Implantology

Annals of Oral & Maxillofacial Surgery
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Critical review

Synthetic materials used for the substitution of bone defects

SY Ivanov*, RF Mukhametshin, AA Muraev, DV Solodkaya

Abstract

Introduction

The need for bone substitution materials has been increased due to teeth loss, trauma, tumour and bone reconstructive surgery. Various types of bone grafts have been developed to repair craniofacial bone defects over many years. Here, an analysis of Russian and foreign sources of literature, reflecting the characteristics of synthetic bone graft materials used in modern dental practice to fill bone defects, has been done. The importance of developing a new generation of synthetic material to replace bone defects is emphasized. The aim of this critical review is to discuss the synthetic materials that can be used as a substitute for bone defects.

Conclusion

New materials will allow bone tissue regeneration and defect reconstruction. We call on more research into this topic to increase our understanding and improve materials we currently use or discover a better suited material.

Introduction

Various materials are used in modern dental and maxillofacial surgery for bone tissue substitution and reconstruction. All osteoplastic materials can be divided into four groups by origin: autogenic (the donor is the patient), allogenic (the donor is another person), xenogenic (the donor is an animal) and synthetic (on the basis of calcium salts).

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Successes achieved in the development of xenogenic and synthetic biomaterials, which possess osteoconductive and osteoinductive properties, allow a decrease in the use of auto- and allotransplantation methods that possess a certain number of disadvantages. Autogenous bone graft harvesting may be accompanied by complications including vessel and nerve damage, hematoma formation or development of an inflammatory infection process. Apart from that, autobone grafts are often resorbed faster than their integration and reconstruction of the bone defect[1]. Bone allotransplants, on the contrary, are characterized by slow osteointegration. Their use implies a risk of transferring various diseases of bacterial or viral aetiology from the donor to the recipient because of the possibility of developing a histoincompatibility reaction and chronic granulomatous inflammation[2].

The main drawback of synthetic materials, unlike auto-, allo- and some xenomaterials, is the fact that they lack osteoinductive properties. The term 'osteoinduction' is defined by some authors as the ability of an osteoplastic material to form *de novo* ectopic (outside the bone) bone tissue[3]. However, the ability of bone graft materials to stimulate regeneration of the bone tissue may be attributed to osteoinduction. Such biological activity may be determined by including sulphated glycosaminoglycans, amino acids, growth factors and morphogens into the bone graft material. The ability to cause ectopic osteogenesis is characteristic for a number of representatives of the bone morphogenic protein (BMP) family and was first demonstrated by MR Urist in 1965[4]. The main inducing action of BMPs includes their impact on the proliferation of osteoblasts and the differentiation of mesenchymal precursor cells in the direction of osteogenesis and angiogenesis.

The development of new medical technologies enables use of achievements in material science, biochemistry, molecular biology and genetic engineering while creating new combined synthetic materials for bone grafting (osteoplasty). Modification of their bulk structure, which brings their structure closer to natural bone tissue, including cytokines—growth factors and morphogens—into their composition enables to provide synthetic materials with not only osteoconductive but also osteoinductive properties. This also enables to control the speed of biodegradation, bringing it closer to the kinetics of osteogenesis.

The aim of this critical review is to assess the synthetic materials that can be used as replacements of bone defects.

Discussion

In the present critical review, an attempt has been made to summarize and analyse the results of studies and developments in the field of synthetic osteoplastic materials.

Synthetic resorbable materials were intended as an inexpensive substitute for natural hydroxyapatite (HAP)[5]. Synthetic graft materials include various types of calcium phosphate ceramics: tribasic calcium phosphate (CP); bioglass; HAP and its compositions with collagen, sulphated glycosaminoglycans such as keratan and chrondroitin sulphate as well as with sulphate and CP[6]. At present, many various forms of porous nanostructured CP ceramics, bone cements, biohybrids and biocomposite compounds have been created on the basis of HAP.

For citation purposes: *Ivanov SY, Mukhametshin RF, Muraev AA, Solodkaya DV.* Synthetic materials used for the substitution of bone defects. Critical review. Annals of Oral & Maxillofacial Surgery 2013 Feb 01;1(1):4.

Competing interests: none declared. Conflict of Interests: none declared.
All authors contributed to the conception, design, and preparation of the manuscript, as well as read and approved the final manuscript.
All authors abide by the Association for Medical Ethics (AME) ethical rules of disclosure.

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Synthetic materials on the basis of artificial HAP surpass HAP of animal origin by a number of features. They exclude the possibility of carrying communicable diseases and enable the regulation of resorption speed due to peculiar features of the synthesis and various ratios of phosphate and hydroxyl group within the apatite structure. This characterizes synthetic HAP as a promising osteoplastic material to be used in all areas of bone reconstructive surgery.

Synthetic preparations are differentiated by dissociation and resorption degree, which is largely related to the amount of intercellular fluid and osteoclastic activity. Materials with a low dissociation and resorption degree may include certain synthetic granulated HAP, bioglass and biositall preparations[7].

Among materials with a high resorption, solution and dissociation rate and, consequently, a high degree of metabolic activity, tribasic calcium phosphate (TCP) and calcium sulphate can be named[8].

TCP materials belong to the group of bioactive materials, which facilitate the formation of newly-formed bone on their surface and firm chemical linkages. These biomaterials facilitate attaching, proliferation, migration and phenotypic expression of the bone cells, which leads to apposition growth of the bone on the graft surface. They are also capable of adsorbing proteins, which stimulate the function of osteoclasts and osteoblasts and inhibit the function of competing cells, in particular fibroblasts responsible for the formation of connective tissue[9,10].

Despite the aforementioned positive biological properties, the drawback of most CP materials is poor mechanical durability and slow resorption in the body tissues.

Ceramic materials

Synthetic HAP is used in the form of non-porous (non-resorbable) and porous (resorbable) ceramics. Non-porous ceramics as if ‘gets immured over itself’ by bone during a long period within the body. No osteogenesis takes place directly in the area occupied by the bone[11].

Porous HAP ceramics is an osteoconductor, i.e. a conductor of the regenerate, which grows through the implant. One of the forms of porous ceramics used is its granulate. After implantation of high temperature ceramic granulates into bone defects, histological evaluation shows extension growth of the connective tissue and the osteogenic cells present within it. This served as the base for using this material as a surface coating for endoprostheses, osteosynthesis constructions and dental implants. The process is most intensive primarily near the surface of HAP particle conglomerates close to the source of osteogenic cells (bone defect walls)[12].

Nanosized HAP

Within bone tissue, HAP is present in the form of nanosized crystals; therefore, the next stage of developing materials on the basis of CP and HAP became the creation of nanocrystals. CF nanocrystals possess two properties which are most important for the physiology of bone tissue: they are in a dynamic equilibrium with their biological environment in the remodelling cycle (resorption/mineralization and manifest a high level of mechanical properties. Nanocrystalline HAP possesses an enhanced capability to adsorb proteins required for the vital activity of the cells, as well as discrimination regarding the function of the cells which form osseous and fibrous tissues[13]. It has been demonstrated on a model of nano-HAP heterotopic implantation that certain CP materials possess osteoinductive properties that are largely determined by the geometrical characteristic of the material[14,15].

Earlier preclinical studies have shown that nanostructural HAP obtained at temperatures below 60°C possesses a significantly larger capability to stimulate reparative osteogenesis compared with its polycrystalline (high-temperature) analogue[16]. Nanocrystals of biological HAP make the bone harder and stiffer, whereas collagen fibres ensure elasticity and high cracking resistance as well as an adequate resorption and bone regeneration rate[17].

Combined synthetic materials

Using fine-dispersed forms of the material is not convenient in clinical practice. Therefore, combined forms are developed which consist of a polymeric matrix (on the basis of polylactide, polyoxybutyrate, polyglycolic acid and their combinations) and nano-HAP as a filler. The appearance of composites made of synthetic HAP in the form of powders, granules and gels in combination with the polysaccharides chitosan, alginate[18,19], hyaluronic acid, the protein collagen, peptides[20], embryonic stem cells[21], medications and other preparations expanded the possibilities of reconstructing pathologically modified mineralized tissues[22,23].

BMPs are true osteoinductors and are able to facilitate ectopic bone formation. The combination of BMP with materials, which can deliver proteins, demonstrated maximum therapeutic effect of BMP. HAP with its osteoconductive properties is the best carrier for BMP. As studies performed by Rohanizadeh demonstrated, the best way of combining them is including BMP into the composition of HAP[24].

It has been demonstrated that CP paste in combination with rhBMP-2 accelerates the healing of bone tissue and leads to the restoration of mechanical properties equivalent to those in a normal bone. In an experimental model, on the fibula of primates after osteotomy, the use of rhBMP-2/α-BSM paste accelerated the healing of the bone by approximately 40%[24].

CAD/CAM technologies are actively used in dentistry for the manufacturing of inlays, veneers, crowns and dental bridges when restoring teeth. Computer modelling, based on CT scans of bones, and manufacturing individual bone grafts

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Competing interests: none declared. Conflict of interests: none declared.
All authors contributed to the conception, design, and preparation of the manuscript, as well as read and approved the final manuscript.
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is a promising technology for reconstruction of irregularly shaped bone defects of the jaws and facial bones.

In an experimental animal study[25], interesting results have been demonstrated in the reconstruction of multi-wall bone defects in the alveolar process of the maxilla by using ceramic implants produced by three-dimensional impression method. The implants had smooth microarchitectonics with the size of the pores being 120 ± 20 µm; their shape fully corresponded to the formed defects. The osteoinductive properties were determined by introducing BMP-2 into the implant composition. Data obtained in the work demonstrate that ceramic materials on the basis of HAP manufactured by 3D prototyping in combination with morphogenetic proteins have distinct possibilities regarding their use for bone tissue engineering, with the main advantage being a fully configurable 3D structure and shape.

Conclusion

Thus, the analysis of the available literature enables us to conclude that the development of new osteoplastic bone grafting materials pursues two main goals: optimization of bone tissue regeneration and bone defect reconstruction. Apparently in the future, individual artificial ceramic implants on the basis of HAP, containing a combination of growth factors and morphogens, e.g. BMP and vascular endothelial growth factor, will be created. Such an approach may possibly offer the possibility of effectively implementing bone tissue bioengineering in various clinical situations.

Abbreviations list

BMP, bone morphogenic protein; CP, calcium phosphate; HAP, hydroxyapatite; TCP, tribasic calcium phosphate.

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FOR CITATION PURPOSES: *Ivanov SY, Mukhametshin RF, Muraev AA, Solodkaya DV.* Synthetic materials used for the substitution of bone defects. Critical review. Annals of Oral & Maxillofacial Surgery 2013 Feb 01;1(1):4.

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All authors contributed to the conception, design, and preparation of the manuscript, as well as read and approved the final manuscript.
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