## EFFICACY OF THE JAWBONE DEFECT ELIMINATION

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The regenerative medicine methods are being actively developed both in Russia and abroad due to relevance of this direction, especially in the field of the jaw osteoplasty. Autologous, allogeneic and xenoplastic materials, as well as the calcium phosphate ceramics synthetic preparations are conventionally used to normalize and stimulate osteogenesis, however, the treatment outcomes are not always unequivocal. The study was aimed to substantiate the use of the biocomplex consisting of plasma rich in growth factors (PRGF) and xenoplastic material to improve the jawbone osteogenesis efficacy. The study involved 136 patients (105 females and 31 males aged 21–67) divided into four groups based on the method of bone defect restoration. In group 1, no osteoplastic material was used; in group 2, osteoplasty involved the use of the PRGF fibrin gel; in group 3, the Osteobiol Gen-Os material was used; in group 4, osteoplasty involved using the combination of the Osteobiol Gen-Os material and plasma rich in growth factors (PRGF). Computed tomography and digital densitometry were performed before surgery and 3, 6, 12 months after it to assess the dynamics of osteogenesis. A year later restoration of the lost bone tissue volume was reported in 100% of patients in group 4, 70.27% of patients in group 3, 43.47% of patients in group 2, 37.5% of patients in group 1; Fisher's exact test revealed significant differences in the osteoplasty outcomes in groups 3 and 4 ($p$ = 0.00002). There were significant differences in bone density between patients of groups 1 and 2 twelve months after surgery ($p$ = 0.044), between patient of groups 3 and 4 three ($p$ = 0.004), six ($p$ = 0.0001) and 12 ($p$ = 0.0001) months after surgery. The findings show that the method proposed is effective.

**Keywords:** jaw defect, osteoplasty, plasma rich in growth factors, xenograft, osteostimulation, osteoconduction

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**Compliance with ethical standards:** the study was approved by the Ethics Committee of the Pirogov Russian National Research Medical University (protocol № 131 of 27 January 2014), the patients submitted the informed consent to study participation.

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## ЭФФЕКТИВНОСТЬ УСТРАНЕНИЯ КОСТНЫХ ДЕФЕКТОВ ЧЕЛЮСТЕЙ

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Методы регенеративной медицины в России и за рубежом активно развиваются в связи с актуальностью этого направления, особенно в вопросах костной пластики челюстей. Для нормализации и стимуляции остеогенеза традиционно применяют ауто-, алло- и ксенопластиченские материалы, а также синтетические препараты на основе кальций-фосфатной керамики, но результаты лечения не всегда однозначны. Целью исследования было обосновать применение биокомплекса плазмы крови, богатой факторами роста PRGF, и ксенопластического материала для повышения эффективности остеогенеза костных дефектов челюстей. В исследовании участвовало 136 пациентов (105 женщин и 31 мужчина, в возрасте 21–67 лет), в зависимости от метода замещения костного дефекта разделенных на четыре группы. В 1-й группе остеопластические материалы не применяли, во 2-й пластику проводили фибриновым гелем PRGF, в 3-й — материалом Osteobiol Gen-Os, в 4-й — материалом Osteobiol Gen-Os совместно с препаратом плазмы, богатой факторами роста PRGF. Для динамической оценки процесса остеогенеза проводили компьютерную томографию с цифровой денситометрией до операции и через 3, 6, 12 месяцев после нее. Через год восстановление утраченного объема костной ткани в 4-й группе зафиксировано у 100% пациентов, в 3-й — у 70,27%, во 2-й — у 43,47%, а в 1-й у — 37,5%, точный критерий Фишера выявил статистически значимые различия результатов костной пластики в 3-й и 4-й группах ($p$ = 0,00002). Статистически значимо различаются показатели плотности костной ткани у пациентов 1-й и 2-й групп через 12 месяцев после операции ($p$ = 0,044), у 3-й и 4-й групп — через 3 ($p$ = 0,004), 6 ($p$ = 0,0001) и 12 ($p$ = 0,0001). Полученные результаты говорят об эффективности применения предложенной нами методики.

**Ключевые слова:** дефект челюсти, костная пластика, плазма, богатая факторами роста, ксенографт, остестимуляция, остеокондукция

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The features of reparative regeneration of the jawbone defects result primarily from the high degree of the oral cavity microbial contamination. One milliliter of oral fluid contains billions of microorganisms that form associations consisting of various bacterial species (streptococci, neisserias, vibrios, spirilla and spirochetes), the majority of which are obligate or facultative anaerobes that maintain viability over a long time and actively replicate [1].

Chemical composition of the saliva has a significant impact on the jawbone tissue spontaneous regeneration, since the increased activity of proteolytic enzymes and fibrinolytic activators promotes the blood clot dissolution and washing

out of the defect cavity, thereby complicating the course of postoperative period and disrupting the organotypic bone graft formation [2].

Some clinical and experimental studies have shown that extraction of maxillar and mandibular teeth is followed by bone resorption in the tooth extraction sockets. Furthermore, bone deterioration is more prominent on the buccal side than on the lingual and palatal sides [3, 4]. Two thirds of the alveolar bone tissue is lost three months after tooth extraction [5]. Six months after surgery, the average clinical width and height loss in the tooth socket is 63% and 22% of the baseline, respectively [4], that is why many clinicians point to the need to preserve the alveolar process (part) after tooth extraction using various osteoplastic materials [6, 7].

Bacterial contamination of the bone defect adversely affects regeneration by distorting bone repair, therefore, there is no full bone cavity replenishment. A similar pattern is observed in the projection of bone defects caused by benign neoplasms of the jaw, the invasion of which results in bone tissue resorption and causes compression of the trigerminal nerve branches with typical neurological symptoms [8].

To date, numerous studies have been published reporting good outcomes of spontaneous jawbone defect regeneration after enucleation of cysts, including in cases of large defects [9–11]. Comparative assessment of the use of xenografts, allografts and synthetic material to preserve the volume of the alveolar process (part) of the jaw for the 25-year period was performed. Computer analysis of the data obtained revealed no clinically significant differences between application of osteoplastic materials and barrier membranes of different origin used for preservation of the alveolar process (part) of the jaw. Furthermore, postoperative complications significantly slowed bone tissue repair and thwarted formation of the full-fledged organotypic graft [12]. This suggests the need for further study of the methods for bone tissue regeneration stimulation using various materials and their combinations, as well as for identification of standard indications for the use of osteoplasty techniques.

The study was aimed to substantiate the use of the biocomplex consisting of plasma rich in growth factors and osteoplastic material to improve the effectiveness of osteogenesis in the limited jawbone defects.

## METHODS

The clinical x-ray study was performed at the Pirogov City Clinical Hospital № 1, department of maxillofacial surgery and dentistry of the Pirogov Russian National Research Medical University of the Ministry of Health of the Russian Federation, in 2014–2022.

To assess the dynamics of the jawbone tissue regeneration, we performed the clinical x-ray study and surgical treatment of 136 patients aged 21–67, among them 105 (77.2%) females and 31 (22.8%) males. The patient inclusion criteria were as follows: the established diagnosis of chronic periodontitis, periapical abscess with a fistula, root cyst, follicular cyst, incisive canal cyst. Exclusion criteria: decompensation of concomitant disorder, malignant neoplasms of any stage or remission for less than five years, circulatory system diseases, hepatitis B and C, diabetes mellitus, thrombocytopenia, moderate to severe generalized periodontitis. Pregnancy and the history of concomitant disorder with complications during the study period were also considered to be the exclusion criteria. In 15 cases (11.03%), resorption of mandibular canal and incisive canal walls with the development of trigeminal neuropathy was reported. The bone cavities were divided into three subgroups based on their size: small cavities (volume up to 1 $cm^3$) were diagnosed in 52 cases (39%), medium cavities (volume up to 2 $cm^3$) were observed in 53 patients (38.2%), large cavities (volume exceeding 2 $cm^3$) were reported in 31 cases (22.8%).

Clinical groups were formed based on the jaw osteoplasty method. Group 1 consisting of 24 individuals (17.65%) showed spontaneous bone tissue regeneration due to filling the cavity with a blood clot; in group 2 consisting of 23 patients (16.91%), the bone defect was filled with plasma rich in growth factors (PRGF) in the form of gel. Group 3 included 37 patients (27.20%), among them seven patients showed resorption of the alveolar canals and compression of the trigerminal nerve branches. In this group osteoplasty was performed using the Osteobiol Gen-Os xenogeneic material (Tecnoss; Italy). Group 4 consisted of 53 patients, among them eight patients had neurological symptoms associated with compression of the inferior alveolar and nasopalatine nerves in the mandibular and incisive canals, respectively. The jaw defects in this group were repaired using a complex consisting of the Osteobiol Gen-Os material and plasma rich in growth factors (PRGF). The complex was obtained by polymerization of the xenogeneic material granules in the liquid phase. In group 4, the PRGF fibrin membrane was used to ensure decompression of the neurovascular bundle and separation of the augmentation area from the canal cavity. The PRFG Sistema IV centrifuge (BTI Biotechnology Institute; Spain) was used to obtain the plasma preparation rich in growth factors (PRGF). Preoperative dental examination and treatment were conducted in accordance with the general guidelines “Periapical Tissue Diseases” [13].

During the postoperative period, clinical assessment of patients was performed on days 1, 3, 5, and 7. All patients were recommended to rinse the oral cavity with an antiseptic solution, to apply antiseptic gel to the surgical wound area, to use the methods to ensure local hypothermia in the operated areas within 3 days after surgery for 10–15 min every hour. The broad-spectrum antibiotics and medium therapeutic doses of non-steroidal anti-inflammatory drugs were prescribed. Suture removal was performed on day 10–14 after surgery.

To study the jaw structure and determine the studied materials’ capability of full-fledged bone tissue volume restoration, the data of cone beam computed tomography scans obtained using the Galileos (Sirona; Germany) or KaVo 3D eXam (KaVo; Korea) dental computed tomography system before treatment and 3, 6, 12 months after surgery were used. The Galileos Viewer and Vidar Dicom Viewer 3.1 software tools were used to determine the defect shape, size, and localization, as well as the contact with adjacent anatomical structures; the jawbone volume and density were measured in the Hounsfield units (HU).

Mathematical and statistical processing of the data obtained was performed using the IBM SPSS Statistics 21.0 software package, the following modules were used: descriptive statistics, t-test for independent samples (Student's t-test), nonparametric Mann–Whitney *U* test for two independent samples. The medstatistic.ru online resource (calculator) was also used. The following programs were applied: analysis of contingency tables using the $\chi^2$ test, two-sided Fisher's exact test.

## RESULTS

The analysis of the jawbone tissue regeneration dynamics performed a year after surgery suggested that the best osteoplasty outcomes were observed in group 4, where the lost volume of bone tissue was restored in all 52 cases (100%),

while in group 3 a full-fledged filling of bone cavity with the graft was reported only in 26 cases (70.27%) ($p$ = 0.00002, < 0.05). In groups 1 and 2, complete restoration was reported for small defects only, in 9 cases (37.5%) among patients of group 1 and 10 cases (43.47%) among patients of group 2, while no restoration of volume was reported for medium to large cavities; no significant advantage of one of the groups was also found ($p$ = 0.905, > 0.05; $p$ = 0.77, > 0.05). However, the slightly higher x-ray intensity values were reported for clinical group 2 on month 3, 6 and 12 after surgery.

Patients of groups 1 and 2 demonstrated significant differences in the digital densitometry data 12 months after surgery ($p$ = 0.044, < 0.05), which suggested that the use of the PRGF preparation in the form of gel significantly improved the bone tissue regeneration qualitative characteristics. In patients of clinical group 4, the average jawbone density values obtained three months after surgery were 721.73 ± 24.41 HU, while in group 3 these were significantly lower: 445.11 ± 7.92 HU ($p$ = 0.004, < 0.005). After 6 months the difference between the average bone tissue x-ray intensity values became smaller; the values of group 3 were within in range of 600.54 ± 11.68 HU, while that of group 4 were in the range of 843.58 ± 19.7 HU. However, significant differences persisted ($p$ = 0.0001, < 0.05). The average bone density value of patients of control clinical group 3 did not change significantly over a year after surgery, it was 608.95 ± 18.71 HU. In group 4, this indicator slightly increased (898.64 ± 20.18 HU), but it was still significantly different ($p$ = 0.0001, < 0.05).

## DISCUSSION

Auto-osteoplasty is considered to be a gold standard of osteoplasty in surgical practice, however, allogeneic bone, xenografts and synthetic materials are extensively used to restore medium to large bone defects, when a large amount of bone is needed [14–18]. Good outcomes of the jawbone defect osteoplasty were achieved when using plasma preparations rich in autologous and allogeneic platelets and growth factors [19–22]. The results of the randomized controlled trial involving comparative analysis of bone tissue repair following the use of xenogeneic and allogeneic osteoplastic materials, as well as plasma rich in growth factors, showed that plasma preparation was significantly superior to other studied materials [23]. Many authors note that it is necessary to combine materials of different origin in order to enhance the augmentation material regeneration potential [24–28].

## CONCLUSIONS

Comparative analysis of the dynamic changes in the volume and density of bone tissue in the projection of limited defects in all clinical groups demonstrated that the use of biocomplex of the Osteobiol Gen-Os bone material and plasma rich in growth factors (PRGF) was superior to that of the conventional method used in control group 1, as well as to the separate use of Osteobiol Gen-Os and plasma rich in growth factors (PRGF) in the form of gel. Simplicity and accessibility of the method to generate the plasma preparation rich in growth factors (PRGF), along with the relatively low cost, absolute level of biological safety and no toxic effects on the organism, make this technique one of the methods to address the issues of regenerative medicine. The study results obtained based on the informative clinical x-ray data have shown that the proposed method of using the Osteobiol Gen-Os osteoplastic material in combination with plasma rich in growth factors (PRGF) is promising for everyday use in clinical practice.

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