

## CLINICAL AND MORPHOLOGICAL SUBSTANTIATION OF ELIMINATING OF THE ALVEOLAR BONE DEFECTS USING BIOACTIVE LONG-ACTING COMPOSITE “MEDICAL GLUE”

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**Annotation.** *At the present stage periradicular chronic inflammatory lesions contribute to the development of odontogenic cysts of jaws and is a leading factor in the partial or total loss of teeth, which leads to changes in the morphology of the alveolar bone of the jaws and adjacent tissues with the formation of bone defects. The purpose of this study was to substantiate of eliminating of the alveolar bone defects using bioactive long-acting composite “Medical Glue”. The study involved 42 patients (w-15, m-27) with radicular cysts of the jaws, an average age was  $33.8 \pm 9.1$  years. Additional method of study was computed tomography (CT) with the determination of the size of lesions of bone tissue, an X-ray density assessment of the bone tissue in the cystic defect on the Hounsfield index (HU). According to the density of bone regenerate on 12 months after the operation, this figure was  $369.2 \pm 47.7$  units HU ( $p = 0.38$  versus  $370.8 \pm 84.7$  units HU in a blood clot group), indicating a compliance of terms and phases of material's biodegradation and reparative osteogenesis, its biocompatibility and efficacy.*

**Key words:** *odontogenic cyst, alveolar bone defects, bioactive composite, folic acid, implantation, biodegradation, computed tomography, reparative osteogenesis.*

**Introduction.** At the present stage periradicular chronic inflammatory lesions contribute to the development of odontogenic cysts of jaws, a quantitative advantage of which is given to radicular and residual cysts (up to 84%), which during exacerbation stage cause abscesses, phlegmon, periostitis and osteomyelitis of the maxillofacial area, and is a leading factor in the partial or total loss of teeth, which leads to changes in the morphology of the alveolar bone of the jaws and adjacent tissues with the formation of bone defects [1, 2, 4, 5, 6].

From a biological point of view, the restoration of the alveolar bone integrity is prevented by a number of interrelated factors: the preservation of pathogenic microflora, the inhibitory effect of the epithelium on the regeneration of bone tissue, low reparative potential of solid tissues of the periodontal complex due to the absence of osteogenic precursor cells of the bone marrow in this region [3,7].

The correlation between the size of the bone defect, the term and the quality of its

healing is proved. The size of the pathological bone defect more than 10 mm worsens the conditions for reparative bone regeneration and increases the risk of complications in the early stages and remote postoperative period [8]. In addition, large periradicular defects are sometimes accompanied by displacement of teeth, which can be continued throughout the healing period and depends on the anatomical structure, localization and functional load of the teeth [1].

According to modern clinical protocols, elimination of defects of the alveolar bone is preferred to the surgical methods of directed bone and soft tissue restoration, which involves the use of: free auto-bone graft and / or connective tissue graft to fix it on the alveolar sprout, bone substitute materials, including synthetic bioactive composites, membranes, distraction methods, and a combination of these methods, etc. [9, 10, 11, 12].

On the basis of the Institute of Macromolecular Chemistry of the National Academy of Sciences of Ukraine, Kyiv, the bioactive long-acting composite based on polyurethane mesh – Medical Glue (MG) has been received, which has the ability to dissolve, as well as polymerize in the bone cavity, takes its form and forming adhesive bond on the polymer–bone–soft tissue boundary [13].

After polymerization, the microporous structure (pore size: 231 – 806  $\mu\text{m}$ , interconnected mesopores: 45 – 270  $\mu\text{m}$ ) of the composition contributes to stability and gradual penetration of the newly formed tissues back into the depth as the material biodegrades, the adhesion of blood cells and regenerative cells to its surface (Tabl. 1), the diffusion of biological fluids, which creates a potential opportunity to optimize conditions for the course of reparative osteogenesis

*Table 1*

**Dimensions of cells and cellular elements ( $\mu\text{m}$ ) by V.I. Sevastyanov, 1999**

<b>Erythrocyte</b>	7,5	<b>Lymphocyte</b>	4,5-12
<b>Neutrophil</b>	9-12	<b>Monocyte</b>	12-18
<b>Basophile</b>	9	<b>Platelet</b>	2-3
<b>Eosinophil</b>	12-17	<b>Fibroblasts</b>	20
<b>Collagen fibers</b>	length – 300 thickness – 1.5	<b>Macrophage</b>	10-30

It has characteristics of strength and microstructure, close to the natural spongy part of the bone. The biocompatibility of the composite is due to the proximity of the chemical composition of the urethane group – CO-NH – to the peptide group of proteins [13, 14].

The process of biodestruction of the bioactive composite MG occurs as a result of a combination of non-enzymatic hydrolysis and cellular resorption of the polymer in two major groups of cells: macrophages that phagocyte microparticles of polymer and giant cells of foreign bodies that penetrate the implant through lysis and its separation into fragments.

According to radioisotope analysis, biodegradation products are gradually removed

from the body through the urinary system and the gastrointestinal tract without accumulation in the liver and kidneys [15].

Folic acid (vitamin B9, N-pteroyl-L-glutamic acid) manifests its biological activity by forming tetrahydrofolic acid, which is very important for the further synthesis of nucleic acids (RNA and DNA), increases the binding of nitric oxide synthase and its synthesis that will influence to the angiogenesis, release from free radicals, protection against oxidative modification of human low density lipoprotein and improvement of antioxidant protection of cells [16, 17].

The study of the biocompatibility and bioactivity of folate-containing composites conducted on white laboratory rats showed good adhesion and strength characteristics, for a long time (up to 30 days) retained their structure during implantation, did not cause a chronic inflammatory reaction. After 30 days there was a gradual germination of the connective tissue deep into the polymer implant. The duration of the replacement of the polymer composition with bone took place within 6–8 months [18, 19].

**Purpose.** To substantiate of eliminating of the alveolar bone defects using bioactive long-acting composite “Medical Glue”.

**Materials and methods.** The study involved 42 patients (w-15, m-27) with radicular cysts of the jaws, an average age was  $33.8 \pm 9.1$  years, with no bleeding disorders, severe liver and kidney diseases, or allergic reactions to medical drugs. The patients were treated at the Dental Medical Center of Bogomolets National Medical University.

The diagnosis of the disease was verified on the basis of data from a clinical examination, aspiration of cystic fluid with cholesterol crystals through the root canals of causative teeth, and computed tomography (CT) on the Planmeca ProMax 3D machine.

Clarified the patients' complaints, the cause and duration of the disease, the characteristics of its course, the presence of concomitant pathology were found out. An objective examination took into account the state of transitional fold, percussion and mobility of the teeth, the degree of displacement of the crowns of the teeth, the presence of the Dupuytren's symptom, the presence of the periodontal pocket and its connection with the cystic defect, the data of dental pulp test (DPT).

Additional method of study was computed tomography (CT) with the determination of the size of lesions of bone tissue, an X-ray density assessment of the bone tissue in the cystic defect on the Hounsfield index (HU) [20].

All patients received pre-endodontic treatment of root canals and their filling with zinc-oxide-eugenol cement with gutta-percha filling material. The next day, a Cystectomy operation was performed with apicoectomy of the teeth and retrograde filling of root canals with MTA (mineral trioxide aggregate). The pre- and postoperative antibiotic complex, anti-inflammatory therapy (Cyprinol 750 mg – 2 times a day, Movixicam ODT 15 mg – 1 time a day) was prescribed for 5-7 days.

In the main group, after removal of pathological tissues and retrograde filling of root canals, the bone defect was filled with bioactive long-acting composite MG. In the comparison group – a blood clot.

The evaluation of the clinical study results was carried out according to general

clinical and radiological examination methods (measurement of the volume of the periradicular defect and the density of the newly formed bone regenerate according to CT data). Repeated CT scans were performed 3, 6, 12 months after surgery.

The analysis of the obtained research results was processed by the method of variation statistics using the MedStat and EZR v.1.35 for Windows 8.0 computer-aided software for medical statistical calculations.

**Results and discussion.** The patients were divided into 2 groups: the main group – 11 persons, the comparison group – 31 persons. The average age is  $33.8 \pm 9.1$  years; the average size of the bone defect is  $1.26 \pm 0.29$  cm<sup>3</sup>.

The majority of patients – 40 (93,8 %) included in this study had complaints about the change in the color of the crown/s of the tooth/teeth and the periodically occurring dull ache in the protruding area, and its slow increase in size.

The average duration of the disease in patients of both groups was approximately the same and was in the main group  $2.8 \pm 1.8$  years, and in the comparison group –  $2.1 \pm 0.9$  years.

In patients of both groups, the defects of the alveolar process were mainly localized in the frontal area of the maxilla – 27 (64.3 %) persons, of which in the main group were 7 (63.6 %), and in the comparison group, 20 (64.5 %) persons. The remaining 15 (35.7 %) patients from both groups had radicular cysts in the following areas: the lateral and frontal areas of the mandible were respectively 8 (19.1 %) and 4 (9.5 %) persons, the lateral area of the maxilla was 3 (7.2 %) person. All patients did not have periodontal pockets in the areas of teeth, the roots of which had a connection with cystic defect.

An assessment of the condition of the mucous membrane was shown in 8 (72.7 %) patients in the main group and in 19 (61.3 %) of the patients in the comparison group, the presence of an explosion in the size of 1 to 2 cm in diameter in the area of the alveolar process of the jaw in the projection of the roots of causative teeth. During palpation it was dense or dense-elastic consistency, somewhat compliant, painless. Dupuytren's symptom was positive. Palpation of the transitional fold in the area of these teeth was painless, color of the mucous membrane is unchanged. None of the patients showed any periodontal pockets.

In 18 (58.1 %) patients of the comparison group and in 2 (18.2 %) patients of the main group, scars from the fistulas that functioned earlier were found. Scars from previously performed cystectomy were detected in 3 (7.2 %) patients among all the subjects. Palpation of the transitional fold in the area of causative teeth was painless in 36 (85.7 %) patients, and 6 (11.1 %) patients noted slight pain during palpation.

According to objective data, in 1 (9.1 %) of the patient in the main group and 1 (3.2 %) of the patient in the comparison group, the vertical displacement of the causative (11) tooth was detected 1.2 mm below the level of the adjacent (21) tooth. In 15 (48.4 %) patients in the comparison group, there was a diagnosis of convergence and divergence of teeth, among which 2 patients (6.5 %) of patients revealed a vestibular displacement of causative tooth to  $1.2 \pm 0.3$  mm in relation to adjacent teeth.

A slight pain and discomfort during percussion were noted by the majority of patients

in the main and comparison groups, respectively 8 (72.7 %) and 24 (77.4 %) persons. The percussion of the teeth was painless in 3 (27.3 %) patients in the main group and 7 (22.6 %) patients in the comparison group.

Mobility of the causative tooth of the 1st degree was diagnosed in 2 (18.2 %) patients in the main group and 16 (51.6 %) in the comparison group.

According to the DPT, 100 % of the patients in both groups had indices  $\geq 100\mu A$ , indicating no viable pulp in the causative teeth. During endodontic treatment of teeth, 32 (76.2 %) patients of both groups were aspirated with a light straw colored liquid containing cholesterol crystals.

After a series of CT images after endodontic treatment, the teeth were of the usual shape and size, the crown part was partially restored with a filling, root canals were traced along the entire length, hermetically filled with a contrast filling mass to the tops of the roots.

Patients in both groups had focal lesions of bone tissue of the jaws in the projection of the apex of the teeth roots, which were approximately the same in patients with the main and the comparison group and were respectively  $1.26 \pm 0.29 \text{ cm}^3$  and  $1.19 \pm 0.32 \text{ cm}^3$ . Along the contour of the focal lesion, the bone density enhancement was visualized.

In the main study group, the operation of cystectomy with apicoectomy of the teeth was carried out and the cystic defect was filled with bioactive long-acting composite "Medical Glue." After removal of pathological tissues, the walls of the bone cavity were treated with the antiseptic solution – Dekasan 0,02%. The, the filler (folic acid) and the accelerator of polymerization were sequentially added to the phial with glue base, mixed for 30 seconds until small bubbles appeared, and injected into the cavity of the bone defect. The mucoperiosteal flap was placed in place, tightly pressing the material that filled the defect, after which the wound was sutured with a 5/0 polyamide thread. Aseptic pressure bandage, cold. Postoperative antibiotics use, anti-inflammatory therapy.

Table 2

**Changes of the frequency of edema and hyperemia in patients in the main group**

Index		Abs. (%)			The level of significance of the difference, p
		2nd day	5th day	7th day	
Edema	no	–	7 (63,6)*	11 (100)*	<0,001
	yes	11 (100)	4 (36,4)	–	
Hyperemia	no	–	7 (63,6)*	10 (90,9)*	<0,001
	yes	11 (100)	4 (36,4)	1 (9,1)	

Note: when compared, the Cochran criterion for related samples is used; for posterity comparisons McNemara's criterion is used, taking into account the Bonferroni correction, is used: \* - the difference from the index on the 2nd day is statistically significant ( $p < 0,05$ ).

There was a tendency for a faster reduction of postoperative inflammatory symptoms in patients of the main group: 5 days, 7 (63.6 %) patients had no edema and hyperemia, whereas in most of the persons in the comparison group, 23 (76.7 %) were edema and hyperemia persisted and significantly decreased mainly on day 7. In the main group for 7 days, almost all patients had no edema and hyperemia, which remained in 7 (23.3 %) patients in the comparison group and were over at 9-10 days (Tabl. 2). This served as the basis for the removal of sutures in shorter terms in the main group, an average of  $5.5 \pm 0.9$  days, while in the comparison group, this figure was  $6.6 \pm 1.0$ . The difference between the groups is statistically significant ( $p=0.001$  by the Mann-Whitney criterion). Thus, the filling of the postoperative cystic defect of the alveolar bone can accelerate ( $p=0.001$ ) the healing period, on average by 1.1 days compared with the control group.

The complications in the early postoperative period were only in the patients in the comparison group: the suture line disruption was in 1 (3.2 %) person, the suppuration of the wound – 1 (3.2 %) person.

At follow-up examinations 1 month after surgery, patients had hardly noticeable scars at the site of intervention, the mucosa was pale pink in color, without visible pathological changes, even gingival margin.

In the patients of the main group, there was no displacement of teeth after osteotomy and apicoectomy, while in 3 (9.7 %) patients in the comparison group, a vertical displacement of the teeth was revealed, the roots of which prolapsed into the cavity of the bone defect. After 3 to 6 months, 11 (35.5 %) of the persons in the comparison group showed a hernial mucosal ingrowth at the area of postoperative bone defect.

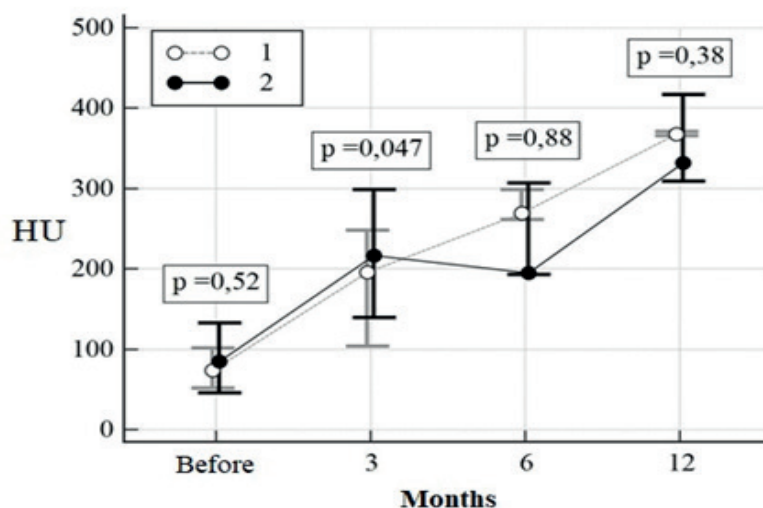


Fig. 1. Dynamics of changes of the roentgenological density index of the newly formed bone in patients of the comparison group (1) and of the main groups (2).

Among 16 (51.6 %) patients in the comparison group, the teeth mobility of the 1st degree disappeared for 1 month in 2 patients, while in 14 (45.2 %) patients, the teeth mobility of 1st degree was maintained for up to 3 months. After 6 months, the mobility of the teeth was absent in all patients in the comparison group.

Palpation of the transitional fold at the postoperative area and percussion of the teeth in all patients was painless.

According to CT data, the structure of the newly formed bone regenerate gradually changed and acquired signs with a characteristic trabecular structure. After 3, 6, 12 months the radiological density on the Hounsfield scale was similar in patients of the comparison group and in the main groups (Fig. 1), indicating similarity of the course and terms of reparative osteogenesis.

The structure of the newly formed bone regenerate gradually changed and acquired roentgenological characteristics of the typical trabecular structure, marked an appositional growth of bone tissue, roentgenological density according to the Hounsfield scale increased.

**Conclusions.** The applied technique of the surgical method for elimination of bone defects of the alveolar processes by the bioactive long-acting composite MG allowed to accelerate ( $p = 0.001$ ) the period of soft tissue healing, on average 1.1 days (95 % confidence interval (CI) 0.5 days – 1, 8 days) compared with the group with the blood clot and allowed to decrease ( $p=0.02$ ) the risk of complications, in particular, postoperative teeth displacement and hernial ingrowth of the mucous membrane to the area of bone defect, to 9.1 % (95 % CI 0 % – 35.9 %), (relative risk (RR) = 0.18 (95 % CI 0.03 – 0.99).

According to the density of bone regenerate on 12 months after the operation, this figure was  $369.2 \pm 47.7$  units HU ( $p=0.38$  versus  $370.8 \pm 84.7$  units HU in a blood clot group), indicating a compliance of terms and phases of material's biodegradation and reparative osteogenesis, its biocompatibility and efficacy.

The obtained data suggest that the bioactive long-acting composite MG has a high level of biocompatibility, gradual biodegradation, expressed adhesion and strength properties, and in terms of clinical and instrumental studies, it contributes to faster postoperative healing of alveolar bone defects and reduction of risks and number of complications compared with blood clot

An important part of successful and predictable treatment of periradicular defects is a combination of biologically justified concepts and methods with clinical application of modern equipment, tools and materials.

**Conflict of interest.** The authors claim there is no conflict of interest that could call into question the integrity of the article.

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