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Cardoso, Camila L.; Curra, Cláudia; Santos, Pâmela L.; Rodrigues, Maria F.M.; Ferreira-
Júnior, Osny; de Carvalho, Paulo S.P.

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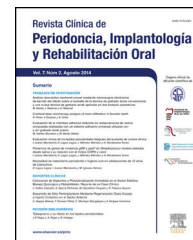
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REVIEW ARTICLE

Current considerations on bone substitutes in maxillary sinus lifting



Camila L. Cardoso^a, Cláudia Curra^a, Pâmela L. Santos^{a,*}, Maria F.M. Rodrigues^a, Osny Ferreira-Júnior^b, Paulo S.P. de Carvalho^b

^a Department of Oral and Maxillofacial Surgery, University of Sagrado Coração, Bauru, São Paulo, Brazil

^b Department of Oral and Maxillofacial Surgery, University of São Paulo, Bauru, São Paulo, Brazil

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Abstract The procedure of maxillary sinus lifting using autogenous bone was considered the reference standard choice for oral rehabilitation in cases of severe atrophic maxilla. However, it is not always a viable option, due to the limitations or morbidity caused by grafting techniques. This has led to the development of bone substitutes, which have been elaborated and improved. Choosing the best biomaterial becomes difficult due to the wide variety of bone substitutes. The aim of this article is to present some of these materials that are reported in the current scientific literature for maxillary sinus lifting.

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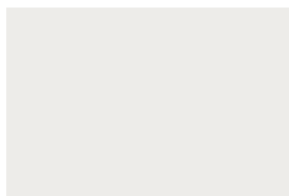
Seno maxilar;
Sustitutos de huesos;
Materiales
biocompatibles

Consideraciones actuales sobre sustitutos óseos en elevación del seno maxilar

Resumen El procedimiento de elevación del seno maxilar utilizando hueso autógeno se consideraba la opción estándar de oro para la rehabilitación oral en casos de maxilar atrófico grave. Sin embargo, no siempre es una opción viable, debido a las limitaciones o a la morbilidad causada por técnicas de injerto, lo que justifica la existencia de sustitutos óseos que han sido elaborados y mejorados. En cuanto a la amplia variedad de sustitutos óseos, se hace difícil la mejor elección de biomaterial. El objetivo de este informe es presentar una variedad de

* Corresponding author.

E-mail address: pamelalsantos@hotmail.com (P.L. Santos).



sustitutos óseos respetados en la literatura científica actual, usados en la elevación del seno maxilar.

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Introduction

Over the past 40 years, the dental implant osseointegration has been considered the greatest scientific discovery for dentistry, since its first description by offering an alternative of oral rehabilitation.¹ However, there are some individual limitations including the bone insufficiency, which is common after tooth loss associated with absence of functional stimulus in the site.² After tooth extraction, the alveolar bone undergoes an additional atrophy as a result of natural remodeling process. This process begins immediately after extraction and may result up to 50% of ridge width resorption, within 3 months.³ Deficiency in bone volume in the posterior maxilla is one of the most common problems to the implantodontist to plan an implant supported prosthesis. This is because the maxillary sinus in the absence of teeth tends to pneumatized reducing the height of alveolar ridge, hindering the installation and/or initial stability of the implant required to the prosthetic support. Against this problem, authors have created a procedure to increase bone volume of atrophic jaws through the maxillary sinus lifting.^{3,4}

In the literature, the autogenous bone graft is considered as "gold standard", because it presents the characteristics considered ideal: osteogenesis, osteoinduction and osteoconduction.⁵ However, the techniques of bone grafting and partial reconstruction of the jaws are planned according to the degree of bone loss, surgical prosthetic planning, the patient's systemic condition and the viability of the donor area. The major limitation of intraoral autogenous bone is the need of more surgical intervention and the morbidity of the donor area, apart from the limited amount of autogenous bone. Extraoral donor areas also have some disadvantages or limitations such as the need for hospitalization, morbidity of the donor area, higher cost and, particularly, in the case of the Iliac crest, one post-operative riskier in relation to infections, injuries to nerves and functional disability.⁶ In addition, there are reports on significant levels of bone reabsorption when only the autogenous bone is used, requiring an alternative consideration of bone substitutes.^{7,8}

As a priority to minimize patient's morbidity, bone substitutes are becoming increasingly improved. On the wide variety of bone substitutes, it becomes difficult to choose the best product.^{9,10} The aim of this paper is to present to surgeon dentist the variety of bone substitutes applied in maxillary sinus lifting, enshrined in the current scientific literature.

Materials and methods

The proposal of this study was to inform the surgeon on suitable bone substitutes regarding the world scientific literature. The search was based on scientific researches published in English including systematic reviews and also animal and human studies. The exclusion criteria were case reports and discussion articles. The inclusion criteria assumed the studies published in English from 1980 to 2014 searched at Medline (Pubmed) and Bireme databases. The keywords "bone substitute," "bone repair", "bone modeling", "maxillary sinus lifting", "biomaterials" and "grafting" were used for searching.

Literature review

Fundamental considerations on bone substitutes

There are four main characteristics considered ideal in bone regeneration, those of which at least one bone substitute must present.^{8,9} The first main feature is the osteogenesis or osteogenic activity (ability of bone formation from viable osteoblasts or pre-osteoblasts derived from the graft donor area, which are capable of generating cellular proliferation and producing new bone).⁸⁻¹¹ The second property is the osteoconduction (the capacity of the graft for support or allow cell migration, formation of blood vessels and the bone growth in surface), and the osteoinductivity (refers to the ability of a graft to induce nondifferentiated stem cells or osteoprogenitor cells to differentiate into osteoblasts).^{8,9} Finally, the osseointegration, which is the ability of chemical contact between the bone surfaces without the fibrous tissue's presence.¹⁰ It is fundamental the presence of at least one of the characteristics described above and only autogenous bone presents them all.

Other characteristics considered ideal include: the remodeling of the bone initially formed in mature lamellar bone as a function of time passing, ability to stabilize implants when installed simultaneously to the grafting procedure, low risk of infection, good availability, low antigenicity and physiologically stable, not cause rejection and be ideally be absorbed after the regeneration.¹¹

Classification of bone substitutes

Considering the limitations, disadvantages and morbidities associated with use of autogenous bone in maxillary sinus lifting, bone substitutes were introduced as an alternative,

using two criteria for clinical success: osteoconduction and/or osteoinduction. The major advantages are easy sterilization, storing, handling and purchasing the bone substitute based on the preferences and needs of each case. They are totally synthetic or present animal origin. The bone substitutes of animal origin may be derived from xenogenic and allogenic and, those fully synthetic or alloplastic, can be divided into: polymers, ceramics, metallic and composites. In addition, growth factors have been used more recently.⁹ In this work, the classification on bone substitutes follows some authors,⁹ which takes into consideration its main composition, since they may present associations of more than one material.

Allogenic bone graft

The allogenic bone implant is a bone substitute widely used in reconstructive surgery and it can be used alone or in combination with other biomaterials. It is an alternative that offers great similarity with autologous bone, except for the preservation of osteogenic cells. Furthermore, it has osteoconductive properties.^{11,12} Its main advantage compared to autogenous bone is the elimination of a second surgical site to reduce morbidity to the patient.⁹ Furthermore, they may be available in large volumes in large bone defects, also they are capable of providing structural support.¹⁰ However they present some limitations such as the absence of many bone bank, high cost and strict control to prevent disease transmission, besides presenting negative aspects such as risk of infection. There are no studies presenting long follow up.

The allogenic bone grafts are demineralized freeze-dried bone allograft (DFDBA) and demineralized bone matrix (DBM). The DBM is able to improve bone regeneration by their ability osteoconductive. They can often be associated with alloplastic biomaterials or xenogenic grafts to supply some deficiencies property.¹³ Authors demonstrated that the amount of bone formed depends on how the DFDBA is used.¹³

Although the allogenic bone grafts are treated by various methods considered safe such as freezing, gamma radiation and ethylene oxide, the risk of disease transmission from donor to receptor is not completely removed.⁹ The risk of bacterial infection is superior with increasing size of the graft and can be seen in more than 10% of cases. Viral transmission is a potential hazard, especially in relation to hepatitis B, C and HIV, although it has been documented unusual coming from cadaver donor.¹⁴ 25 cases of infection have been linked to this type of implant.¹⁴ It is noteworthy that, although many methods of sterilization are able to reduce the risk of infection, proteins and others factors responsible for osteoinductivity tissue are eliminated. It is noteworthy that this type of graft is banned in Europe and elsewhere.

Complications associated with allogenic bone graft include fractures, lack of osseointegration and infection.¹⁰ When allograft is performed it is difficult to evaluate the osseointegration. Some discrepancies were found between the radiological, clinical and microscopic findings. Absence of radiographic aspects of osseointegration can be expected in up 17% of cases using allogenic bone graft.⁹

Xenogenic bone graft

Bone substitutes whose main component is derived from xenogenic bone is called xenogenic bone graft. Xenogenic bone graft most commonly used is from bovine, after to

treat chemically the organic components and to leave their mineral structure. Equine and porcine sources are also common. Another source is from the exoskeleton of coral. Xenogenic bone grafts have show excellent osteoconductive properties.¹² Bio-Oss® (Geistlich Pharmaceutical, Wolhusen, Switzerland) is a bone substitute derived from deproteinized bovine bone marrow, with the hydroxyapatite structure of the highly porous bone, similar to the cortical bone of the human species. The organic components are removed chemically or heat leaving a skeletal support for osteogenic cells. In the literature, there are many studies which demonstrated excellent performance as a bone substitute, in its particulate form to fill bone defects.^{15,16} Also, it presents osteoconductive property acting as a scaffold for the deposition of new bone. Studies showed a slow degradation (between 3 and 4 years) or may be not completely degradable.^{16,17}

Several studies on animals and humans have demonstrated that this material is promising in comparison with other bone substitutes, because in maxillary sinus lifting Bio-Oss® demonstrated good clinical outcomes.¹⁷ Authors described an efficacy about 80–100% using Bio-Oss®, suggesting as effective as autogenous bone.¹⁸ Authors showed evidence of an increased radiographic density and stability of pure mineralized bovine bone as a graft to 1.5 years later, in the absence of dental implants.¹⁹

Evaluation of dental implants, installed in the region of maxillary sinus lifting using mineralized bovine bone (MBB), showed 63% of bone formation in contact with the implant surface,²⁰ 27%,²¹ and 38%²² after six months of follow up. Using only the MBB, 23% of newly formed bone was observed at 12 weeks, so it proved to be slowly reabsorbed and seems to behave as a semi-permanent bone substitute.¹⁶

Randomized clinical study evaluated 10 patients, two different forms of treatment in each maxillary sinus: a resorbable rigid membrane on the maxillary sinus and in the other, 100% of Bio-Oss®. The results after 6 months, demonstrated a statistically significant increase of bone between the groups and the microscopy of the bone was formed on the side of Bio-Oss® (36.1%) group compared to the membrane group (24.2%).²³ Authors analyzed these patients after one year and they did not demonstrate statistically significant difference in bone loss between the two groups (mean 1.5 mm in the membrane group and 1.7 mm in the in Bio-Oss® group).¹² In addition, differences statistically significant were not presented in the failure of implants, neither in the prostheses between the two groups.

Ceramic compounds

The bone substitutes made of ceramic are widely used associated or no with another biomaterial. There are many types of calcium phosphate (CaP) obtained by different methods of synthesis and nowadays, tricalcium phosphate (TCP) and hydroxyapatite (HA) are highly sought. Compounds of the base of calcium phosphate (CaP) have excellent biocompatibility,^{9,24} osteoconductive activity, and they are biodegradable.²⁵ HA is an inorganic compound which is very similar to the structure of the mineral phase of bone, but shows weak and slow degradation (1–2%/year).¹² However, TCP presents a very fast biodegradation rate, and is not always concurrently with the bone deposition.²⁶

The BoneCeramic® (Straumann®, Basel, Switzerland) is a completely synthetic biomaterial with osteoconductive property which favors the formation of vital bone.²⁷ It is composed of biphasic CaP (BCP), a combination of HA (60wt% and 40% TCP-B). Studies in peri-implant defects demonstrated bone around dental implants which have been placed in alveoli regeneration, immediately after tooth extraction. Microscopic and radiographic evaluation demonstrated regenerated bone with characteristics similar to those of bone located in areas without defect.²⁷ However, there are few reports using such material in humans or animals so that the authors suggest further studies.²⁷

Authors classify bioactive glasses and ceramics as the most promising fully synthetic ceramics, because they are inert, biocompatible and they present osteoconductive properties.²⁸ Bone substitutes composed of bioactive glass are reinforced by oxides (sodium oxide, calcium oxide, phosphorus pentoxide and silicon dioxide) and they allow an osseointegration with bone tissue, although not having good mechanical strength.

Several studies have examined the efficacy of bone substitutes compounds of bioactive glass and they demonstrated osteoconductive and they potentially can combine ability to bond to tissues (bioactivity).²⁹ When used in maxillary sinus lifting of 25 patients, Biogran® (Orthovita e 3i, ImplantInnovations, Inc, Palm Beach Gardens, FL) demonstrated bone growth, proving their osteoconductive properties.²⁹ Studies demonstrated high osteoconductive property followed maxillary sinus lifting, using hydrate bioactive glass with saline and later implant placement, suggesting its use isolated or associated with autogenous bone.³⁰ Other clinical studies have also indicated this bone substitute in maxillary sinus lifting procedure.³¹ The main advantages offered by bioactive glass is being absorbable, to present no risk of disease transmission and immune responses and to assist in hemostasis. The bioactive ceramics exhibit improved mechanical properties relative to bioactive glass, but they are still brittle enough to fracture when subjected to cyclic loading. In order to improve its resistance to fracture, methods of incorporating stainless steel and zirconia fibers have been performed. The use of Cerabone® (Botiss dental GmbH, Berlin, Germany) is referred to, in a systematic review, to be as effective as the use of autogenous bone in severe maxillary atrophy.¹² NanoBone® (Artoss GmbH, Rostock-Warnemünde, Germany) was also evaluated as a bone substitute and authors concluded that their use is reliable.³² Moreover, it seemed to be partially resorbed and replaced by new bone.³²

Polymeric bone substitutes

The use of biodegradable polymers as a scaffold for cell culture has emerged as an alternative in bone regenerative therapy. Several natural and synthetic polymers are being studied and biodegradable polymers are considered as the best candidates for the construction of scaffolds for the tissue repair.³⁹ Polylactic acid (PLA), polyglycolic acid (PGA) of polycaprolactone (PCL) and their copolymers are widely used in manufacturing scaffolds.³³ The choice of the biopolymer as a bone substitute is due to biocompatibility, reproducibility, porosity, cell adhesion ability, besides being easily manipulated.³⁴ Examples of biopolymers used

as tissue substitutes are polylactic acid (PLA), glycolic acid (PGA), polylactic-coglycolic acid (PLGA), polyethylene, polycaprolactone (PCL) and polymethyl methacrylate (PMMA). They can be used as a tissue scaffold or as a carrier of growth factors.

Authors evaluated microscopically the behavior of Fisiograft® (Ghimas SpA Casalecchioldi Reno, Italy) alone or associated with Bio-Oss® after maxillary sinus lifting in 16 patients.³⁵ They observed no inflammatory reaction in all samples. Fisiograft® was present after 7 months after surgery and the newly formed bone with or without beads of Bio-Oss® were within conjunctive, with primary structure of an immature bone associated with a good amount of lamellar bone.³⁵

A polymeric, biodegradable, biocompatible and osteoconductor bone substitute formed by the union of PLGA with two phases of CaP and an outer layer of CaP from 3 to 5 µm thick, was developed and its trade name is OsteoScaf™ (BoneTecCorp – TRT, Toronto, Canada).^{35,36}

OsteoScaf™ is manufactured by a process of leaching and phase inversion, from PLGA and two CaP phases both of which are resorbable by osteoclasts; the first a particulate within the polymer structure and the second a thin ubiquitous coating. The outermost layer, 3–5 µm thick osteoconductive surface CaP abrogates the putative foreign body giant cell response to the underlying polymer, while the internal CaP phase provides dimensional stability in an otherwise highly compliant structure. Still, it has sufficient mechanical strength to surgical manipulation and it can be easily fabricated, according to the desired shape and porosity. The aspects of porosity, of around 81–91% and size between 350 and 1200 µm, favor the absorption capacity of blood, allowing the retention of clots and resulting in an osteoconductive support for the growth of the host bone. Studies have revealed that it is a completely resorbable three-phase matrix, with highly interconnected macropores. Three dimensional matrices (scaffolds) made from this material, with similar porosity to human cancellous bone, have shown bone growth both in vitro and in vivo and offer great potential for application in bioengineering.^{34,36} As bone substitute in maxillary sinus lifting, OsteoScaf™ demonstrated both clinically and microscopically great performance and clinical success after two years of final rehabilitation with implants in one patient.³⁷

Discussion

In order to restore the bone volume of this region, the technique of elevation of the maxillary sinus membrane was developed without damaging the sinus membrane and over the years this procedure has been performed with a high degree of predictability and low rate of complications.³⁸ Currently, in order to reconstruct the atrophic maxillae, different bone grafting techniques have emerged as autogenous, homogenous and heterogenous grafts, as well as synthetic biomaterials.³⁹ The ideal bone graft should possess features like an unlimited supply, donor site without morbidity, lack of risk of disease transmission, high promotion in bone repair, provide immediate stability, versatility, excellent handling properties, adequate life cycle and affordable cost.⁴⁰

In order to overcome the limitations of autogenous bone, several studies, in humans and animals, searching the ideal bone substitute have been performed, in which the biomaterials are evaluated by their clinical, radiographic, histological and biomechanical aspects.⁴¹ However, despite the vast number of papers related to the rehabilitation of the posterior maxilla associated with bone substitutes, there is no standardization of the methods used for analysis hindering the election of the best biomaterial. Thus, this study aimed to present the clinical variety of bone substitutes applied in maxillary sinus lifting, enshrined in the current scientific literature.

Authors compared the response of the Bio-Oss® and the autogenous bone, in maxillary sinus lifting of dogs, in periods of 90 and 180 days, through histologic analysis. At 90 days showed that the percentage of the contact area bone/implant was 11.46% and 52.16% in the autogenous bone and Bio-Oss®, respectively. At 180 days, the Bio-Oss® continued with greater bone graft contact rate 63.43%, while the autogenous (42.22%). The authors believe that these results happened because Bio-Oss® acts as a permanent graft.²⁰ In the same experimental model, other authors evaluated histologically the simultaneous installation of endosseous implants after maxillary sinus lifting, including the filling of the cavity with lyophilized human cortical bone, resorbable hydroxyapatite or Bio-Oss®, at 150 days period.²¹ The results showed that in the maxillary sinuses filled with lyophilized bone grafts there was no new bone formation, different from those filled with natural hydroxyapatite or with Bio-Oss®, which showed new bone formation, with direct contact in the surface of implant.²¹

Authors compared different materials in maxillary sinus lifting in humans: autogenous bone, demineralized lyophilized bone graft, Bioglass®, PepGen P-15® (association of anorganic bovine material (Ca₂PO₄) with a synthetic biomimetic of the 15 amino acid sequence of Type I collagen, that is responsible for cell binding), calcium sulfate and Bio-Oss®.⁴² The sample comprised of 94 patients and 362 implants inserted, and each patient underwent biopsy within a 6 months period for subsequent histological analysis. The authors concluded that all particles of biomaterials used were surrounded by bone and all the analyzed biomaterials were biocompatible and improved the formation of new bone in maxillary sinus lifting. The data are very encouraging due to the high number of patients successfully treated and the good quality of the bones which were found in the specimens recovered.⁴³

Finally, the use of autogenous bone is not always a viable option, as seen previously, being the reason for the existence of bone substitutes. Despite the wide variety of bone substitutes available, more clinical studies are necessary, with high level of scientific evidence, analyzing the behavior of the implant with a long follow up, after maxillary sinus lifting, so that we can better conclude about the bone substitutes.

Conflicts of interest

The study was supported Drs. Camila Lopes Cardoso, Cláudia Curra, Pâmela Leticia Santos, Maria Flávia Milagre

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