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DIAGNOSTIC AND TREATMENT METHODS

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THE USE OF STEM CELLS IN OSTEOPLASTY OF JAW DEFECTS: A CELL - ENGINEERING APPROACH

The use of stem cells in osteoplasty of jaw defects is one of the most promising areas of modern cellular engineering regenerative medicine. Traditional osteoplasty methods have a number of limitations, from the risk of infections and pain to the limited amount of available graft. In this regard, stem cells open up new possibilities for creating biologically active structures capable of stimulating osteogenesis and restoring complex structures of the maxillofacial region. The review systematizes current data on the use of periodontal ligament (PDLSC), dental pulp (DPSC) and jawbone (JBMSC) stem cells in osteoplasty of jaw defects. Their morphological and molecular characteristics, osteogenic potential, interaction with the microenvironment of the defect, as well as integration with biomaterials and growth factors are considered. Special attention is paid to the results of preclinical and clinical studies confirming the safety and effectiveness of cellular therapies aimed at restoring the cement–periodontal ligament–bone complex and improving the osseointegration of implants. In addition, the work analyzes existing preclinical models of jawbone defects in small and large animals, providing an experimental basis for evaluating the effectiveness of cellular engineering structures and developing safe protocols for clinical use. The importance of DPSC and JBMSC exosomes as biologically active factors enhancing osteogenic differentiation and tissue regeneration is noted. The obtained data emphasize the high prospects of using stem cells from the oral cavity for bone tissue regeneration, the development of new biocompatible materials and individualized therapeutic strategies. The presented review can serve as a scientific basis for creating effective, safe and clinically justified approaches to the treatment of maxillofacial defects and improving the results of implantation therapy.

Keywords: stem cells, osteoplasty, jaw defects, tissue engineering, PDLSC, DPSC, JBMSC, bone regeneration

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Introduction. Jawbone defects remain one of the urgent problems of modern maxillofacial surgery, as they can occur due to congenital anomalies such as cleft lip and palate, injuries, tumors, or tooth extractions. [1, 2, 4, 5, 7]. According to the World Health Organization, about 15-20% of the population face problems with restoring the bone tissue of the jaw after injury or surgery, while in Russia more than 25 thousand cases of maxillofacial defects requiring osteoplasty are registered annually [6]. Delayed healing and non-healing of jaw defects can lead to functional disorders of chewing, aesthetic deformities and speech problems, which underlines the high clinical significance of the problem.

Traditional bone repair methods, including autogenic, allogeneic, and xenogenic grafts, distractive osteogenesis, and targeted bone regeneration, have limitations such as the risk of infection, mechanical complications, pain, prolonged rehabilitation, and limited volume of autografts [3, 6, 9, 17]. In this regard, cellular engineering approaches and tissue engineering open up new opportunities for bone structure regeneration by combining materials, biology and medicine. Stem cells, possessing multipotent differentiation and the ability to self-renew, are able to transform into osteoblasts upon transplantation into a defect, accelerating the restoration of the shape and function of the jaw. Choosing the optimal cell type and defect models requires a systematic approach, taking into account the features of the structure and physiology of the oral cavity [12, 24, 27, 47, 48].

Therefore, the relevance of the topic is due to the need to improve osteoplasty methods to accelerate bone tissue repair and reduce complications in the treatment of maxillofacial defects. The aim of this work is to analyze current data on the use of stem cells in osteoplasty of jaw defects, as well as to evaluate their osteogenic potential, interaction with the microenvironment, and integration with biomaterials to develop effective cellular engineering approaches to bone and periodontal tissue regeneration.

Materials and methods. The article is based on a systematic analysis of the literature on the use of stem cells in osteoplasty of the jaw and cellular engineering regeneration of bone tissue. The search was conducted in leading databases (eLIBRARY.ru, PubMed, Scopus, Web of Science, ScienceDirect, Google Scholar, ResearchGate) with keywords related to stem cells, bone defects, and cell models, with a focus on publications from 2010 to 2025. Clinical and preclinical studies, systematic reviews, and meta-analyses reflecting current understanding of stem cell types, their osteogenic potential, and cellular engineering structures were included. To systematize the data, content analysis and descriptive analytical methods were used to identify the relationship between cell types and recovery efficiency. Special attention was paid to the choice of the cell source, methods of cultivation and integration with biomaterials for the formation of bone regenerate. The approach to finding, evaluating, and structuring information is presented in Table 1, which ensures transparency and reproducibility of the study.

Results and discussion. This section discusses the results of using various types of stem cells (PDLSC, DPSC, JBMSC) for bone and periodontal tissue regeneration, including their interaction with the microenvironment and the possibilities of clinical application. In the future, the features of each cell population, preclinical models of maxillofacial defects, and prospects for the use of cellular and biomaterial therapies to restore the jawbone will be discussed in detail.

The use of stem cells for the reconstruction of jaw defects. There are several types of stem cells for jaw defect reconstruction: Ashour et al. [44] described PDLSC, Bi and colleagues [11] studied DPSC, and M.G. Semenov et al. [8] investigated JBMSC. In comparison with long bone stem cells, jaw cells demonstrate higher proliferation and osteogenic potential, which makes them effective for bone tissue repair [5, 7]. These cells actively interact with the microenvironment of the defect, including vascular and nervous components, which enhances regeneration [1, 2]. Therapy based on jaw stem cells provides accelerated restoration of anatomical shape and function, as well as differentiation into various bone and connective tissue lines [8, 9, 17]. Genetic models of mice are used to trace the lineage of stem cells in vivo and to study the role of nervous tissue, including Schwann cells, in the regulation of osteogenesis [1, 2]. The optimal combination of stem cells with biomaterials and growth factors significantly increases the speed and quality of osteoplasty, which makes the approach promising for clinical use [17].

Periodontal ligament stem cells (PDLSC) are multipotent postnatal cells localized in the periodontal ligament, capable of differentiating into osteoblasts, adipocytes, collagen-forming cells, and cement-like cells [12]. PDLSCS were first isolated and amplified in vitro by Seo and colleagues, and their molecular markers, including CD44, CD90, CD105, STRO-1, and SSEA4 in the absence of CD34 and CD45, were characterized in detail in studies by Kawasaki et al. [37] and Duan et al. [40]. Chopra et al. [29] demonstrated that PDLSCS have a high ability for osteogenic differentiation in vitro, forming calcium nodules and activating alkaline phosphatase, which confirms their potential for bone tissue regeneration. Moreover, Wang L. et al. [36, 43] showed that PDLSC transplantation onto biomaterial scaffolds promotes the restoration of the cement-periodontal ligament-bone complex in preclinical animal models, ensuring the formation of a functional periodontal structure. Clinical studies of L.Gan et al. [18] and Yu.I. Chergeshtova et al. [9] confirmed the safety and efficacy of autologous PDLSC cell membranes for the treatment of periodontitis, improving the depth of probing, bone height, and the level of clinical attachment of periodontitis.

Mesenchymal dental pulp stem cells (DPSC) are a rapidly proliferating population of cells isolated from the pulp of an adult tooth, capable of multipotent differentiation, including odontogenesis, adipogenesis, and myogenesis. A. Machavariani et al. [22] showed for the first time that the combination of DPSC with osteoplastic materials can promote targeted regeneration of jawbone defects, opening up prospects for clinical use in dental surgery. H. Sun et al. [41] demonstrated that exosomes secreted by DPSC enhance osteogenic differentiation and cell migration in graphene-porous titanium-aluminum frameworks, thereby improving the formation of new bone tissue. N.V. Popova et al. [4] contributed to understanding the characteristics of DPSCs by describing in detail their surface markers and the possibilities of integration with biomaterials for tissue engineering. Z. Jing and colleagues [21] demonstrated the effectiveness of 3D-printed skeletons for targeted bone regeneration using DPSC, and I. Mitra et al. [10] have shown that such structures increase the biocompatibility and osteogenic potential of cells. Finally, the research of S. Nikfarjam and colleagues [30] emphasized the importance of DPSC exosomes as modern biologically active factors capable of enhancing cell proliferation and differentiation, opening up new approaches for regenerative medicine.

Jawbone mesenchymal stem cells (JBMSC). JBMSCS originating from the jawbone have a high proliferative ability and are able to repair not only bone, but also cementoid and periodontal ligamen-

tous tissue, which makes them preferable for the regeneration of jaw defects compared to BMSCs [36]. Implantation of autologous JBMSCS into bone defects has shown efficacy in the treatment of maxillary defects and promotes osseointegration of implants by stimulating osteogenic differentiation [38]. Recent studies have identified osteogenic precursors of JBMSC with high Fat4 expression, which enhance the osteogenic potential of these cells. [12, 17, 27, 47, 48]. Additionally, the effect of DPSC exosomes increases the osteogenic differentiation of JBMSC, which further accelerates the regeneration of the jawbone [24].

Preclinical models of maxillofacial defects and their application. Animal experiments create a critically important bridge between basic research and clinical practice, allowing us to study the mechanisms of healing of jaw defects and test new therapeutic approaches [26]. Various types of jaw defects, including postextractional, traumatic, and congenital, may vary in location and degree of damage, which requires the use of specific preclinical models [16]. Both large animals (pigs, dogs, goats, rabbits) and small animals (rats, mice) are used to model jawbone defects, while the choice depends on the research objectives, accessibility, and complexity of surgical intervention [16, 25]. Large animals provide more anatomically approximate results, but their use is limited by the high cost and complexity of procedures, while small animals are more often used because of convenience and cost-effectiveness [25]. Collectively, the use of various preclinical models makes it possible to optimize bone regeneration strategies and pre-evaluate the effectiveness of implants and cell therapies, including stem cells and biomaterials [16, 25].

Further prospects for the use of stem cells (SC) in bone tissue regeneration. In recent decades, tissue engineering using oral SCS has shown significant progress in the regeneration of bone and periodontal tissue, including alveolar bone, dentin, pulp, and cement, with active contributions from S. Subramaniam et al. [25], Y. Wen et al. [16] and S.K. Boda et al. [31]. The development of preclinical models of jaw defects, including maxillary and mandibular models of drilling and tooth extraction, has made it possible to study the effectiveness of various SCS in vivo, as shown in the studies of E.S. Willett et al. [39]. However, unresolved issues remain, including the selection of the most suitable tissue for cell production, the safe use of allogeneic SCS, immunomodulation, and the

Clinical and preclinical studies using stem cells for jaw defect reconstruction

The authors' research	Year of research	A country	The type of stem cells	Main effects / benefits	Number of cases/ models	The control group
Popova N.V. et al. [7]	2024	Russia	DPSC / PDLSC	Characteristics of surface markers, possibilities of integration with biomaterials, application in orthodontics	15 patients	10 patients
Khlusov I.A. et al. [5]	2018	Russia	MSC	Modeling of the mesenchymal stem cell microenvironment, perspectives of tissue engineering	10 animals	5 animals
Chergeshtov Yu.I. et al. [9]	2014	Russia	BMSC / PDLSC	Dynamics of reparative regeneration of mandibular defects with implants and stem cells	12 animals	6 animals
Ashour et al. [44]	2020	Jordan	PDLSC	Increased osteogenic differentiation, restoration of periodontal structure	15 animals	5 animals
Bi et al. [11]	2023	China	DPSC	Accelerated bone formation, improved integration with biomaterials	20 animals	10 animals
Cai et al. [32]	2021	China	JBMSC	Restoration of bone and cement periodontal tissue, stimulates osteogenesis	12 animals	6 animals
Gan et al. [46]	2020	USA	PDLSC	Safety and effectiveness of autologous cell membranes, improvement of bone tissue height	10 patients	10 patients
Machavariani et al. [22]	2019	Georgia	DPSC	Targeted regeneration of jaw defects, increased osteogenic potential	8 animals	4 animals
Sun et al. [41]	2022	China	DPSC	Exosomes enhance osteogenic differentiation and cell migration	10 animals	5 animals
Jing et al. [21]	2020	China	DPSC	Effectiveness of 3D-printed skeletons for bone regeneration	6 animals	3 animals
Mitra et al. [10]	2021	USA	DPSC	Increasing biocompatibility and osteogenic potential in 3D printing	5 animals	5 animals
Willett et al. [39]	2017	USA	PDLSC / BMSC	A standardized rat model for assessing the effects of inflammation and transplantation on healing	24 animals	12 animals

development of optimal delivery systems. Despite this, fundamental and preclinical studies have provided convincing evidence of the potential of oral SC for bone tissue regeneration [39]. In the future, it is necessary to integrate these data to develop clinically safe, effective and economically viable methods of jawbone tissue engineering.

Conclusion. The analysis showed that the stem cells of the periodontal ligament, tooth pulp and jawbone have a high osteogenic potential and the ability to multipotent differentiation, which makes them effective for the regeneration of bone and periodontal tissue. The use of these cells in combination with biomaterials and growth factors accelerates the restoration of the anatomical shape and functional structure of jaw defects. Preclinical models have confirmed the safety and effectiveness of cell-based therapies, making it possible to optimize delivery methods and predict clinical outcome. The practical significance of the work lies in the possibility of applying these approaches to develop safe and effective strategies for jawbone tissue engineering, including the treatment of periodontitis, defects, and improved osseointegration of implants.

The authors declare that there is no conflict of interest.

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