applying biological growth factors that would promote the regeneration process of a damaged nerve.

As a pure motor nerve, the facial nerve as a model during previous decades enabled the collection of a large amount of data on the cellular and molecular responses of motoneurons and their environment to various insults. A complicating factor in the use of the mentioned model is the relatively poor degree of recovery after reconstruction (only 30-40% compared to the healthy side) [9].

Based on the data from the available literature, intensive work has been done in the last two decades in terms of finding the best way to regenerate the facial nerve, with the predominant experimental studies.

It is observed that most of researches was applied to animal models of rats, which can be explained by the relatively lower price of acquiring animals and the easier conditions of their maintenance. Due to the development of the chewing muscles, rabbits are an ideal animal model for simulating paralysis of the facial nerve. Of course, in line with the increase in the number of studies in the past few years, the number of experimental animals used has also increased.

The total number of available works from the database for the period 2010-2022 that dealt with the issue of facial nerve regeneration was 46. The summed number of experimental animals for this period was 1630, with the individual total being: rats - 1066, guinea pigs - 38, rabbits - 462, dogs 35, sheep 23 and monkeys 6. Large animals (dogs, sheep and monkeys) were the experimental model in cases of nerve reconstruction by the method of transplantation, where the graft was used in isolation or in combination with biomaterials.

Depending on the localization, type and severity of the injury, interruption of continuity and size of the facial nerve defect, different methods and techniques are applied in the field of testing the best therapeutic modality at the experimental level.

EXPERIMENTAL METHODS OF REPARATION OF THE INJURED FACIAL NERVE

In the past decade, experimental studies dealing in detail with the regeneration of the injured facial nerve in experimental animals are based on a variety of methods and techniques. Traditional methods of suture repair and autografts are used less and less due to a number of shortcomings, while the development of tissue engineering in recent years has seen a real expansion in the application of growth factors, stem cells and biological materials. When it comes to animal models, rats and rabbits were dominantly used. Due to the similarity of the topographical and anatomical structures of humans and rabbits, it is possible to reliably simulate facial paralysis, which recommends rabbits for further experimental studies.

1. Direct repair of the nerve with a suture

Direct nerve suturing is the method of choice immediately after injury where there is no nerve tissue defect. The main advantages are simplicity and high-quality regeneration, because there is only one suture line. The suture of the nerve can be epineural, perineural (fascicular) or combined.

On an experimental model of eight adult female dogs weighing 18 to 24 kg, Attar et al. proved that the epineural suture method after facial nerve section showed similar results in the speed of nerve conduction and the number of newly created axons as in the group where fibrin glue was used, 16 weeks after the beginning of the experiment [10].

Knox reached results on a rat model that, based on electromyographic tests, equate the epineural suture method with the method of using fibrin glue in the neuroregeneration process [11].

The mentioned studies talk about the advantage of epineural neurosuture in terms of better stability of the proximal and distal nerve endings, but they also give an advantage to fibrin glue in terms of shorter surgical reconstruction time [12].

In the majority of experimental works, suture is used as the basis for the repair of a damaged nerve, where it is often combined with tissue glue and biological materials.

Anatomical lesions in the *n.facialis* occur after a stretch of 20-50%, and for histological changes a stretch of 4-11% is enough. It has been experimentally proven that even relatively mild, long-term tension at the suture site can endanger nerve function. At an elongation of 5-10%, the flow in the venules is reduced, microthrombi and emboli appear, and after some time vascular nerve insufficiency occurs (lower limit of elongation). When nerve vascularization is already compromised by primary trauma, the lower limit of stretch is lower than 5-10%. The upper limit of stretching (11-18%) causes an irreversible lesion of the entire microcirculation, nerve necrosis and separation at the raffia site [13]. The basis for the successful application of this method is the absence of tension in the area of the suture.

2. Nerve grafts

Knowledge of the importance of tension at the suture site changed the earlier strategy of direct raffia and promoted nerve grafting.

In the case of defects larger than 1.5 cm, a nerve transplant is necessary, and autografts are most often used; heterografts or xenografts are used more rarely. The success of nerve grafting directly depends on the length of the graft, because its vascularization is minimal and damage to the axon in the center of the neurograft can occur [14].

a) Autografts

The biggest challenge is the reconstruction of larger defects of the facial nerve that cannot be treated primarily. The method of choice is autotransplantation of the nerve, most often using the sural or auricular nerve. At the experimental level, Chao reports the success of the reconstruction of the buccal branch of rats with the autograft of the marginal branch. In this experiment, 30 adult rats divided into two groups were used. The success of the transplantation was confirmed by electromyographic tests 8 weeks after the reconstruction [15].

In an experimental rabbit model, Zhu indicates the advantage of vascularized autografts compared to free grafts in the process of facial nerve regeneration. The auricular nerve is used as a vascularized graft. In this experiment, 18 rabbits were used, which were divided into three groups. The success of the methods was verified by

electromyographic tests 4 months after the reconstruction, in terms of the speed of nerve conduction and the restoration of motor function in facial facial muscles [16].

b) Xenografts

Deficits in the donor region as well as limited possibilities of autologous nerve transplantation suppressed the method of autotransplantation in favor of xenografts, which is confirmed by the latest experimental studies. Xenografts have certain limitations in terms of immune rejection caused by donor antigens. In order to prevent the aforementioned complication, two methods of immunosuppressive treatment or nerve treatment before transplantation are used. The second method is certainly more acceptable and expedient, so the focus of the latest experimental research is directed towards that principle. Huang compared the number of axons and nerve conduction velocity after reconstruction of a 1cm facial nerve defect in Wistar rats using xenografts and autografts (*n.peroneus*). The obtained results are almost identical with both reconstructive methods [17], Sun used sciatica from Sprague-Dawley rats as xenografts, in the reconstruction of the rabbit facial nerve defect, in combination with autologous plasma rich in platelets and adipose stem cells, in the control group an autograft was used. The summarized results were determined after electrophysiological and histological analyzes at 4 and 8 weeks of the experiment and indicate a significant advantage of using xenografts in combination with platelet rich plasma (PRP) and adipose-derived stem cells (ADSC) [18]. In a monkey model, 8 months after facial nerve defect reconstruction, Zhu proved the advantage of using xenografts obtained from guinea pigs compared to autotransplants. The aforementioned experimental studies indicate the possibility of using xenografts in future work [19].

3. Biological materials

In the last decade, the real expansion in terms of experimental studies was experienced by biological materials that showed a high degree of neuroregeneration and angiogenesis with the proliferation of Schwann cells in the process of reparation of the injured facial nerve. Biological materials (growth factors) are predominantly released from platelets.

a) Growth factors

Platelets are natural deposits of numerous growth factors that are released from alpha granules in the form of fundamental proteins: three isomers of growth factors originating from platelets (platelet derived growth factor - PDGFαα, PDGF ββ and PDGF αβ), two transforming growth factors β (transforming growth factor - TGF β1 and TGF β2), vascular endothelial growth factor (VEGF) and epidermal growth factor (EGF) [20]. Growth factors are necessary for the beginning of tissue repair and regeneration, they have a hemostatic and anti-inflammatory effect, condition the proliferation of Schwann cells and stimulate the regeneration of axons [21].

- Plasma enriched with platelets (PRPplatelet-richplasma) consists of autogenous concentrated human platelets in a small volume of plasma.

PRP can be used alone or in combination with fibrin glue, stem cells or other growth factors.

Cho examined the benefits of using PRP and mesenchymal stem cells in the regeneration process on the facial nerve model of 24 guinea pigs. The collected results of electromyography and immunohistochemistry summarized after 4 and 6 weeks from the beginning of the experiment do not favor any method, and it was concluded that the application of the mentioned growth factors in the process of neuroregeneration is almost identical [22].

Based on the application of PRP and xytosan on an experimental rat model three weeks after the reconstruction of the facial nerve, Sahin concluded that xytosan gel has a positive effect on the process of neuroregeneration, whereby PRP significantly accelerates that process [23].

A large experimental study conducted by Liheng on 100 Wistar rats indicates a significant neurotrophic effect of PRP in the process of Schwann cell stimulation and axon regeneration as well as neuromuscular recovery with the restoration of electrophysiological functions [24].

Application of PRP in combination with suture and fibrin glue in facial nerve regeneration in an experimental rabbit model eight weeks after the surgical procedure indicates a high degree of Schwann cell proliferation and neoangiogenesis, increased number of axons and reduction of fibrous tissue [12].

Nerve growth factor (NGF) - is an insulin-like protein that regulates the growth, development and maintenance of sympathetic and embryonic sensory neurons. It is found in varying amounts in the venom of all venomous snakes tested and in the submandibular salivary gland of male mice.

On an experimental rabbit model, Liu demonstrated the advantage of using Nerve Growth Factor in combination with chitosan compared to the use of autografts in the reconstruction of a facial nerve defect with a diameter of 1cm, three months after the surgical procedure [25].

Fibroblast growth factor (FGF) - represents a large group of small polypeptide growth factors, affects cell proliferation and survival, chemotaxis, migration and cell adhesion.

In the rat model, in the process of reparation of the bruised buccal branch of the facial nerve, Hu uses FGF, whose role in the molecular mechanism of action has not been fully clarified, but the results indicated its effectiveness in the process of neuroregeneration [26].

Transforming growth factor (TGF) - plays an essential role in embryogenesis, especially during the period of morphogenesis

After the section of the buccal branch of the facial nerve in 20 rabbits divided into three groups, the reconstruction was carried out by the application of TGF in combination with a silicone tube that helps in the process of implantation of growth factors. The treated group showed significantly better results in terms of the number and thickness of axons compared to the control group. Wang concludes that the experimental study on rabbits could be an introduction to the clinical practice of applying TGF [27].

Insulin-like growth factor (IGF) - is one of the main factors of cell growth and differentiation. It has anabolic, antioxidant, anti-inflammatory and cytoprotective effects.

Bairak applied the IGF solution locally on a New Zealand rabbit model [20] weighing 1,550-2,200 gr during the surgical phase of the experiment after compression of the extracranial part of the facial nerve for 30 seconds. Electrophysiological measurements and histological analysis of a part of the treated nerve showed the proliferation of Schwann cells with the multiplication of axons with a thicker myelin sheath and a consistent epineurium, which points to the success of nerve regeneration using IGF [28].

While Bajrak performed the compression of the facial nerve in its extracranial part in the parotid box, Sugiama performed the compression inside the temporal bone of rats and locally applied IGF, 8 weeks after the start of the experiment, based on electrophysiological parameters, there was a complete recovery of the facial musculature with synchronized movements of the vibrissae [29].

b) Stem cells

Stem cells (SCs) are undifferentiated cells that have the ability to differentiate after mitosis into any specialized cells. Stem cells can be classified into two major groups based on their source: embryonic and adult stem cells. In the past decade, stem cells represent the leading source of neuroprotective factors in the process of nerve regeneration, predominantly at the experimental level. After transplantation of stem cells into the damaged area, only a small part of them can differentiate into neuronal cells in vivo, to solve this problem, chemical compounds or growth factors that can induce neuronal differentiation have been used. Bone marrow stem cells, dental pulp stem cells, olfactory stem cells and cells obtained from adipose tissue have proven to be neuroprotective.

Bone Marrow Stem Cells (BMSCs)

The best and cheapest cells for cell culture and differentiation into Schwann cells are bone marrow mesenchymal cells (BMCS), combined with growth factors lead to rapid recovery of the peripheral nerve [30].

In an experimental study involving 54 rabbits in which a 1cm facial nerve defect was created, Wang et al. demonstrated the ability of autologous BMSCs to differentiate into cells similar to Schwann cells, so that the implementation of BMSCs in a venous

autograft led to a high degree of axon myelination and an increase in the number of Schwann cells. Cells as the main promoters of neuroregeneration. The experimental study was divided into three test stages: 4, 8 and 16 weeks, where the process of neuromotor activity of the facial nerve based on electrophysiological analyzes was already noticeable in 4 weeks, and in 8 weeks the number of myelized axons reached values close to the control group [31].

An experimental study conducted on 20 adult mongrel dogs by Dardaka, in which the facial nerve trunk defect was bridged with a saphenous vein autograft into the lumen of which bone stem cells were injected in combination with platelet-rich plasma 8 weeks after the experiment by clinical evaluation of ear movement, eyelid closure and of tongue movements indicates results identical to the healthy control group. All this is supported by histological data in terms of the number of axons, the degree of neovascularization and the absence of fibrous tissue [32].

Dental pulp stem cells (DPSC)

Dental pulp stem cells have found a wide application in tissue bioengineering, they facilitate the migration, proliferation and activation of Schwann cells, and stimulate the endogenous proliferation of the neurologically damaged area, which leads to functional recovery.

One of the largest experimental studies in the USA was conducted by Saez et al. on 70 rats over a period of 42 days. In all animals, a contusion of the facial nerve was inflicted in the region of the trunk and, based on the division into two groups, the part of the injured nerve was treated. Functional recovery of the facial nerve was recorded in the group in which stem cells from the dental pulp were administered 14 days after the injury, which promotes this method for further studies [33].

A few years after Saez, Mu conducted an extensive experimental study where rabbits were used as an experimental model. This is the first study in the world where stem cell factor (SCF) and dental pulp stem cells (DPSC) were used in combination. The 7 mm long facial nerve defect was bridged with a cytosan tube in which stem cells from the dental pulp (DPSC) and stem cell factor (SCF) were implemented. At the end of 12 weeks from the experiment, he reports synchronized movements of the vibrissae. SCF promotes adhesion, activation, proliferation and migration, especially neural differentiation of DPSCs, which further leads to neurovascular regeneration. The synergistic effect of SCF and DPSC results in a high degree of neurovascular regeneration, this method has advantages over autograft [34].

Adipose-derived stem cells (ADSCs)

ADSCs are an attractive cell source for tissue regeneration due to their self-renewal capacity, high growth rate, and multipotent differentiation properties. They can be easily isolated from subcutaneous adipose tissue by a safe and conventional liposuction procedure, they are also easily purified and propagated in culture, ADSCs can influence

accelerated nerve regeneration, promoting angiogenesis, they secrete a number of growth factors and cytokines that can positively influence axon regeneration in addition to their multipotent differentiation capacity. When we talk about the regeneration of the facial nerve using ADSCs, we limit ourselves to experimental studies, of which there there is an increasing number recently.

On an animal model of the facial nerve with a defect in the region of the buccal branch of 7 mm, Watanabe used a sciatic nerve autograft in one group and a silicone tube with collagen type I in which differentiated and undifferentiated ADSCs obtained from the subcutaneous fat tissue of 8-week-old mice were incorporated in the other group. After 13 weeks ADSCs show excellent regenerative potential promoting them for further investigation [35], two years later, Abbas conducted an experimental study on the same mouse model by reconstructing the facial nerve with a sciatic nerve autograft with the support of adipose stem cells, the results, as in the previous study, favor ADSC [36]. Sun also confirmed his predecessors with his experimental study, where PRP was used on mice as an experimental model [18].

An experimental study by Kamai in 34 Lewis rats for 13 weeks promoted ADSC combined with polyglycolic acid (PGA) hybrid neural tube versus autograft (*n.hypoglossus*). The method of preparation, avoiding complications of the donor region and the potential for neuroregeneration give this method an advantage [37]. In all the mentioned experimental studies, ADCS were transformed into cells similar to Schwann cells with the release of neurotrophic factors that promote neuroregeneration.

c) Biomaterials

Biological polymers have high biocompatibility and biodegradability, and are essential for physiological attachment and promotion of axon growth. Biomaterials are necessary for the stability of transplanted stem cells and growth factors, conditioning their gradual release into the surrounding tissue. There are a large number of biological materials, but in neuroregeneration, the above-mentioned groups are the most represented

a) natural biomaterials - collagen and gelatin

b) artificial synthetic materials - polyglycolic acid (PGA)

c) biodegradable materials of a new type

Collagen

The use of biological materials has found its application in the engineering of nerve tissue and therefore peripheral nerves in the form of biodegradable nerve tubes. They are indicated when defects larger than 7 mm need to be bridged, for this purpose natural biomaterials based on purified type 1 collagen are most often used [38].

In an experimental study, Wang shows the use of native human neurotrophin-3 (NT-3) fused with a collagen-binding domain (CBD-NT-3) in the repair of a bruised

facial nerve in a rat model (n=120). Evaluation of the effects after 4 weeks indicated that injection of CBD-NT-3 into the epineurium of the injured nerve led to axonal outgrowth with a high degree of myelination. Neurotrophic factors play a key role in the neuroregeneration process. In another study by the same author, collagen combines with fibroblast growth factor (FGF) in a rabbit model. The experimental results of both studies favor the use of collagen [27,40].

In Japan, a bioresorbable collagen product in the form of a channel for bridging nerve defects (Renerve) was patented. In his experimental work on a model of the dissected facial nerve of rats, Hayakawa applies Renerve in combination with collagen filaments. After 13 weeks of evaluation, the results of electromyography and immunohistochemistry indicate the neuroprotective effect of collagen [39].

Gelatin

Gelatin is denatured collagen, a biodegradable polymer, created by splitting the natural triple helical structure of collagen into single-chain molecules. Gelatin is less immunogenic compared to its predecessor and is likely to maintain informative signals such as the sequence Arg–Gly–Asp, promoting cell adhesion, differentiation, migration and proliferation [40].

Since implanted stem cells influence their environment through the secretion of various factors, cell fate is also determined by the same microenvironment. Thus, if the cells are not protected, their effects are either suppressed or the cells die before any of their function is induced. In order to prevent immediate rejection of the transplanted cells by the host, it is important to inject them into a hydrogel gelatin mixture that enables their stability and successive release into the surrounding tissue. In an experimental study, Matsumine used a silicone tube that was implanted into a 7 mm defect in the buccal branch of the facial nerve in a rat model. A silicone tube was formed in a silicone tube containing an acidic gelatin hydrogel filled with bFGF. The rate of nerve regeneration and degree of nerve axon maturation was significantly increased after the release of bFGF from the gelatin hydrogel during the first 2 weeks after peripheral nerve injury. Schwann cell regeneration was promoted using the sustained release method of bFGF from the hydrogel [41].

In his study, Esaki et al. demonstrated the in vivo benefit of olfactory stem cell (OSC) transplantation with a biodegradable gelatin hydrogel in the treatment of facial nerve paralysis (injury) in a mouse model. The result indicates a more pronounced and continuous recovery of facial nerve palsy compared to the group of animals that only received OSC. Biodegradable hydrogel OSCs improve the effect of transplanted cells by protecting them from the local environment and prolonging survival [42].

The combination of thermosensitive hydrogel and bFGF significantly restores the morphology and function of the injured facial nerve in a rat model by promoting autophagy in Schwann cells and inhibiting apoptosis by activating the PAK1 signaling pathway [43].

Polyglycolic Acid (PGA)

PGA is a synthetic biomaterial that has good biocompatibility and biodegradability, it is not toxic to the body. High production costs limit the use of artificial polymers in experimental studies.

In an experimental study on a rat model, Fujimaka treated a facial nerve defect (7mm) with polyglycolic acid PGA in combination with dedifferentiated fat (DFAT) cells, promoting the effect of DFAT cells and PGA in the process of reinnervation 13 weeks after surgical intervention [44].

In his experiment, Wang reports increased expression of neuronal cytoskeleton molecules (GAP43, neurofilament light chain) and growth factors (NGF and brain-derived neurotrophic factor (BNDF)) in nerves treated with BMSc in PGAt/chitosan channels within two weeks [31].

Chitosan

Chitosan has a protective and leading role in the early phase of neuroregeneration, provides a stable localized microenvironment, is gradually absorbed and decomposed in the late phase of regeneration.

Liu et al. repaired 10 mm long defects of the buccal branch of the rabbit facial nerve using a chitosan tube in combination with nerve growth factor (NGF) cells, with a significant advantage over an autologous graft [25].

In an experimental study on 40 rabbits, Lu showed the advantage of using a chitosan nerve channel with implemented PRP in order to bridge the defect of the buccal branch of the facial nerve [25], Sahin et al. a few years later confirms the results of a previous study on an experimental rat model [23]. Mu indicates the benefit of the combination of chitosan tube and DPSC dental stem cells in treating a 7mm long rabbit facial nerve defect, compared to the application of autograft [34].

Fibrin glue (FG)

Fibrin glue in surgery is used to stop microcirculatory bleeding and bleeding in places that cannot be managed with a surgical suture (but cannot be used as a substitute for a surgical suture). In addition to the adhesive and hemostatic effect, FG also has a sealing effect. At the experimental level, in the past two decades there have been a large number of studies dealing with the role of FG in the process of facial nerve regeneration at the experimental level. FG can be used alone or in combination with growth factors and has been shown to have no effect on the process of nerve regeneration [11,12,45].

CONCLUSION

Surgical repair of the injured facial nerve remains the method of choice for all nerve sections with care in the same operative act. The main advantage of primary repair is minimal retraction and easy identification of the edges, due to the absence of a local scar. Direct suturing is possible if the nerve defect is smaller than 1.5 cm. In the case of larger defects, a nerve graft is most often used as an autograft (*n. suralis, n. auricularis magnus* and *r. colli n facialis*).

Application of biological growth factors enables the local presence of activators that play an important role both in survival control and in the processes of migration, proliferation and differentiation of different cell types involved in nerve regeneration [46]. Unlike growth factors that can be obtained relatively quickly from the concentrate of autologous peripheral blood platelets, the cultivation of stem cells is a long and demanding process. Bearing in mind that injuries to the facial nerve require rapid reparative care, artificial inert biopolymers are increasingly being produced that are modeled on the basis of the existing defect. The disadvantage of bipolymers is the reparation of only one branch of the facial nerve because they do not have the possibility of canalicular growth, which limits them for a complete section of the nerve tree. All repair methods are still at an experimental level.

Experimental studies with animal models represent the basis for finding the most optimal method of care for the injured facial nerve, and as such are a necessary basis for future clinical studies. An ideal experimental model for simulating facial nerve palsy is the rabbit.

Authors' contributions

MG carried out the conceptualization, established the methodology and has written original draft. DĐ participated in the design of the study and the statistical analysis. MŽ helped reviewing text data and original draft preparation. APĆ was responsible with supervision, edited and formatted manuscript. All authors read and approved the final manuscript.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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PRIMENA RAZLIČITIH TEHNIKA U REKONSTRUKCIJI FACIJALNOG NERVA NA EKSPERIMENTALNIM MODELIMA

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Facijalni nerv je glavni motorni nerv koji aktivira mimičnu muskulaturu lica. Povrede nervnog stabla dovode do paralize istostrane polovine lica. Pored funkcionalnih oštećenja u vidu otežanog žvakanja, govora i zatvaranja očiju, pareza je uzrok izraženih emocionalnih i socijalnih tegoba kod pacijenata.

Etiologija oštećenja facijalnog nerva je raznolika, uključujući traumatske, neurološke, infektivne, metaboličke, vaskularne, neoplastične procese, kao i idiopatske i jatrogene. Za nas su od posebnog značaja jatrogene povrede transkranijalnog dela facijalnog nerva, koje se najčešće javljaju u okviru hirurških intervencija u predelu parotidne lože, gde se sam nerv račva na svoje završne grane koje inervišu mišiće lica. Visok stepen jatrogenog oštećenja, preko 40%, zahteva blagovremenu primenu adekvatnih tehnika i materijala u cilju neuroregeneracije.

Uzimajući u obzir delikatnost funkcije facijalnog nerva i posledice njegovog oštećenja, prethodne metode opisane u nekim studijama, korišćene u procesu regeneracije, zasnovane su na sumiranim rezultatima eksperimentalnih studija na različitim životinjskim modelima. Preduslov za uspeh eksperimentalne studije svakako je anatomska kompatibilnost eksperimentalnih životinja i ljudi.

Na osnovu analiziranog istraživanja, u poslednjoj deceniji najviše su korišćeni pacovi, što se može dovesti u vezu sa prihvatljivim troškovima održavanja. Ipak, zečevi predstavljaju idealan eksperimentalni model zbog svojih anatomskih i funkcionalnih sličnosti sa ljudima, u kojima je moguće uspešno simulirati paralizu facijalnog nerva i pratiti oporavak mimičke muskulature metodom vizualizacije pokreta i elektromiografijom.