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Review article

Overview of the Possibility of Bone Replacement for the Purpose of Pre-Prosthetic Preparation of the Patient

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SUMMARY

Introduction. The loss of the jaw bone, especially in the area of the alveolar process, can significantly complicate the procedure of prosthetic rehabilitation of prosthetic patients. The reason for the loss of the jaw bones are physiological and pathological processes.
Materials. Bone replacements are widely used in the reconstruction of bone defects. The optimal characteristics of these materials are biocompatibility, bioinertness, biofunctionality and a special canalicular and intercanalicular system. Alloplastic bone replacements are inorganic, synthetic, biocompatible and bioactive bone replacements with osteoinductive potential. Hydroxyapatite is a preparation based on calcium phosphate. It has high biocompatibility, low immunogenicity and good osteoconductive characteristics. Poor properties are poor mechanical resistance as well as a low degree of resorption. Therefore, the research of chemically modified hydroxyapatites containing different ions was started.
Conclusion. Calcium ions can be replaced by various metal ions like cobalt, aluminum, nickel, manganese, chromium, copper in a liquid medium.

Keywords: **bone replacements, hydroxyapatite, biocompatibility, metal ions**

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INTRODUCTION

Loss of the jaw bone, especially in the area of the alveolar process, can significantly complicate the procedure of prosthetic rehabilitation of prosthetic patients. Oral conditions often require additional skills to complete surgical augmentation of the alveolar process.

Physiological and pathological processes are the cause of the jaw bones' loss. In accordance with the systemic loss of bone mass, there is a decrease in the amount of jaw bone, primarily in the height of the alveolar process. Usually, atrophic changes are combined with resorption of the alveolar ridge, e.g. after tooth extraction or advanced changes to the tooth support structures (1).

There are many causes that lead to bone loss, so that defects can occur that can make prosthetic rehabilitation difficult or in rare cases impossible. The alveolar ridge can be resorbed in the vertical (height) and in the horizontal direction (width), as well as in combination. Bone loss is more common in the elderly when the body's regenerative and reparative capabilities are reduced (2).

Periodontal disease is of the greatest importance for the loss of the jaw bone tissue, considering the frequency of the disease and the chronic course. Periodontitis leads to the formation of bone pockets that sometimes reach the very top of the tooth root, and in the final stage, a complete loss of the supporting structures of the tooth. The use of alloplastic materials can be of great help in order to preserve teeth whose supporting structures are affected by a pathological process.

With the growth of cysts, bone tissue is suppressed, resulting in bone defects that can reach significant dimensions. In such cases, the use of biomaterials is of great importance because the reparative abilities of bone tissue are usually not sufficient to repair the resulting bone defects.

Resorption of the ridge after tooth loss can interfere with the production of total dentures especially in the lower jaw, making it impossible to achieve a valve effect. Bone deficiency disrupts the implantation procedure.

BONE REPLACEMENTS

Bone replacements are widely used in the reconstruction of bone defects. The optimal characteristics of these materials are biocompatibility, bioinertness, biofunctionality and the existence of a special canalicular and intercanalicular system. Their application is based on their properties to act (3):

- osteogenetic (material contains cells responsible for bone synthesis - osteoblasts)
- osteoinductive (material induces the differentiation of pluripotent stem cells into the osteoblast phenotype leading to bone synthesis)
- osteoconductively (the material stimulates the growth of bone over its surface by representing a matrix for the growth of new bone and a depot of minerals).

Bone grafts and bone replacements are classified into four groups: autogenous bone grafts, allogeneic bone grafts, xenogeneic bone grafts, and alloplastic bone substitutes. An autogenic graft (autotransplant) belongs to the same organism, an allograft is from another person, while a xenograft is of animal origin (4).

Donor sites for autotransplantation are localized in the oral cavity if the bone defect is small or extraoral (crista iliaca and calvaria), in case of major bone damage. In any case, there must be no consequence at the donor site after taking the transplant (5, 6).

Bone is the most commonly transplanted tissue in the human body. Given the shortcomings (rejection and resorption) and partial obsolescence of bone grafts, alloplastic bone implants can be considered modern bone substitutes (7).

ALLOPLASTIC BONE REPLACEMENTS

Alloplastic bone replacements are inorganic, synthetic, biocompatible and bioactive bone replacements with osteoinductive potential. They are divided into resorptive (beta-tricalcium phosphate, calcium sulfate, calcium carbonate) and non-resorptive (porous and non-porous hydroxyapatite, bioglass and polymers).

Calcium orthophosphates

Calcium orthophosphates are widespread in nature. The mineral part of bones as well as teeth is tricalcium phosphate (Ca_3 (PO_4) 2) which is equated with hydroxyapatite (HA) in the literature. There are certain differences between biological and stoichiometric apatites, small crystal dimensions as well as a lower degree of crystallization. Biological apatites also contain other ions, either bound in the crystal lattice itself or adsorbed on the crystal surface. Calcium phosphates that occur in biological tissues include amorphous calcium phosphate, dicalcium phosphate dihydrate, octacalcium phosphate, Mg-altered-β-tricalcium phosphate (1). These materials are placed in bone defects in order to stimulate the regeneration of lost tissue. β-tricalcium phosphate (β-TCP) is very rapidly resorbed or encapsulated with a binder with minimal bone regeneration and incomplete regeneration of other parts of the periodontium.

Hydroxyapatite

Hydroxyapatite (HA) is a preparation based on calcium phosphate ($Ca_{10}(PO_4)_6(OH)_2$). It is used in the form of resorptive and non-resorptive particles. From a chemical and structural point of view, it is a material that is most similar to the mineral components of bones and teeth (8). Better bone replacement acceptance is provided by the use of a matrix, most commonly polylactic acid/polyglycolic acid copolymer (PLGA) (9).

Hydroxyapatite has high biocompatibility, low immunogenicity and good osteoconductive characteristics. Poor properties are poor mechanical resistance as well as a low degree of resorption. Therefore, the research of chemically modified hydroxyapatites containing different ions was started.

Calcium ions can be replaced by various metal ions (cobalt, aluminum, nickel, manganese, chromium, copper) in a liquid medium. The surface configuration, morphology and crystal structure change depending on the amount of metal ions. It has been observed that the addition of lead, nickel and copper ions to hydroxyapatite changes the activity of this material (10). The surface structure of hydroxyapatite in which calcium ions are replaced by metal ions is not sufficiently known. Data on the surface of modified hydroxyapatite can give us new insights not only in the mechanism involved in the adsorption and catalysis of this material, but also in the surface characteristics of bones and teeth where such material has been applied (11).

Manganese is an important element for the synthesis of mucopolysaccharides and its deficiency causes a decrease in the synthesis of the organic matrix and slows down enchondral osteogenesis, which results in a decrease in bone thickness or length and their deformation. Manganese ions (Mn^{2+}) are thought to have an effect on the activation of integrins, receptors that are important for mediation between cells and the extracellular matrix and ligands on the cell surface (12). In the presence of these ions, the activity of ligands increases and cell adhesion is enhanced. Manganese regulates bone remodeling. Its low concentration leads to an increase in the concentration of calcium, phosphate and phosphatase outside the cells. Manganese deficiency is considered a predisposing factor for osteoporosis (13, 14).

The cytotoxic effect of manganese-modified hydroxyapatite (Mn-HA) was investigated on human osteoblast cell lineage (15). Compared with pure hydroskiapatite, Mn-HA showed slightly higher absorbance values, and it can be concluded that Mn-HA does not possess cytotoxic properties, although additional research related to cell adhesion is needed to confirm the increase in bioactivity compared to pure hydroxyapatite (15).

Bigi et al. determined the effect of Mn^{2+} on osteoblast proliferation. They reported that synthetic HA with added manganese on the titanium surface allows for similar osteoblast differentiation as in bone tissue, although there is a significant difference in the degree of crystallization (16)

Paluszkiewicz et al. found in their study (17) that the number of cells grown on the surface of hydroxyapatite with Mn^{2+} was reduced compared to unmodified hydroxyapatite and positive control. In contrast, adequate cell morphology determined by their adherence and proliferation was confirmed.

Hydroxyapatite containing iron particles can be synthesized by the method described by Suchanek et al. (18). The Fe_3O_4 particles obtained in this way were scanned by TEM (19), where it was found that iron oxide nanoparticles were incorporated into the hydroxyapatite layer. The nanoparticles had similar properties after binding to hydroxyapatite.

The research of De Lima et al. on hydroxyapatite modified with lead, strontium, cobalt, zinc, iron, copper and magnesium ions is included. Although the materials proved similar in most physicochemical tests, there was a difference in biocompatibility. Cell cultures incubated with iron, cobalt, lead, and strontium-modified hydroxyapatite behaved very similarly to incubation with pure hydroxyapatite, while incubation with magnesium-modified hydroxyapatite led to a significant increase in fibroblast density. The analysis in this study also confirmed that hydroxyapatite cannot cause apoptosis. In contrast, samples of hydroxyapatite modified with cobalt as well as magnesium led to a high degree of apoptosis (20).

Calcium ions can be replaced by copper ions as well as titanium ions. In the conducted research (21), the nanoparticles of modified hydroxyapatites observed by SEM did not differ significantly in relation to the particles of pure hydroxyapatite. Antibacterial tests showed a positive correlation between the presence of copper ions and antibacterial effect. In contrast, the antibacterial effect of titanium ion-modified hydroxyapatite was negligible (21).

Calcium sulfate

Calcium sulfate is a mineral that is quite widespread in nature in various forms (alabaster, plaster, selenite). It consists of calcium sulfate dihydrate ($CaSO_4x2H_2O$). It is white, hard, insoluble in a large number of organic solvents. Lowering the pH of the medium increases its solubility. Medical calcium sulfate has satisfactory resistance to pressure, while its resistance to stretching is weaker compared to spongy and cortical bone. The disadvantage of the application of calcium sulfate is its rapid resorption if used in the treatment of bone defects, crumbliness and contamination with blood and fluid, which negatively affect the properties of the material. Therefore, it is necessary to apply a material with sufficient chemical purity and particle size; the place for implantation must be as moist as possible and with as many supporting bone walls as possible. The advantage of using calcium sulfate is its biocopatibility. After implantation of this material, inflammatory reaction is not present.

Polymers can also be used to fill bone defects. The most commonly used is non-resorptive copolymer of polymethyl methacrylate (PMMA) and polyhydroxymethyl methacrylate (PHEMA) coated with calcium hydroxide and polymer-resorbable polylactic acid (PLA).

Bioactive glasses or bioglass (SiO_2, Na_2O and P_2O_5) can be resorptive and non-resorptive depending on the size of the granules. A double layer of silicon gel and calcium phosphate is formed on their surface under the influence of tissue fluids.

CONCLUSION

The use of bone substitutes is invaluable for the outcome of dental prosthetic therapy. The use of biomaterials has become a routine procedure in the treatment of numerous pathological conditions. Hydroxyapatite has the greatest application due to its great resemblance to bone tissue. With the development of manufacturing technology, it is possible to further improve the material by modifying the chemical structure, which results in better material characteristics in order to regenerate the lost bone tissue.

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Pregled mogućnosti nadoknade kosti u cilju pretprotetske pripreme pacijenta

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SAŽETAK

Uvod. Gubitak kosti vilica, posebno u predelu alveolarnog nastavka, može značajno otežati proceduru protetske rehabilitacije protetičkih pacijenata. Razlog gubitka viličnih kosti jesu fiziološki i patološki procesi.
Materijal. Koštani zamenici imaju široku primenu i u rekonstrukciji defekata kostiju. Optimalne karakteristike ovih materijala su biokompatibilnost, bioinertnost, biofunkcionalnost i poseban kanalikularni i interkanalikularni sistem. Aloplastični koštani zamenici su neorganski, sintetski, biokompatibilni i bioaktivni zamenici za kost sa osteoinduktivnim potencijalom. Hidroksiapatit predstavlja preparat na bazi kalcijum–fosfata. Poseduje visoku biokompatibilnost, nisku imunogenost i dobre osteokonduktivne karakteristike. Loše osobine su slaba mehanička otpornost kao i nizak stepen resorpcije. Zbog toga se pristupilo istraživanju hemijski modifikovanih hidroksiapatita koji u sebi sadrže različite jone.
Zaključak. Joni kalcijuma mogu biti zamenjeni različitim metalnim jonima kao što su kobalt, aluminijum, nikl, mangan, hrom, bakar u tečnoj sredini.

Ključne reči: **koštani zamenici, hidroksiapatit, biokompatibilnost, joni metala**