



Main Approaches to the Use of Biomaterials in Oral and Maxillofacial Surgery: A Brief Systematic Review

Henrique Esteves Magalhães^{1,2}, Priscilla Janaína de Lima Borelli Bovo^{1,2}, Luciano Rodrigues Neves^{1,2}, Marcelo Henrique Batista Santos^{1,2}, Rogério Luiz de Araújo Vian^{1,2,3}, Idiberto José Zotarelli Filho^{4,*}, Elias Naim Kassis^{1,2}

¹ University Center North Paulista (Unorp) - São José do Rio Preto – SP, Brazil.

² Post graduate and continuing education (Unipos), Street Ipiranga, 3460, São José do Rio Preto SP, Brazil 15020-040.

³ Santa Casa Hospital-Bucomaxillo Facial Traumatology Center- Ribeirão Preto/SP, Brazil.

⁴ Zotarelli-Filho Scientific Work of Sao Jose do Rio Preto/SP, Brazil.

*Corresponding author Email: m.zotarelli@gmail.com

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Abstract: Introduction: In recent years, procedures with the use of dental implants have increased worldwide, reaching approximately one million dental implants per year. In recent years, a platelet concentrate called FRP (fibrin-rich plasma) has been the subject of clinical studies. Associated with this, the biomaterial Bio-Oss® (Geistlich), as it is biodegradable, biocompatible, non-toxic, and has low immunogenicity, and bio stimulators can act in the regeneration of bone tissue, as it establishes with the cells the appropriate biological niche (favorable microenvironment) for bone growth. **Objective:** Therefore, the present study aimed to evaluate, through a brief systematic review, the results that involve bone formation for dental implantation, with the use of biomaterials such as fibrin-rich plasma and Bio-Oss®. **Methods:** The model used for the review was PRISMA. Was used databases such as Scopus, Scielo, Lilacs, Google Scholar, PubMed. **Results:** Fibrin-rich plasma (FRP) as an autologous biomaterial for use in oral and maxillofacial surgery presents most leukocytes, platelets, and growth factors, forming a fibrin matrix, with three-dimensional architecture. The Bio-Oss® biomaterial (Geistlich), as it is biodegradable, biocompatible, non-toxic, and has low immunogenicity and bio stimulators can act in the regeneration of bone tissue, since it establishes with the adenomatous mesenchymal stem cells the appropriate biological niche for bone growth and, thus, allowing the dental implant to be as effective as possible. **Conclusion:** The use of FRP associated with Bio-Oss® seems to illustrate high success rates with minimal costs, which may reduce the amount of bone graft needed to fill the sinus cavity, reducing the costs of the procedure.

Keywords: Biomaterials, Bio-Oss®, Fibrin-rich plasma, Bucomaxillofacial surgery, Bone augmentation.

Introduction

In recent years, procedures with the use of dental implants have increased worldwide, reaching approximately one million dental implants per year [1]. In this sense, the development of biomaterials for use in dental clinics in recent years has represented a powerful therapeutic tool in the correction of bone defects and consequent effective action for the dental implant process [1,2].

Thus, maxillary atrophy is an increasingly frequent clinical condition and the causes that lead to focal or generalized atrophy are in multiple factors [3,4]. After the loss of the affected teeth, resorption is maximum in the first year and more pronounced in the anterior areas than in the posterior ones. Thus, in the

following years there is a minimal, but constant, decrease in the residual bone quantity [5,6].

Also, bone density influences the operative protocol and the choice of the type of implant used to replace missing teeth [6]. For a graft material to assume the role of insufficient bone substitute, it meets the criteria of biocompatibility, it has an optimal response to biomechanical stress, and a great capacity to replace the functions of synthesis/remodeling of the bone structure [1].

In this scenario, the gold standard is the use of autologous bone from the intraoral area with the greatest biocompatibility, due to the same embryogenic derivation and the presence of bone morphogenetic protein (BMP) favoring osteoinduction,

being the perfect material for sinus elevation. [7]. Also, it is the only material with osteogenic properties, in addition to osteoinductive and osteoconductive properties [2,8].

In this context, from the second half of the 1990s, the attention of the "Oral and Maxillofacial Surgery Community" was attracted by a series of scientific studies, which claimed that a platelet-derived growth factor could be valid not only for homeostasis but also bone graft field [9]. Thus, in recent years, a platelet concentrate called FRP (fibrin-rich plasma) has been the subject of clinical studies [10].

FRP belongs to a new generation of platelet concentrates. After the artificial and inflammatory hemostatic phenomenon induced by centrifugation, this concentrate releases different cytokines slowly and gradually, in addition to growth factors such as the vascular endothelial growth factor (VEGF). Thus, the FRP is then able to regulate inflammation and stimulate the immune process of chemotaxis [10,11].

Associated with this, the biomaterial Bio-Oss® (Geistlich), as it is biodegradable, biocompatible, non-toxic, and has low immunogenicity, and bio stimulators can act in the regeneration of bone tissue, as it establishes with the cells the appropriate biological niche (favorable microenvironment) for bone growth. With the use of Bio-Oss®, it is possible to obtain orthodontic movement in patients after treatment with bone regeneration. Also, resorbable membranes proved to be superior to non-resorbable membranes in the generation of vertical bone filling [2].

Therefore, the present study aimed to evaluate, through a brief systematic review, the results that involve bone formation for dental implantation, with the use of biomaterials such as fibrin-rich plasma and Bio-Oss®.

Methods

Clinical studies were included (case reports, retrospective, prospective and randomized studies) with qualitative and/or quantitative analysis. Initially, the keywords were determined by searching the DeCS tool (Descriptors in Health Sciences, BIREME base) and then verified and validated by MeSH System (Medical Subject Headings, the US National Library of Medicine) to achieve a consistent search.

Descriptors (MeSH Terms)

The main descriptors (MeSH Terms) used were "Biomaterials", "Bio-Oss®", "Fibrin-rich plasma", "Bucomaxillofacial surgery" and "Bone augmentation". For further specifications, the description "bone regeneration" for refinement was added during the research, following the rules of the systematic review-PRISMA (Transparent reporting of systematic reviews and meta-analyses- <http://www.prismastatement.org>).

The bibliographic search was performed using online databases Scopus, Scielo, Lilacs, Google Scholar and PubMed. The deadline and related research have been stipulated covering all available literature on virtual libraries.

Series of Articles and Eligibility

102 articles were found involving implantology and biomaterials. Initially, duplication of articles was excluded. After this process, abstracts were evaluated and a new exclusion was performed, removing articles that did not contemplate bone regeneration with the use of Biomaterials (allogeneic bone) and plasma rich in fibrin. A total of 49 articles were evaluated in full and 29 were included and evaluated in the present study.

Selection of studies and risk of bias in each study

Two independent reviewers (1 and 2) carried out research and study selection. Data extraction was performed by reviewer 1 and completely reviewed by reviewer 2. A third investigator decided on some conflicting points and made the final decision to choose the articles. Only studies reported in Portuguese and English were evaluated. The Cochrane Instrument was adopted to assess the quality of the included studies [12].

Major Results of The Review and Discussion

Risk of bias

Considering the Cochrane tool for risk of bias, the overall assessment resulted in 5 studies with a high risk of bias and 3 studies with uncertain risk. The domains that presented the highest risk of bias were related to the number of participants in each study approached, and the uncertain risk was related to the time of bone maturation for the implantation. Also, there was an absence of the source of funding in 4

studies and 3 studies did not disclose information about the conflict of interest statement.

Major Findings

The maxillary sinus is the largest of the paranasal sinuses and has the function of contributing to the resonance of phonation, conditioning of the air we breathe, and aid in the production of mucus in the nasal cavity [11]. It also acts to equalize barometric pressures in the nasal cavity, which is covered by a membrane called the Schneider membrane. This membrane is constituted by a pseudostratified ciliated cylindrical epithelium with calciform cells that produces mucus. The importance of knowing the constitution of this epithelium is because these hair cells play a fundamental role in the physiology of the maxillary sinus. While the calciform cells produce mucus, these cilia generate movements that cause this mucus to move to the drainage site of the maxillary sinus. The maxillary sinus drains through its ostium in the nasal cavity, which usually happens in the middle meatus. Around 25% of all the maxillary sinuses, there is an accessory bone that is located a lower part than the main ostium, and all the mucus produced and the particles trapped in this mucus are directed through the ciliary beat to the ostium. [11].

When the loss of a dental element occurs in the posterior region of the maxilla, there is natural resorption of the alveolar process and at the same time, there will be pneumatization of the maxillary sinus. It will increase its volume towards the place where the roots existed and this will often make it difficult or impossible to restore implants in the place. For this reason, the procedure for lifting the maxillary sinus floor should be performed, or short implants when possible [11]. When grafting procedures are needed, our focus is often on the type of biomaterial to be used and in fact, the success and predictability of our results do not depend only on the biomaterial. It is also necessary to consider the type of defect to be treated, its morphology. The morphology will impact mainly because the defects have different vascularization capacity, different osteogenic cell recruitment capacity, different natural graft stabilization capacity, therefore, we must consider the characteristics of the biomaterial that we must use, but also, the characteristics of the bed and the bone defect that we intend to treat [11].

Several surgical techniques can be used to reconstruct the atrophic alveolar ridge, techniques isolated or associated with autogenous, allogeneic,

xenogenous grafts, and alloplastic biomaterials. The autogenous bone graft is the only one capable of presenting three important biological properties (osteogenesis, osteoinduction, and osteoconduction) guaranteeing a regenerative self-potential [13]. As a disadvantage to the autogenous bone graft, the need for second surgical access in the donor area stands out, resulting in longer surgical time, morbidity, and a consequent greater resistance of the patient to the proposed treatment. In this context, allogeneic, xenogenous, and alloplastic bone grafts are presented as an alternative for the treatment of bone defects in the jaws, since they avoid the need for a second surgical access.

But due to the need for processing to eliminate antigenic components, these grafts are only osteoconductive with a lower bone formation potential compared to autogenous bone grafting. To increase the bone formation potential of these grafts, combinations have been proposed to obtain better regenerative conditions through the preservation of volume (osteoconduction) and the induction of differentiation of cell migration (osteoinduction) [14].

In the past 20 years, platelet concentrates have been proposed as regenerative materials in tissue regeneration procedures. Among the platelet concentrates proposed in the literature, there is PRP (platelet-rich plasma) and FRP (fibrin-rich plasma) that act as autogenous platelet aggregates with osteoinductive properties. These biomaterials, due to low morbidity and possible regenerative potential, have been indicated for use in combination with other biomaterials or even alone. FRP is a second-generation concentrate, that is, no anticoagulant is used for its acquisition. The blood of the patient, after being collected, is subjected to a specific centrifugation force, and thus, the figured elements are separated according to their density. From this, the part corresponding to the erythrocytes is discarded and the resulting platelet concentrate is used for the regenerative purpose. Leukocytes and platelets synthesize and release a variety of cytokines and growth factors that act in chemotaxis, angiogenesis, differentiation, and cell inhibition [15].

Xenografts are bone minerals derived from animals or algae and corals. The organic component is removed to eliminate the risk of immunogenic responses or disease transmission. Animal derivatives are the most used in guided bone regeneration (ROG), especially the sterile deproteinized bovine medullary bone (OBMED), which has been extensively researched

and shown to have similarities with human medullary bone. OBMED is a great osteoconduction, providing a framework favorable to bone formation. Its slow reabsorption contributes a lot to the maintenance of the graft volume. It has good wettability and a good surface contact angle, favoring contact with the blood clot. Elevations of the maxillary sinus floor performed using only OBMED demonstrate good osteoconductive capacity and excellent biological integration, which facilitates bone neof ormation. A study with OBMED used alone or mixed with autogenous bone in several percentages in elevation of the maxillary sinus floor demonstrated bone formation similar to that of autogenous bone after 9 months [16].

The xenografts most used in guided bone regeneration procedures are the deproteinized bovine bone mineral, commercially known as Bio-Oss®, which is the most researched product in regenerative dentistry worldwide. It is a bone of bovine origin processed to produce natural bone mineral without organic elements. After thermal and chemical treatments, the inorganic phase of the bovine bone consists mainly of hydroxyapatite (HA) which retains the porous architecture. The excellent osteoconductive properties of Bio-Oss® lead to predictable and efficient bone regeneration, Bio-Oss® particles become an integral part of the newly formed bone structure and retain their volume in the long term [5]. Due to its great similarity to human bone, Bio Oss® is incorporated into the natural process of modeling and remodeling. The highly porous structure of Bio Oss® offers a lot of space for the formation of blood vessels (angiogenesis) and the deposit of newly formed bone (osteogenesis) [5].

The surface microstructure of Bio Oss® assists in the excellent growth of osteoblasts that are responsible for bone formation. In this way, the Bio Oss® particles become an integral part of the structure of the new bone in the formation and the low conversion rate into Bio Oss®'s own (remodeled) bone, stabilizes the structure and allows the graft volume to be maintained long-term. These biofunctional processes make Bio Oss® unique [17].

For the success of dental implant practice, osseointegration is essential. However, it is a complex process with many factors interfering with the formation and maintenance of bone tissue around the implant, such as topography and surface roughness, biocompatibility, and loading conditions. Also, it is necessary to have a bone layer of the host that is

healthy, compatible and that allows primary stability [1].

Dental implants are being used more and more due to the high success rates. However, a large portion of the patients do not have sufficient minimum bone conditions for the installation of the implants, therefore, previous reconstructive bone surgery is necessary. It is essential that the dental surgeon master the knowledge in the healing process of the post-extraction alveoli, to provide correct planning of the cases [18].

In this sense, after an extraction, the repair process occurs in the internal region of the socket together with the formation of a clot rich in cells and growth factors, promoting neof ormation, bone remodeling, and soft tissue epithelialization [19-21]. During this process, the alveolar ridge undergoes relevant changes, both in height and in thickness, which influence the possibility of installing the implants [22,23]. Thus, the optimized processes of implantology and biomaterials allow the installation of implants in areas of thin thickness, width, and bone height, with the performance of simpler surgeries and with a higher rate of success and comfort for the patient [24,25].

The lack of bone in the alveolar ridges has been a major problem in functional aesthetic recovery in patients who have suffered dentoalveolar trauma, traumatic tooth extractions, congenital tooth absence, maxillary and mandibular pathologies. To fill large bone defects, the development of bone regeneration improves epithelial barriers for a bone graft, favoring greater predictability in alveolar and peri-implant reconstructions and has a good prognosis [26]. In this sense, the filling biomaterials can be fibrin-rich plasma (FRP), Bio-Oss®, hydroxyapatite, lyophilized and ground demineralized bone marrow, autogenous bone, which is considered the gold standard, among others [1].

Thus, fibrin-rich plasma (FRP) as an autologous biomaterial for use in oral and maxillofacial surgery presents most leukocytes, platelets, and growth factors, forming a fibrin matrix, with a three-dimensional architecture [27,28]. The Bio-Oss® biomaterial (Geistlich), as it is biodegradable, biocompatible, non-toxic, and has low immunogenicity and bio stimulators can act in the regeneration of bone tissue, since it establishes with the adenomatous mesenchymal stem cells the appropriate biological niche for bone growth and, thus, allowing the dental implant to be as effective as possible [1].

Based on this, two important studies reported results on the combined use of Bio-Oss® and FRP. Thus, the first study investigated clinically and histologically the potential of FRP as grafting material in pre-implant reconstructive surgery for severe maxillary atrophy after breast elevation procedures in 106-120-180 days, to determine whether the use of FRP can accelerate the bone regeneration process, which is essential to promote the stability of the implant. This study also includes a control group, in which only deproteinized bovine bone (Bio-Oss®) was used as a reconstructive material. As a result, the use of FRP has optimized bone formation [29].

The second study compared the use of Bio-Oss® mixed with FRP and Bio-Oss® with Tisseel® to improve bone regeneration. After elevating the sinus membrane in both maxillary sinus cavities, an implant was placed in the sinus cavity. In one of the sinus cavities, the FRP/Bio-Oss® composite was grafted and the Tisseel®/Bio-Oss® composite was grafted into the other sinus cavity. After a healing period of 6 months, bone formation at the graft sites and bone-implant contact were assessed. The average rate of osseointegration was $43.5 \pm 12.4\%$ and the rate of new bone formation was $41.8 \pm 5.9\%$ at the compound sites FRP/Bio-Oss®. In the composite sites, Tisseel® / Bio-Oss® was $30.7 \pm 7.9\%$ and $31.3 \pm 6.4\%$. There were statistically significant differences between the groups. The findings of this study suggested that when FRP is used as an adjunct to Bio-Oss® particles for bone augmentation in the maxillary sinus, bone formation at the graft sites is significantly greater than when Tisseel® is used [5].

Conclusion

The use of the FRP associated with Bio-Oss® seems to illustrate high success rates with minimal costs, which may reduce the amount of bone graft needed to fill the sinus cavity, reducing the costs of the procedure.

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Data sharing statement

No additional data are available

Ethics Approval

Approval was sought and granted by the Departmental Ethics Committee.

Informed consent

Informed written consent obtained from the participant

Conflict of interest

The authors declare no conflict of interest.

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