



Maxillary sinus surgery and use of fibrin-rich plasma: a systematic review

Talysson Silva de Oliveira Morais^{1,2}, Abner da Rocha Cardoso Costa^{1,2},
Fabio Alarcon Idalgo^{1,2}, Alvaro José Cicareli^{1,2}

¹ UNORTE - University Center of Northern São Paulo, Dentistry department, São José do Rio Preto, São Paulo, Brazil.

² UNIPOS - Post graduate and continuing education, Dentistry department, São José do Rio Preto, São Paulo, Brazil.

*Corresponding author: Prof. Me. Fabio Alarcon Idalgo.

Unorte/Unipos – Graduate and Postgraduate education,

Dentistry department, São José do Rio Preto,

São Paulo, Brazil.

E-mail: dridalgo@gmail.com

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Abstract

Introduction: In around 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. When a dental element is lost in the posterior region of the maxilla, there is natural reabsorption of the alveolar process and at the same time, pneumatization of the maxillary sinus occurs. **Objective:** It was to carry out a systematic review to elucidate the main clinical approaches to the use of fibrin-rich plasma in the bone regeneration process in maxillary sinus surgeries.

Methods: The PRISMA Platform systematic review rules were followed. The search was carried out from October to December 2023 in the Scopus, PubMed, Science Direct, Scielo, and Google Scholar databases. 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:** A total of 115 articles were found, 40 articles were evaluated in full and 25 were included and developed in the present systematic review study. Considering the Cochrane tool for risk of bias, the overall assessment resulted in 20 studies with a high risk of bias and 25 studies that did not meet GRADE and AMSTAR-2. Most studies did not show homogeneity in their results, with $X^2=55.5\%>50\%$. It was concluded that to improve osseointegration and bone anchorage, surface modifications can be chemical, such as calcium phosphate (Ca-P), or physical impregnation, being

related to the microtopography of the implant. Several variables affect the biological activity of FRP preparations, such as the number of centrifuges used, centrifugation speed, and other protocols that result in preparations with various volumes, platelet numbers, amount of growth factors, and concentration of fundamental white blood cells and erythrocytes. Some researchers recommend avoiding tissue exposure to FRP-containing leukocytes, arguing that an inflammatory reaction may occur. On the other hand, other authors have described beneficial effects due to increased immunological and antibacterial resistance, although there is no clinical evidence to support its effect. FRP has gained prominence in the scientific community because it does not require the addition of an activator or anticoagulant, making the product more autologous, and featuring a fibrin network that protects growth factors, keeping them in place for longer.

Keywords: Maxillary sinus surgery. Fibrin-rich plasma. Biomaterials. Bone regeneration.

Introduction

The maxillary sinus is the largest of the paranasal sinuses and its function is to contribute to the resonance of speech, conditioning the air we breathe and helping to produce mucus in the nasal cavity [1]. It also acts to equalize barometric pressures in the nasal cavity, which is lined by a membrane called Schneider's membrane. This membrane is made up of a pseudostratified cylindrical ciliary epithelium with calciform cells that produce 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 goblet cells produce mucus, these cilia generate movements that direct this mucus to the drainage site of the maxillary sinus [2].

The maxillary sinus drains through its ostium in the nasal cavity, which usually occurs in the middle meatus. In around 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. [two]. When a dental element is lost in the posterior region of the maxilla, there is natural reabsorption of the alveolar process and at the same time, pneumatization of the maxillary sinus occurs. It will increase its volume towards the location where the roots existed and this will often make it difficult or unfeasible to restore implants in that location [1-3]. For this reason, the maxillary sinus floor elevation procedure should be performed, or short implants should be performed when possible. When graft procedures are required, our focus is often on the type of biomaterial to be used and the success and predictability of our results do not depend solely on the biomaterial [4].

It is also necessary to consider the type of defect to be treated, and its morphology. 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 the grafts, 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 [4,5].

Furthermore, several surgical techniques can be used to reconstruct the atrophic alveolar ridge, techniques alone or associated with autogenous, allogeneic, xenogeneic grafts, and alloplastic biomaterials. Over the last 20 years, platelet concentrates have been proposed as regenerative materials in tissue regeneration procedures. Among the platelet concentrates proposed in the literature are PRP and FRP, which 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 [6,7].

Thus, fibrin-rich plasma (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 biomaterial Bio-Oss® (Geistlich), as it is biodegradable, biocompatible, non-toxic, and has low immunogenicity and biostimulation,

can act in the regeneration of bone tissue, as it establishes with adenomatous mesenchymal stem cells the appropriate biological niche for bone growth and, thus allowing dental implants to be carried out as efficiently as possible [7-10].

According to some authors, FRP acts to protect growth factors from proteolysis, which can therefore maintain their activity for a longer period and stimulate tissue regeneration. The use of autogenous bone, especially the osteoinductive capacity, has been recommended for filling the antral cavity [7-9].

Therefore, the present study carried out a systematic review to elucidate the main clinical approaches to the use of fibrin-rich plasma in the bone regeneration process in maxillary sinus surgeries.

Methods

Study Design

The present study followed the international systematic review model, following the rules of PRISMA (preferred reporting items for systematic reviews and meta-analysis). Available at: <http://www.prisma-statement.org/?AspxAutoDetectCookieSupport=1>. Accessed on: 11/18/2023. The methodological quality standards of AMSTAR-2 (Assessing the methodological quality of systematic reviews) were also followed. Available at: <https://amstar.ca/>. Accessed on: 11/18/2023.

Data Sources and Research Strategy

The literary search process was carried out from October to December 2023 and was developed based on Scopus, PubMed, Lilacs, Ebsco, Scielo, and Google Scholar, covering scientific articles from various eras to the present. The descriptors (MeSH Terms) were used: "*Maxillary sinus surgery. Fibrin-rich plasma. Biomaterials. Bone regeneration*"; and using the Boolean "and" between the MeSH terms and "or" between historical discoveries.

Study Quality and Risk of Bias

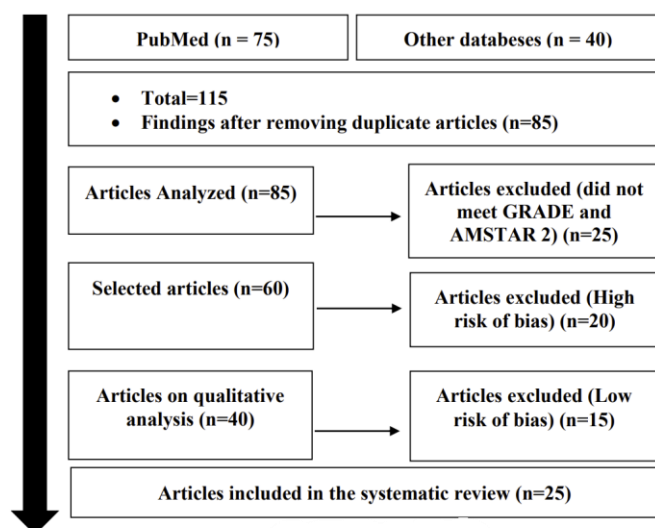
Quality was classified as high, moderate, low, or very low in terms of risk of bias, clarity of comparisons, precision, and consistency of analyses. The most evident emphasis was on systematic review articles or meta-analyses of randomized clinical trials, followed by randomized clinical trials. The low quality of evidence was attributed to case reports, editorials, and brief communications, according to the GRADE instrument. The risk of bias was analyzed according to the Cochrane instrument by analyzing the Funnel Plot graph (Sample size versus Effect size), using the Cohen test (d).

Results and Discussion

Summary of Findings

A total of 115 articles were found that were subjected to eligibility analysis, with 25 final studies being selected to compose the results of this systematic review. The studies listed were of medium to high quality (Figure 1), considering the level of scientific evidence of studies such as meta-analysis, consensus, randomized clinical, prospective, and observational. The biases did not compromise the scientific basis of the studies. According to the GRADE instrument, most studies showed homogeneity in their results, with $X^2=55.5\% > 50\%$. Considering the Cochrane tool for risk of bias, the overall assessment resulted in 20 studies with a high risk of bias and 25 studies that did not meet GRADE and AMSTAR-2.

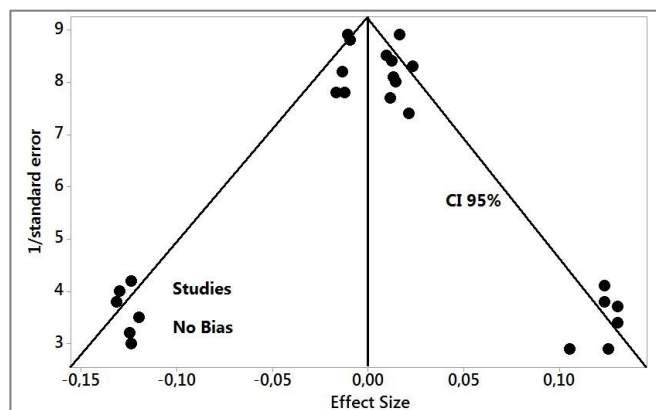
Figure 1. Article selection - exclusion process.



Source: Own authorship.

Figure 2 presents the results of the risk of bias of the studies using the Funnel Plot, showing the calculation of the Effect Size (Magnitude of the difference) using the Cohen Test (d). Precision (sample size) was determined indirectly by the inverse of the standard error (1/Standard Error). This graph had a symmetrical behavior, not suggesting a significant risk of bias, both between studies with a small sample size (lower precision) that are shown at the bottom of the graph and in studies with a large sample size that are presented at the top.

Figure 2. The symmetric funnel plot suggests no risk of bias among the small sample size studies that are shown at the bottom of the graph. High confidence and high recommendation studies are shown above the graph (n=25 studies).



Source: Own authorship.

Major Clinical Outcomes

In the scenario 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 missing teeth, 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 facial region can affect both soft and hard tissues, so these injuries can affect the victim's quality of life and health [3].

Maxillofacial trauma can be considered one of the most devastating injuries found in traumatology and oncology due to the emotional consequences and the possibility of deformity and also the economic impact they cause on the National Health System (NHS) [4]. The face, more than any other region of the body, is affected by aesthetic changes, as it is always visible and damage is noticed immediately. For this reason, facial trauma deserves emphasis in the treatment of polytrauma due to its high incidence and severity [5].

In this context, fibrin-rich plasma (FRP) as an autologous biomaterial was developed in France by Choukroun et al. (2006) [7] for specific use in oral and maxillofacial surgery. This biomaterial contains 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.

Furthermore, 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 [5]. After the start of centrifugation in the

absence of an anticoagulant, the activation of the majority of collected blood platelets begins, upon contact with the tube walls, and the release of the coagulation cascades. As the end product of this process, we have fibrinogen, which is a soluble protein, transformed into insoluble fibrin by thrombin. Fibrin gel constitutes the first scar 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 [6,7].

Also, FRP has the characteristic of polymerizing naturally and slowly during centrifugation. The fibrin network thus formed presents, in particular, a homogeneous threedimensional organization, more coherent than natural fibrin clots [8-10]. 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. Cytokines are thus kept available in situ for a convenient period when cells begin matrix remodeling [11-13].

Furthermore, FRP is based on the protection of growth factors from proteolysis that can maintain their activity for a longer period and stimulate bone regeneration more efficiently [14]. The most critical phase of the sinus membrane elevation procedure after osteotomy of the lateral wall of the maxillary sinus is its detachment [15]. At this stage, ruptures of Schneider's membrane may occur, in around 15.0% of cases, which, depending on the size of the perforation, may 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 curette elevation, excessive pressure on the membrane, and the presence of septa [16-19].

If sinus membrane perforations are present, this should be quantified [20], as small perforations do not require treatment as membrane folds obliterate the perforation. In the case of ruptures greater than 5.0 mm, the use of collagen membranes is indicated [21]. Another study indicated the use of fibrin membranes obtained from FRP to seal perforations. In the presence of perforations greater than 10.0 mm, the surgery must be aborted and reentry performed after 60 to 90 days [22].

The development of optimized implant surfaces is the subject of extensive research to accelerate the osseointegration process, leading to a reduction in

waiting time before loading, in addition to making immediate implant loading safer [23]. It was documented for the first time that the combination of biomaterial and FRP significantly improved bone regeneration in the peri-implant zone. The placement of the implant with the simultaneous use of platelet-rich plasma (PRP) creates a good relationship between the hard tissue and the soft tissue, in addition to the advantage of the psychological relationship with the patient [1].

Cell migration and proliferation on the surface of implants are essential to initiate the tissue regeneration process, while modifications on the surface of implants incorporating growth and differentiation mediators can enhance tissue regeneration for the implant [24]. Xenografts are bone minerals derived from animals 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 (GBR), especially deproteinized sterilized bovine medullary bone (OBMED), which has been extensively researched and shown to have similarities to human medullary bone. OBMED is an excellent osteoconductor, providing a favorable framework for bone formation. Its slow reabsorption contributes greatly to maintaining graft volume. It has good wettability and a good surface contact angle, favoring contact with the blood clot. Maxillary sinus floor elevations performed exclusively using OBMED demonstrate good osteoconductive capacity and excellent biological integration, which facilitates new bone formation. A study with OBMED used alone or mixed with autogenous bone in different percentages in maxillary sinus floor elevation demonstrated bone formation similar to that of autogenous bone after 9 months [16].

The xenograft most used in guided bone regeneration procedures is deproteinized bovine bone mineral, commercially known as Bio-Oss®, it is the most researched product in regenerative dentistry worldwide. It is bone of bovine origin processed to produce natural bone minerals without organic elements. After thermal and chemical treatments, the inorganic phase of 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, the Bio-Oss® particles become an integral part of the newly formed bone structure and retain their volume in the long term. Due to its great similarity to human bone, Bio Oss is incorporated into the natural modeling and remodeling process [25].

Given this, 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® appears to illustrate high success rates with minimal costs, potentially reducing the amount of bone graft needed to fill the sinus cavity, reducing procedure costs [22].

Conclusion

It was concluded that to improve osseointegration and bone anchorage, surface modifications can be chemical, such as calcium phosphate (Ca-P), or physical impregnation, being related to the microtopography of the implant. Several variables affect the biological activity of FRP preparations, such as the number of centrifuges used, centrifugation speed, and other protocols that result in preparations with various volumes, platelet numbers, amount of growth factors, and concentration of fundamental white blood cells and erythrocytes. Some researchers recommend avoiding tissue exposure to FRP-containing leukocytes, arguing that an inflammatory reaction may occur. On the other hand, other authors have described beneficial effects due to increased immunological and antibacterial resistance, although there is no clinical evidence to support its effect. FRP has gained prominence in the scientific community because it does not require the addition of an activator or anticoagulant, making the product more autologous, and featuring a fibrin network that protects growth factors, keeping them in place for longer.

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Ethical Approval

Not applicable.

Informed consent

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Data sharing statement

No additional data are available.

Conflict of interest

The authors declare no conflict of interest.

Similarity check

It was applied by Ithenticate®.

Peer Review Process

It was performed.

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