MedNEXT
Journal of Medical an Health Sciences

REVIEW ARTICLE

DOI: 10.54448/mdnt22S307

Major clinical findings of maxillary sinus surgery and the use of bio stimulators: a systematic review

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DOI: https://doi.org/10.54448/mdnt22S307
Received: 03-07-2022; Revised: 04-26-2022; Accepted: 04-27-2022; Published: 05-10-2022; MedNEXT-id: e22S307

Abstract

Introduction: In the scenario of maxillary sinus surgery, when there is a loss of a dental element 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. For this reason, the maxillary sinus floor elevation procedure should be performed. When grafting procedures are needed, our focus is often on the types of biomaterials and their bio stimulating properties, as well as on other types of bio stimulators to be used. **Objective:** It was to analyze the main clinical findings of maxillary sinus surgery and the use of bio stimulators through a systematic review. **Methods:** The present study followed a systematic review model, following the rules of systematic review – PRISMA. The search strategy was performed in the PubMed, Cochrane Library, Web of Science and Scopus, and Google Scholar databases. The present study was carried out from January to March 2022. The quality of the studies was based on the GRADE instrument and the risk of bias was analyzed according to the Cochrane instrument. **Results and Conclusion:** After analyzing the main clinical findings on maxillary sinus surgery and the use of bio stimulators, it was concluded that bone regeneration processes using biomaterials and the main molecular and cellular constituents such as mesenchymal stem cells, cytokines, platelet-rich plasma, fibrin-rich plasma, exosomes, microRNAs, TNF-α, IL-1, LIF and IL-6 and prostaglandin E2 (PGE2) are strategic for the solution to large bone defects, leading to tissue or bone regeneration. The main filler biomaterials can be fibrin-rich plasma (FRP), Bio-Oss®. However, it is necessary to understand the chemical, physical and biological processes of both the biological material and the biological niche of the host for successful neovascularization and bone filling.

Keywords: Maxillary sinus surgery. Biomaterials. Bio stimulators. Cytokines. Growth factors.

Introduction

In the scenario of maxillary sinus surgery, the maxillary sinus is the largest of the paranasal sinuses and its function is to contribute to the resonance of phonation, conditioning the air we breathe and aid in the production of mucus in the nasal cavity [1,2]. It also acts in the equalization of barometric pressures in the nasal cavity, which is covered by a membrane called Schneider's membrane. This membrane is constituted by a ciliary cylindrical pseudostratified epithelium with goblet cells that produces mucus [3].

Thus, 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 goblet cells produce the mucus, these cilia generate movements that make this mucus go towards the drainage site of the maxillary sinus [4]. The maxillary sinus drains through its ostium in the nasal cavity, which usually happens in the middle meatus. In about 25% of all maxillary sinuses, there is an accessory bone that is located in a lower portion 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 [5].

In this context, when there is a loss of a dental element in the posterior region of the maxilla, there is natural resorption of the alveolar process and, at the same time, pneumatization of the maxillary sinus will occur [6]. For this reason, the maxillary sinus floor elevation procedure should be performed, or short implants when possible. When graft procedures are needed, our focus is often on the types of biomaterials and their bio stimulating properties, as well as on other types of bio stimulators to be used [6].

Still, the morphology will have an impact mainly because the defects have different vascularization capacities, different osteogenic cell recruitment capacities, have different natural stabilization capacities of grafts, therefore, the characteristics of the biomaterials and bio stimulators that must be used must be considered, as well as the characteristics of the bed and the bone defect [7].

Also, several surgical techniques can be used to reconstruct the atrophic alveolar ridge, techniques alone or associated with autogenous, allogeneic, xenogeneic, and alloplastic biomaterials. The autogenous bone graft is the only one capable of presenting three important biological properties (osteogenesis, osteoinduction, and osteoconduction) guaranteeing a self-regenerative potential, mainly with the supply on a larger scale of bio stimulators such as mesenchymal stem cells, cytokines, platelet-rich plasma, plasma rich in fibrin, exosomes, and microRNAs [6-9].

Still in this context, platelet concentrates have been proposed as regenerative materials in tissue regeneration procedures. Among the platelet concentrates proposed in the literature, there are PRP and FRP that act as autogenous platelet aggregates with osteoinductive properties. These biomaterials, due to their low morbidity and possible regenerative potential, have been indicated for use in combination with other biomaterials or even alone. Leukocytes and platelets synthesize and release a variety of cytokines and growth factors that act in chemotaxis, angiogenesis, cell differentiation, and inhibition [10-12].

Although the results do not seem to confirm that FRP is better than other biomaterials, it is suggested that its use may result in a decrease in the total healing time, around 104 days, and improve the handling of the graft material. Furthermore, the use of FRP associated with Bio-Oss® seems to illustrate high success rates with minimal costs, which can reduce the amount of bone graft needed to fill the sinus cavity, reducing the costs of the procedure [8].

Therefore, the present study aimed to analyze the main clinical findings on maxillary sinus surgery and the use of bio stimulators through a systematic review.

Methods

Study Design

The present study followed a systematic review model, following the rules of systematic review - PRISMA (Transparent reporting of systematic review and meta-analysis, access available in: http://www.prisma-statement.org/).

Data Sources

The search strategy was performed in the PubMed, Cochrane Library, Web of Science and Scopus, and Google Scholar databases. The present study was carried out from January to March 2022.

Descriptors (MeSH Terms)

The main descriptors (MeSH Terms) used were "*Maxillary sinus surgery. Biomaterials. Bio stimulators. Cytokines. Growth factors*". For greater specification, the description "*Biostimulation and Bone Regeneration*" for refinement was added during the searches, following the rules of the word PICOS (Patient; Intervention; Control; Outcomes; Study Design).

Selection of studies and risk of bias in each study

Two independent reviewers (1 and 2) performed research and study selection. Data extraction was performed by reviewer 1 and fully reviewed by reviewer 2. A third investigator decided some conflicting points and made the final decision to choose the articles. Only studies reported in English were evaluated. The quality of the studies was based on the GRADE instrument and the risk of bias was analyzed according to the Cochrane instrument.

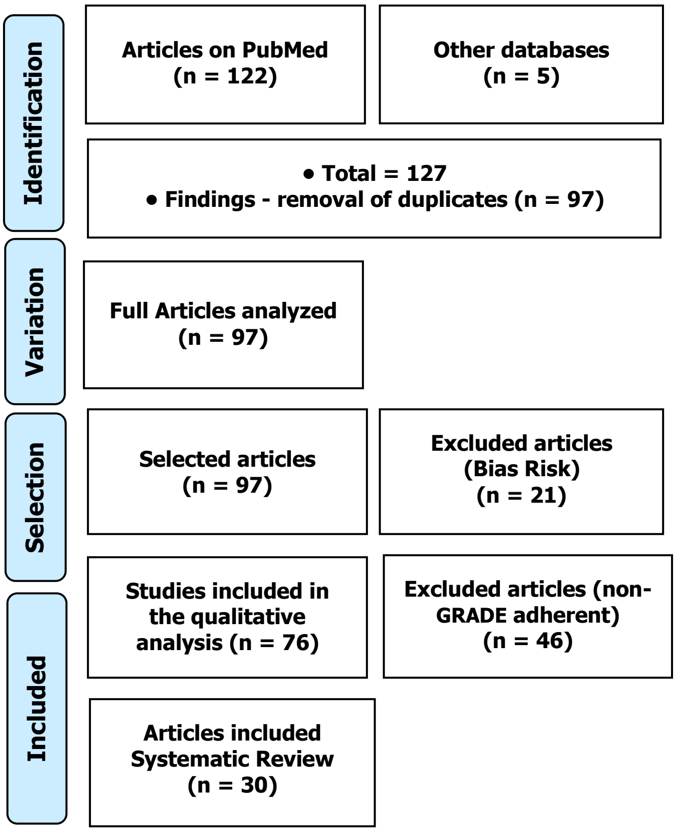
Results and Discussion

A total of 127 articles were found. Articles that presented low-quality scientific evidence according to GRADE, as well as articles that showed research biases, such as a low number of participants and dubious results were also excluded. A total of 76 articles were fully evaluated and 30 were included in this study (**Figure 1**).

Molecular and Cellular Aspects of Biostimulation

In the context of bone formation and tissue repair, the coordinated interaction between bone-forming cells and biological signals is highlighted, with the action of osteoblasts and their precursors [13]. Osteoblasts release Bone Morphogenetic Protein that stimulates the production of new bones along with biomaterials and can initiate the release of biological signals that guide the bone formation and remodeling [14].

Figure 1. Article selection (Systematic Review).



These biological signals attract bone-forming cells to the receptor site. Growth factors and other proteins are some of the biological signals that may be involved in bone neoformation and tissue remodeling. In addition, through chemotaxis, there is a migration of bone-forming cells to the application area, as the stimulation of cell migration occurs in response to chemical stimuli [15].

In this sense, monocytes, macrophages, and endothelial cells contribute to bone remodeling, either through contact with osteogenic cells or through the release of soluble factors such as cytokines and GF [15]. In the skeletal system, TNF-α stimulates bone and cartilage resorption and inhibits collagen and proteoglycan synthesis. IL-1 induces the expression of a wide variety of cytokines. LIF and IL-6 are two such molecules that are known to stimulate the differentiation of mesenchymal progenitor cells in the osteoblastic lineage, they are also potent anti-apoptotic agents for osteoblasts. In bone, the main sources of IL-6 are osteoblasts and not osteoclasts. Prostaglandin E2 (PGE2) is also directly related to the expression of the cytokine IL-6 [16,17].

In the context of maxillary sinus surgery, the lack of bone in the alveolar crests 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, in addition to infections due to emotional and the possibility of deformity and also the economic impact they cause on the National Health System (NHS) [1,2].

Furthermore, bone loss can also occur due to periodontal disease, traumatic surgeries, or even for physiological reasons due to lack of adequate or inadequate prosthetic loading. Trauma to the face region can affect both soft and hard tissues, so these injuries can affect the victim's quality of life and health [6].

Also, maxillofacial trauma can be considered one of the most devastating aggressions encountered in traumatology and oncology due to the emotional consequences and the possibility of deformity and also the economic impact they cause on the Unified Health System (UHS) [7]. The face, more than any other region of the body, is affected by aesthetic changes, as it is always visible and the damage is noticed immediately. For this reason, facial trauma deserves attention in the treatment of multiple trauma due to its high incidence and severity [8].

In this context, FRP as an autologous biomaterial was developed in France by Choukroun et al. (1993) [7] for specific use in oral and maxillofacial surgery. This biomaterial presents the majority of leukocytes, platelets, and growth factors, forming a fibrin matrix with a three-dimensional architecture. It is the second generation of platelet concentrate with a high potential for injury repair.

In addition, obtaining FRP follows an easy and simple protocol. A blood sample is obtained without anticoagulant in 10.0 mL tubes that are immediately centrifuged at 3000 rpm (approximately 400.0 g) for 10.0 minutes [8]. After the start of centrifugation in the absence of anticoagulant, the activation of most of the collected blood platelets begins, from the contact with the tube walls and the release of the coagulation cascades. As a final product of this process, we have fibrinogen, which is a soluble protein, transformed into insoluble fibrin by thrombin. Fibrin gel constitutes the first healing matrix of injured sites. Fibrinogen is concentrated at the top of the tube before circulating thrombin converts it to fibrin. A fibrin clot is then obtained in the middle of the tube, between the red blood cells at the bottom and the acellular plasma at the top [9,10].

FRP has the characteristic of polymerizing naturally and slowly during centrifugation. The fibrin network thus formed presents, in particular, a homogeneous three-dimensional organization, more coherent than the natural fibrin clots [11-13]. In this context, with progressive polymerization, the incorporation of circulating cytokines increases in the fibrin network, implying a longer life for these cytokines, as they will be released and used only in the remodeling of the initial scar matrix, which is long-term [15]. Cytokines are thus kept available in situ for a convenient period when cells initiate matrix remodeling [16].

Furthermore, FRP is based on protecting growth factors from proteolysis that can maintain their activity for a longer period and stimulate bone regeneration more efficiently [17-22]. The most critical phase of the sinus membrane elevation procedure after osteotomy of the lateral wall of the maxillary sinus is its detachment [23]. At this stage, Schneider's membrane ruptures can occur, around 15.0% of the cases, which, depending on the size of the perforation, can make the graft unfeasible, mainly due to the containment nature of the graft material that the membrane exerts. The most frequent causes of these perforations are inadequate osteotomies, incomplete membrane detachments with a lack of bone support for lifting curettes, exerting excessive pressure on the membrane, and the presence of septa [24-27].

If sinus membrane perforations are present, this should be quantified [28] as small perforations do not require treatment as membrane folds obliterate the perforation. In the case of ruptures larger than 5.0 mm, the use of collagen membranes is indicated [29]. Another study indicated the use of fibrin membranes obtained from FRP to seal the perforations. In the presence of perforations larger than 10.0 mm, the surgery should be aborted and reentry performed after 60 to 90 days [30].

The development of optimized implant surfaces is the subject of great research with the objective of accelerating the osseointegration process, leading to a reduction in the waiting time before loading, in addition to making the immediate loading of the implant safer [28]. It was documented for the first time that the combination of biomaterial and FRP significantly improved bone regeneration in the peri-implant zone. Implant placement with the simultaneous use of PRP creates a good relationship between hard and soft tissue, in addition to the advantage of the psychological relationship with the patient [4].

Besides, cell migration and proliferation on the surface of implants are essential to initiate the process of tissue regeneration, while modifications on the surface of implants incorporating growth and differentiation mediators can enhance tissue regeneration for the implant [5-8].

Therefore, although the results do not seem to confirm that FRP is better than other biomaterials, it is suggested that its use may result in a decrease in the total healing time, around 104 days, and improve the handling of the graft material. In addition, the use of FRP associated with Bio-Oss® seems to illustrate high success rates with minimal costs and may reduce the amount of bone graft needed to fill the sinus cavity, reducing procedure costs [28].

Thus, FRP as an autologous biomaterial for use in oral and maxillofacial surgery presents the majority of leukocytes, platelets, and growth factors, forming a fibrin matrix, with three-dimensional architecture. The Bio-Oss® (Geistlich) biomaterial, 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 adenomatous mesenchymal stem cells the appropriate biological niche for bone growth and, thus allowing the most effective dental implant possible [25].

Conclusion

After analyzing the main clinical findings on maxillary sinus surgery and the use of bio stimulators, it was concluded that bone regeneration processes with the use of biomaterials and the main molecular and cellular constituents such as mesenchymal stem cells, cytokines, plasma rich in platelets, fibrin-rich plasma, exosomes, microRNAs, TNF-α, IL-1, LIF and IL-6 and prostaglandin E2 (PGE2) are strategic for the solution to large bone defects, leading to tissue or bone regeneration. The main filler biomaterials can be fibrin-rich plasma, Bio-Oss®. However, it is necessary to understand the chemical, physical and biological processes of both the biological material and the biological niche of the host for successful neovascularization and bone filling.

Acknowledgement
Not applicable.

Funding
Not applicable.

Ethics approval
Not applicable.

Informed consent
Not applicable.

Data sharing statement
No additional data are available.

Conflict of interest

The authors declare no conflict of interest.

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