

Experimental Substantiation of the Use of An Osteoplastic Material Based on Hydroxiapatite in Sinus Lifting

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Abstract:

Modern regenerative medicine is aimed at expanding the capabilities of clinicians in stimulating natural bone regeneration processes and developing artificial biomaterials for the restoration of lost tissues. This work is devoted to the experimental study of the effectiveness and safety of osteoplastic material based on hydroxyapatite, intended for use in surgical dentistry, including during sinus lifting operations.

Keywords: Hydroxyapatite, Osteoplastic Material, Bone Regeneration, Biocompatibility, Toxicological Assessment, Sinus-Lifting, Surgical Dentistry

Introduction

At the present stage, despite significant progress in the field of dental implantology, the issues of rehabilitation of patients with pronounced atrophy of the upper jaw bone tissue remain insufficiently developed. This problem is of particular importance when the upper jaw is affected, where bone volume deficit often necessitates the operation of raising the floor of the maxillary sinus using osteoplastic materials (sinus-lifting) [1]. The effectiveness of this surgical intervention largely depends on the choice of surgical technique, as well as on the physicochemical and biological properties of the osteoplastic material used.

Within the framework of this experimental preclinical study, a comprehensive assessment of the effectiveness and safety of the new osteoplastic material based on hydroxyapatite was carried out. The experiment was conducted on a rabbit model. To study the osteoregenerative potential of the material, it was used in the modeling of sinus lifting in the maxillary sinus [2]. To determine biocompatibility and possible toxic effects, the drug was additionally introduced into the parenchymal organs of experimental animals.

The analysis of the results included a clinical-morphological and toxicological assessment aimed at studying tissue reactions, the severity of the inflammatory response, the presence of degenerative and necrotic changes, as well as the features of reparative processes [3], [4]. The obtained data allow us to assess the prospects of using osteoplastic material based on hydroxyapatite in surgical dentistry and dental implantology, and also testify to its safety during experimental use.



II group - experimental. Animals were modeled on a standard bone defect in the maxillary region with sinus lifting surgery. The defect cavity was filled with osteoplastic material containing 50% hydroxyapatite.



III group - experimental. A similar bone defect was formed with subsequent filling of the cavity with a composite material based on hydroxyapatite and collagen in a 30%:70% ratio.



The removal of animals from the experiment was carried out by the method of euthanasia:

- After 30 days (1 month);
- after 90 days (3 months);

Methodology

For histological analysis, fragments of the upper jawbone in the defect zone were taken from the experimental groups of animals and intact samples from the control animals.

The material was fixed in 10% neutral formalin for 24 hours, then decalcified in a nitric acid solution until the bone tissue was completely softened. Fragments about 1.0 cm in size were extracted from the defect zone.

Further processing included standard histological conduction through increasing concentrations of alcohol, alcohol-chloroform mixture and chloroform, after which the material was impregnated with paraffin. Serial cuts with a thickness of 5-7 μm were made from paraffin blocks.

Slices were stained with hematoxylin and eosin. Microscopic studies were conducted using the BIO BLUE binocular microscope at magnifications of $\times 100$ and $\times 400$.

Result and Discussion

Group I (control, after 1 month.)

The bone tissue of the upper jaw had a typical structure of a compact plate with a clearly expressed osteonal organization. Osteons of correct shape, with centrally located Haversian canals [5]. Osteocytes were evenly distributed in the lacunae, and no signs of inflammatory infiltration, fibrous transformation, or destruction of bone tissue were detected. (Fig. 1-4.)

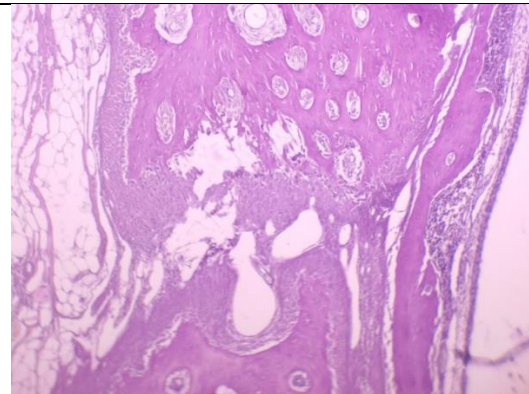


Fig. 1. In the middle of the compact bone plate of the upper jaw, osteocytes, osteons around blood vessels, and dense cellular elements of connective tissue are evenly distributed. Part 1 A. Dyeing: hematoxylin and eosin. Uv. $\times 100$.

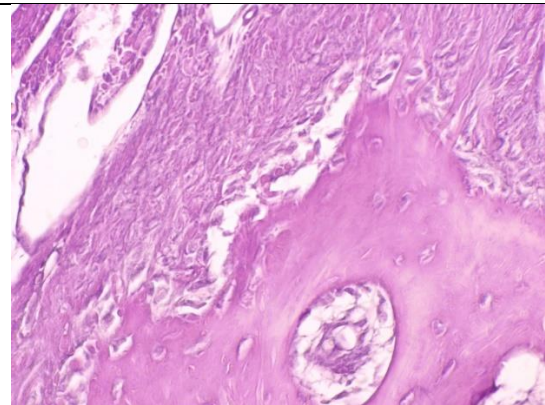


Fig. 2. Fragments of compact bone tissue of the upper jaw with the presence of concentric bone plates of osteon in the center and coarse-fibered connective tissue along the periphery. Part 1 A. Dyeing: hematoxylin and eosin. Uv. $\times 400$.

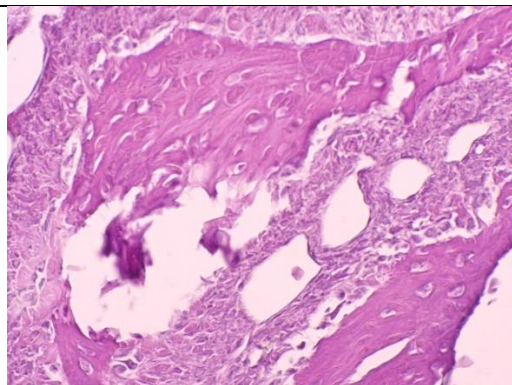


Fig. 3. Bone fragments immersed in a dense cellular stroma with the presence of loose fibers, formation of osteons around blood vessels, differentiation of endothelium and capillaries. Upper jaw Part 1 B. Dyeing: hematoxylin and eosin. Uv. $\times 400$.

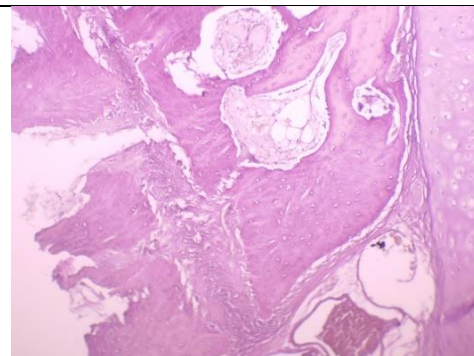


Fig. 4. Layers of cartilage tissue and layers of mature osteogenic fibrous connective tissue in the thickest bone plate of the upper jaw to the right. Part 1 V. Dyeing: Hematoxylin and Eosin. Uv. $\times 100$.

Group II (50% hydroxyapatite + 50% collagen)

30th day

In the area of the defect, dense fibrous-reticular connective tissue with areas of chondroid

differentiation was revealed. On the periphery of the defect, the formation of primary concentric bone plates of osteons around the blood vessels was noted. The vascular network is moderately developed, the endothelium is differentiated [6].

90th day

Progression of osteogenesis with an increase in the volume of newly formed bone tissue was noted. Mature osteons formed, the amount of the fibrous component decreased, and the regenerate restructured towards a compact bone structure.

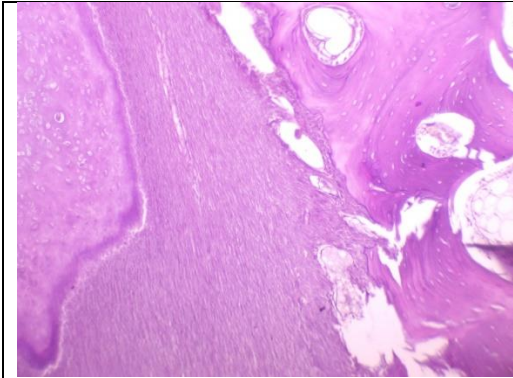


Fig. 5. Compact bone tissue with abundance of osteons and osteocytes, tightly adhering thick fibrous connective tissue, right fragment of chrystalline tissue of the endosteum. Upper jaw to the right 2. Dye: hematoxylin-eosin. Uv. x 100.

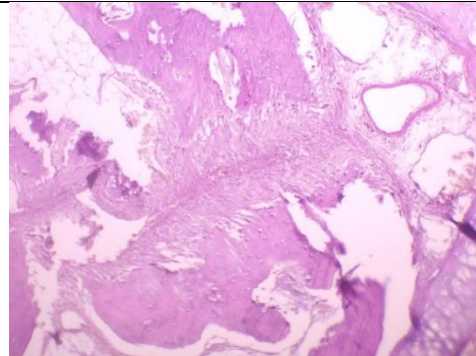


Fig. 6. Formation of primary concentric bone plates of osteons on the surface of the defect wall. Upper jaw A 2. Hematoxylin and eosin staining. Uv. x 100.

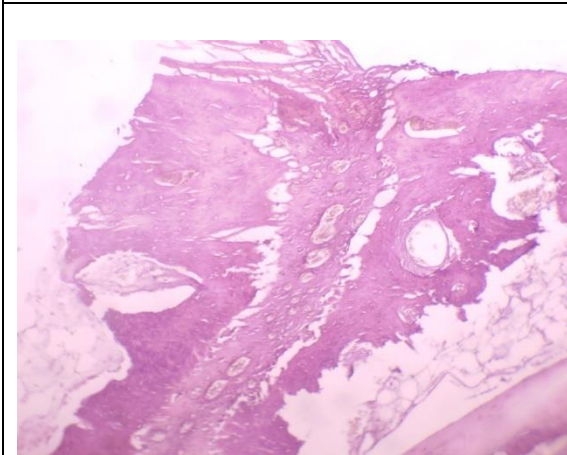


Fig. 7. On the surface of the defect wall, primary concentric bone plates of osteons are formed, and there is an abundance of blood vessels. Upper jaw 2 left G. Hematoxylin and eosin staining. Uv. x 100.

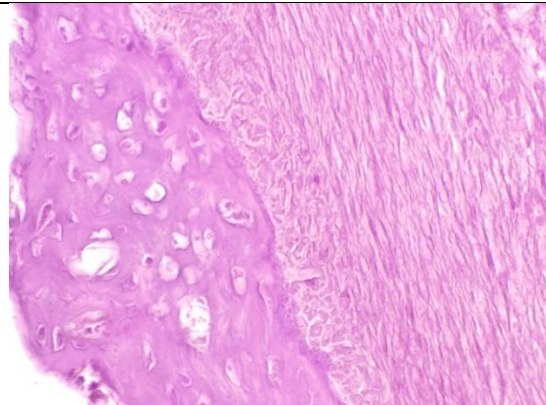


Fig. 8. The wall of the defect is represented by chondroid and fibrous-fibrous tissue. Upper jaw left 2 B. Color: hematoxylin and eosin. Uv. x 400.

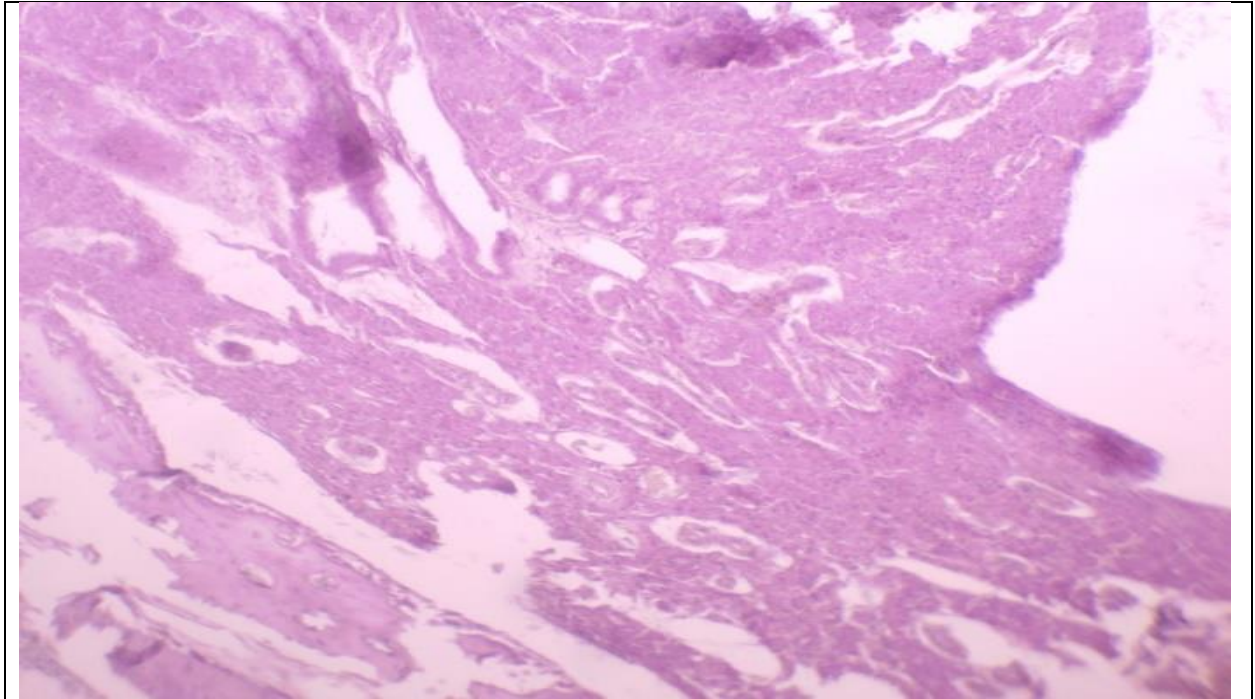


Fig. 9. Cutting of bone tissue with areas of replacement of osteogenic fibrous connective tissue, abundance of fibroblasts, osteoclasts, formation of concentric structures of osteons around vessels. Upper jaw left 3. Staining: hematoxylin and eosin. Uv. x 100.

Group III (30% hydroxyapatite + 70% collagen)

30th day

A pronounced activation of reparative processes was observed in the defect zone. Intensive growth of fibrous fibers, abundance of fibroblasts and osteoclasts, and developed vascular network were determined [7], [8], [9]. Concentric structures of osteons around the vessels were formed, areas of chondroid tissue were noted, which indicated the endochondral type of osteogenesis.

90th day

The regenerate was represented by predominantly mature compact bone tissue with well-formed osteons, narrow lacunae, and a pronounced system of Haversian canals. Fibrous tissue was preserved in minimal volume, which indicated a high degree of osseointegration of the material [10]. In this experimental preclinical study, the effectiveness and safety of a new osteoplastic material based on hydroxyapatite were assessed. The experiment was conducted on a rabbit model. To study the osteoregenerative properties of the material, it was used in sinus lifting in the maxillary sinus area. To determine biocompatibility and possible toxic effects, the drug was additionally administered to the parenchymal organs of experimental animals [11].

Assessment of the research results included clinical-morphological and toxicological analyses to study tissue reactions, signs of inflammation, degenerative and necrotic changes, as well as features of reparative processes [12]. The obtained data allow us to judge the potential of using osteoplastic material based on hydroxyapatite in surgical dentistry and implantology, as well as its safety during experimental use.

Thus, in animals with maxillary defect without osteoplastic materials, granulation tissue formation was observed within 15-30 days, followed by its transformation into dense fibrous connective tissue [13].

The use of osteoplastic material based on hydroxyapatite contributed to the acceleration of bone regeneration processes, however, the best morphological indicators were revealed when using a hydroxyapatite composition with collagen in a 30%:70% ratio [14], [15].

The dynamics of structural tissue restructuring in animals of group III indicates a high biocompatibility and pronounced osseointegrative ability of this material, which confirms its prospects

for use in surgical dentistry and sinus-lifting operations.

Conclusion

The results of histological examination of the parenchymal organs of experimental animals (rabbits) using osteoplastic material based on hydroxyapatite showed the presence of moderately pronounced and unpronounced morphological changes represented by fatty degeneration and venous hyperemia, which may be associated with hypoxic processes. The identified changes are nonspecific and are likely due to a combination of factors, including the conditions of keeping the experimental animals, the peculiarities of the diet, as well as the influence of operational and experimental stress, rather than the direct toxic effects of the studied material. In all series of experiments, the histological structure of internal organs generally maintained its architectonics.

Signs of pronounced toxic effects, including necrotic changes, parenchyma destruction, and gross vascular disorders, were not detected. Thus, the obtained data indicate that the use of osteoplastic material based on hydroxyapatite does not lead to the development of toxic damage to internal organs and can be considered safe under experimental preclinical studies.

References

- [1] J. Arcas-Sanabre, J. Gutierrez-Santamaria, J. López-López, R. Ayuso-Montero, and E. Velasco-Ortega, "Horizontal augmentation of the maxillary alveolar ridge to change the prosthetic profile: Clinical and radiological results of a retrospective study," *Journal of Stomatology, Oral and Maxillofacial Surgery*, vol. 121, no. 1, pp. 25–29, 2020.
- [2] S. A. Bayadilovich and S. K. Erkinovich, "The role of preliminary expansion of soft tissues before GBR," *World Bulletin of Public Health*, vol. 13, pp. 206–209, 2022.
- [3] D. Isanova and O. A. Mukimov, "Evaluation of the sensitivity of microflora of the periodontal pocket to antibacterial agents in the conditions of the rural population," in *Library*, vol. 19, no. 2, pp. 157–159.
- [4] O. I. Radjabov, D. R. Usmanova, K. E. Shomurodov, A. Y. Atazhanov, and A. S. Turaev, "Preclinical studies of injectable collagen solution," in *Proc. III Int. Sci.-Pract. Conf. "Modern Pharmacy: New Approaches in Education and Current Research"*, 2023, pp. 128–129.
- [5] O. I. Radjabov, D. R. Usmanova, A. Y. Otajonov, K. E. Shomurodov, and A. S. Turaev, "Biological activity of collagen-based biomaterials," in *Proc. Int. Conf. "Actual Problems of Development of Bioorganic Chemistry"*, Nov. 13–14, 2023.
- [6] D. R. Usmanova and K. E. Shomurodov, "Analysis of the use of collagen preparations for increasing gingival volume," *Integrative Dentistry and Maxillofacial Surgery*, no. 1, pp. 9–16, 2023.
- [7] A. B. Shukparov, K. E. Shomurodov, and R. S. Mirkhusanova, "Microcirculation of the mucosa of the alveolar ridge during the preliminary soft tissues expansion and guided bone regeneration (clinical trial)," *European Journal of Modern Medicine and Practice*, vol. 2, no. 9, pp. 64–72, 2022.
- [8] K. E. Shomurodov, R. S. Mirkhusanova, and N. Sh. Zhurakulov, "The significance of keratinized gingiva in prosthetics supported by dental implants and methods of increasing its width (review)," *Integrative Dentistry and Maxillofacial Surgery*, vol. 2, no. 1, pp. 82–89, 2023.
- [9] D. Buser, W. Martin, and U. Belser, "Optimizing esthetics for implant restorations in the anterior maxilla," *International Journal of Oral & Maxillofacial Implants*, vol. 19, pp. 43–61, 2004.
- [10] J. Buser, D. Dula, H. Belser, U. Hirt, and H. P. Berthold, "Localized ridge augmentation using guided bone regeneration," *International Journal of Periodontics and Restorative Dentistry*, vol. 13, pp. 29–45, 1993.
- [11] T. Berglundh, I. Abrahamsson, and J. Lindhe, "Bone reactions to long-standing functional load at implants," *Journal of Clinical Periodontology*, vol. 32, pp. 925–932, 2005.

- [12] N. P. Lang and J. Lindhe, *Clinical Periodontology and Implant Dentistry*, 6th ed. Oxford, UK: Wiley-Blackwell, 2015.
- [13] D. Hämmerle and J. Jung, “Bone augmentation by means of barrier membranes,” *Periodontology 2000*, vol. 33, pp. 36–53, 2003.
- [14] M. A. Nevins and H. L. Mellonig, “Enhancement of the damaged edentulous ridge to receive dental implants,” *International Journal of Periodontics and Restorative Dentistry*, vol. 12, pp. 96–111, 1992.
- [15] T. Urban, Z. Lozada, and G. Jovanovic, “Vertical ridge augmentation and guided bone regeneration,” *Clinical Oral Implants Research*, vol. 20, pp. 69–81, 2009.