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Maxillary sinus bone augmentation and injectable plateletrich fibrin (I-PRF) for dental implant: a systematic review

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Abstract

Introduction: In the context of bone regeneration for dental implants, maxillary sinus augmentation is a well-documented surgical technique and is one of the therapeutic options for implant placement in the atrophic posterior maxilla, particularly when the residual bone height is less than 5 mm. Several surgical techniques can be used to reconstruct the atrophic alveolar ridge, techniques alone or associated with autogenous, allogeneic, xenogenous grafts, and alloplastic biomaterials. **Objective:** It was carried out a systematic review to present the main scientific documentation on maxillary sinus augmentation and bone regeneration for dental implants. **Methods:** The PRISMA Platform systematic review rules were followed. The search was carried out from November 2024 to January 2025 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. Experimental and clinical studies (retrospective, prospective and randomized) with qualitative and/or quantitative analysis were included. **Results and Conclusion:** A total of 123 articles were found, and 35 articles were evaluated in full and 26 were included and developed in the present systematic review study. Considering the Cochrane tool for risk of bias, the overall assessment resulted in 25 studies with a high risk of bias and 31 studies that did not meet GRADE and AMSTAR-2. According to the GRADE instrument, most studies presented homogeneity in their results, with X^2=90.8%>50%. It was concluded that the use of small and large bovine xenograft particles for maxillary sinus augmentation provides comparable bone formation, ensuring stable graft dimensions combined with high implant success and healthy peri-implant conditions. However, the small particle size resulted in better bone-graft contact, providing greater osteoconductivity than with the larger particle size. Based on the literary findings, it was shown that the fibrin-rich plasma is favorable for bone formation processes for dental implants, especially when combined with xenografts.

Keywords: Bone augmentation. Maxillary sinus surgery. Fibrin-rich plasma. Bone Graft.

Introduction

In the context of bone regeneration for dental implants, maxillary sinus augmentation is a well-documented surgical technique and is one of the therapeutic options for implant placement in the atrophic posterior maxilla (particularly when the residual bone height is less than 5 mm) [1]. Bone regeneration is performed by elevating the Schneiderian membrane and creating a virtual cavity to be filled with compact bone substitute material. To protect the regenerated region and prevent displacement of the graft material, a resorbable membrane can be placed before suturing. A wide variety of bone substitutes have been studied, such as xenograft, allograft, and synthetic biomaterials [1-3].

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 [1]. 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 pseudo stratified 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 [1,2].

The maxillary sinus drains through its ostium in the nasal cavity, which usually happens in the middle meatus. Around 25% of all maxillary sinuses, there is an accessory bone that is located lower than the main ostium, and all the mucus produced and the particles trapped in this mucus is directed through the ciliary beat to the ostium [3-5].

When a dental element is lost in the posterior region of the maxilla, there is a natural reabsorption 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 place [2,6]. For this reason, the procedure for elevating the floor of the maxillary sinus or short implants should be performed when possible. When grafting procedures are needed, our focus is often on the type of biomaterial to be used and the success and predictability of our results does not depend only on the biomaterial [6].

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 biomaterials that we must use, but also, the characteristics of the bed and bone defect that we intend to treat [1,7].

Also, several surgical techniques can be used to reconstruct the atrophic alveolar ridge, techniques alone 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. As a disadvantage to the autogenous bone graft, the need for a 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 [3,6].

In this context, allogeneic, xenogenous and alloplastic bone grafts are an alternative for the treatment of bone defects in the jaws, since they avoid the need for a second surgical access. However, 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 grafts [8]. To increase the bone formation potential of these grafts, combinations have been proposed to obtain better regenerative conditions through the preservation of volume and the induction of cell migration differentiation [2,3].

Also in this context, in the last 20 years, platelet concentrates have been proposed as regenerative materials in tissue regeneration procedures. Among the platelet concentrates proposed in the literature, injectable platelet-rich fibrin (i-PRF) are found to 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 [2,4].

Thus, the present study carried out a systematic review to present the main scientific documentation on maxillary sinus augmentation and bone regeneration for dental implants.

Methods

Study Design

This study followed the international systematic review model, following the PRISMA (preferred reporting items for systematic reviews and meta-analysis) rules. Available at: http://www.prisma-statement.org/?AspxAutoDetectCookieSupport=1. Accessed on: 10/11/2024. The AMSTAR 2 (Assessing the methodological quality of systematic reviews) methodological quality standards were also followed. Available at: https://amstar.ca/. Accessed on: 10/11/2024.

Search Strategy and Search Sources

The literature search process was carried out from November 2024 to January 2025 and developed based on Web of Science, Scopus, PubMed, Lilacs, Ebsco, Scielo, and Google Scholar, covering scientific articles from various periods to the present day. The following descriptors were used in health sciences (DeCS/MeSH): *Bone augmentation. Maxillary sinus surgery. Fibrin-rich plasma. Bone Graft*, and the Boolean "and" was used between the MeSH terms and "or" between the historical findings.

Study Quality and Risk of Bias

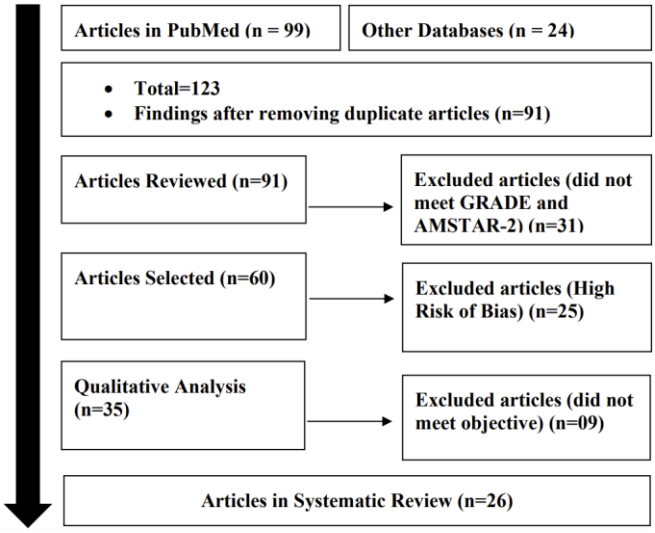
Quality was classified as high, moderate, low, or very low regarding the risk of bias, clarity of

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. 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 Cohen's test (d).

Summary of Findings

A total of 123 articles were found and submitted to eligibility analysis, with 26 final studies selected to compose the results of this systematic review. The listed studies 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. Biases did not compromise the scientific basis of the studies. According to the GRADE instrument, most studies presented homogeneity in their results, with X^2=90.8%>50%. Considering the Cochrane tool for risk of bias, the overall assessment resulted in 25 studies with a high risk of bias and 31 studies that did not meet GRADE and AMSTAR-2.

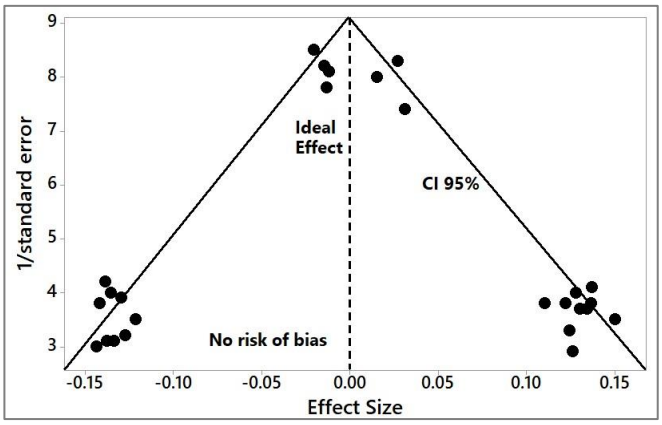
Figure 1. Flowchart showing the article selection process.



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 Cohen's 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 among studies with small sample sizes (lower precision) that are shown at the base of the graph and in studies with large sample sizes that are presented at the top.

Figure 2. The symmetrical funnel plot suggests no risk of bias among the studies with small sample sizes that are shown at the bottom of the graph. High confidence and high recommendation studies are shown above the graph (n=26 studies).



Source: Own Authorship.

Literature Review and Development

Authors Eken et al. (2025) [9] compared, through a randomized clinical trial, the radiographic, histomorphometric, and stability results of titanium-prepared platelet-rich fibrin (T-PRF) and deproteinized bovine bone mineral (DBBM) implants in a two-stage maxillary sinus augmentation technique. Patients with systemic comorbidities and residual bone height > 5 mm in the bilateral posterior maxilla were excluded. The primary outcome was the histomorphometric evaluation of the percentage of new bone between the 2 groups. Secondary outcomes included radiographic assessment of total bone height (ToBH), bone gain, bone density (BD), and graft volume (GV) on cone beam computed tomography 6 months after maxillary sinus augmentation, clinical assessment of primary implant stability at implant placement and secondary stability 3 months after placement, and histomorphometric assessment of the percentage of residual particles, percentage of connective tissue, and percentage of blood vessels from bone biopsy specimens collected 6 months after maxillary sinus augmentation. The sample consisted of 10 patients with bilateral maxillary sinuses, 20 maxillary sinus augmentation regions, 8 (80%) men, and 2 (20%) women with a mean age of 51.30 (9.06) years. The percentage of new bone was 19.48 ± 14.60 μm^2 in the T-PRF group and 8.31 ± 5.47 μm^2 in the DBBM group, and there was no statistically significant difference between the groups (p=0.074). Radiographic measurements showed ToBH, GV, and BD values of 10.64 ± 3.96 mm, 989.89 ± 523.07 mm^3, and 192.09 ± 127.90 Hounsfield units in the T-PRF group and 14.25 ±

1.65 mm, 1,519.39 ± 432.61 mm^3, and 492.77 ± 117.35 hounsfield units in the DBBM group, respectively. The ToBH, GV, and BD values were statistically significant between the groups (p=0.01 and p=0.00). The primary and secondary implant stability in the T-PRF group were 71.11 ± 12.48 implant stability quotient (ISQ) and 68.03 ± 6.81 ISQ, respectively, compared with 67.94 ± 19.84 ISQ and 72.46 ± 11.21 ISQ in the DBBM group.

Also, the authors Krennmair et al. (2024) [10] analyzed the new bone formation assessed histomorphometrically (NB), the graft stability measured radiographically and the clinical outcome of the implant for maxillary sinus augmentation grafted with deproteinized bovine bone mineral (DBBM) with small (Bio-Oss-S, Geistlich) or large (Bio-Oss-L, Geistlich) particles. A total of 22 sinuses from 11 patients were analyzed. Histomorphometric analysis of axially retrieved bone biopsies revealed the presence of NB (S: 25.5% ± 7.0% vs L: 23.6% ± 11.9%; P = 0.640), residual graft particles (S: 19.6% ± 9.2% vs L: 17.5% ± 6.3%; P = 0.365), as well as connective tissue (S: 54.9% ± 9.2% vs L: 58.9% ± 12.5%; P = 0.283), with no significant differences between the use of small (Bio-Oss-S) and large (Bio-Oss-L) particles. However, there was significantly (p=0.021) greater bone-graft contact (BGC) for the small particle graft sites (27.9% ± 14.8%) compared with the large particle graft sites (19.9% ± 12.9%), representing significantly greater osteoconductivity. Both particle sizes showed a significant (p<0.01) reduction in vertical graft height over time (4 years) of approximately 10%, with predominant graft reduction in the period between sinus augmentation and implant placement compared with any follow-up periods after implant placement. In the 3-year implant post-loading evaluation, all implants and prostheses survived (100%), and peri-implant marginal bone loss (S: 0.52 ± 0.19 mm; L: 0.48 ± 0.15 mm) as well as peri-implant health conditions (S: 87.5%, L: 81.2%) did not differ between implants inserted with the two different xenograft particles used.

A randomized controlled clinical trial demonstrated that maxillary sinus augmentation with composite grafts containing minimal amounts of autogenous bone graft yields comparable implant treatment outcomes compared with autogenous bone graft alone after one year of functional implant loading. Extensive autogenous bone graft harvesting in conjunction with maxillary sinus augmentation therefore appears not to be necessary. High patient satisfaction and significant improvement in oral health-related quality of life were also reported in all groups [11].

In addition, among xenografts, deproteinized bovine bone graft is frequently used in sinus floor elevation procedures. Leaving an ungrafted space after membrane elevation has also been shown to have bone regenerative potential. A randomized controlled clinical trial conducted by authors Carmagnola et al. (2024) [12] compared the clinical and histological characteristics of sinus floor elevation surgery performed with or without biomaterials. Patients with severe maxillary posterior atrophy (residual bone height of 2–6 mm and residual crestal thickness ≥4 mm) and requiring sinus floor elevation surgery to allow placement of three implants were enrolled and randomly divided into two groups. They underwent maxillary sinus elevation with deproteinized bovine bone graft (control) or with a graftless technique (test) and immediate placement of two implants (one mesial and one distal), with a follow-up of 5 to 12 years. Ten patients were enrolled in the test group and nine in the control group. The 6-month follow-up showed in the control group a mean increase of 10.31 mm (± 2.12), while in the test group, it was 8.5 mm (± 1.41) and a success rate of 96.3% in the control and 86.7% (p > 0.05). Histological analysis evidenced the presence of new bone tissue surrounded by immature osteoid matrix in the test group, and a variable number of deproteinized bovine bone particles surrounded by an immature woven bone matrix in the control group.

In the scenario of maxillary sinus surgery, 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 dental extractions, congenital tooth absence, jaw, 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]. Bone loss can also occur due to periodontal disease, traumatic surgeries, or even physiological reasons due to the lack of adequate or inadequate prosthetic load. Trauma in the face 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 to the economic impact they cause on the Unified Health System [7]. The face, more than any other region of the body, is affected by aesthetic changes since it is always visible and the damage is noticed immediately. For this reason, facial trauma deserves to be highlighted in the treatment of multiple trauma due to its high incidence and severity [8].

In this context, injectable platelet-rich fibrin (i-PRF) as an autologous biomaterial was developed in France by Choukroun et al. (1993) [4] for specific use in oral and maxillofacial surgery. This biomaterial presents the

majority of leukocytes, platelets, and growth factors, forming a fibrin matrix, with three-dimensional architecture. It is the second generation of platelet concentrate with a high potential for injury repair.

Also, obtaining i-PRF 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 most of the collected blood platelets begins, from the contact with the tube walls, and the release of the coagulation cascades. As the final product of this process, we have fibrinogen, which is a soluble protein, transformed into insoluble fibrin by thrombin. Fibrin gel is the first scar matrix of injured sites. Fibrinogen is concentrated in the upper part of the tube before the circulating thrombin converts it into 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].

The i-PRF has the characteristic of polymerizing naturally and slowly during centrifugation. The fibrin network thus formed has, in particular, a homogeneous three-dimensional organization, more coherent than the natural fibrin clots [8-14]. 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 [15,16]. Cytokines are thus kept available in situ for a convenient period when cells begin remodeling the matrix [17].

Also, i-PRF is based on the protection of proteolysis growth factors that can maintain its activity for a longer period and stimulate bone regeneration more efficiently [18]. The most critical phase of the sinus membrane elevation procedure after osteotomy of the maxillary sinus lateral wall is its detachment [19]. In this phase, Schneider membrane ruptures may occur, in approximately 15.0% of the cases, which, depending on the size of the perforation, may render the graft unfeasible, mainly due to the containment character of the graft material that the membrane exercises. The most frequent causes of these perforations are inadequate osteotomies, incomplete membrane detachments with a lack of bone support to raise curettes, excessive pressure on the membrane, and the presence of septa [20-23].

If perforations of the sinus membrane are present, this must be quantified [24], since small perforations do not require treatment, since the folds of the membrane obliterate the perforation. In the case of ruptures greater than 5.0 mm, the use of collagen membranes is indicated [25]. Another study indicated the use of fibrin membranes obtained from the i-PRF to seal the perforations. In the presence of perforations greater than 10.0 mm, the surgery must be aborted and reentry performed after 60 to 90 days [26].

The development of optimized implant surfaces is the subject of great research to accelerate the osseointegration process, leading to a reduction in the waiting time before loading, in addition to making the immediate loading of the implant safer [26]. It was documented for the first time that the combination of biomaterial and i-PRF significantly improved bone regeneration in the peri-implant zone. The placement of the implant with the simultaneous use of i-PRF creates a good relationship between hard and soft tissue, in addition to the advantage of the psychological relationship with the patient [2]. Migration and cell proliferation on the surface of the implants are fundamental to initiating the process of tissue regeneration, while changes in the surface of the implants incorporating growth and differentiation mediators can potentiate tissue regeneration for the implant [3,4].

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 (ROG), especially the sterile deproteinized bovine bone marrow (OBMED), which has been extensively researched and shown to have similarities with human bone marrow. OBMED is a great osteoconduction, providing a framework favorable to bone formation. Its slow resorption contributes a lot to maintaining the graft volume. It has good wettability and a good angle of superficial contact, 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 neoformation. A study with OBMED used alone or mixed with autogenous bone in several percentages in the floor elevation of the maxillary sinus demonstrated bone formation similar to that of autogenous bone after 9 months [20].

The xenograft most used in guided bone regeneration procedures is the deproteinized bovine bone mineral, commercially known as Bio-Oss®, it is the most researched product worldwide in regenerative dentistry. It is a 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, Bio-Oss® particles become an integral

part of the newly formed bone structure and retain their volume in the long term. Therefore, although the results do not seem to confirm that the I-PRF 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. Also, the use of the I-PRF 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 procedure costs [23].

Implantology stands out as a modern method of oral rehabilitation for total or partially edentulous patients. For this method to develop properly, bone integration of the implant into the recipient bone tissue is necessary, since bone integration is the key to clinical surgical success, which will be completed after the prosthetic phase is over [1-3]. Dental implants are being used more and more due to the high success rates. However, a large portion of patients do not have sufficient minimum bone conditions for the installation of 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 cases [1,2].

Thus, i-PRF as an autologous biomaterial for use in oral and maxillofacial surgery has the majority of leukocytes, platelets, and growth factors, forming a fibrin matrix, with threedimensional architecture. 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 adenomatous mesenchymal stem cells the appropriate biological niche for bone growth and thus, allowing the dental implant to be as effective as possible [21].

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, and 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. In this sense, filling biomaterials can be i-PRF, Bio-Oss®, hydroxyapatite, lyophilized and ground demineralized bone marrow, and autogenous bone, which is considered the gold standard, among others [24].

To improve osseointegration and bone anchorage, surface changes 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 the i-PRF preparations, such as the number of centrifuges used, the speed of centrifugation, and other protocols that result in preparations with various volumes, platelet numbers, the number of growth factors, and concentration of white blood cells and fundamental red cells [25].

Some researchers recommend avoiding tissue exposure to i-PRF-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. The i-PRF has gained prominence in the scientific community for not requiring 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. It also shows other forms of the application making its use simpler. In this sense, the bioactivation of the dental implant surface with i-PRF has been described and discussed by the scientific community as a surface treatment for the stimulation and acceleration of the osseointegration process, as well as to achieve greater primary stability to the implant [26].

The need to rehabilitate edentulous areas that have undergone major resorption is a current need and the maxillary sinus elevation maneuver is a viable way to implant anchorage for implant-supported oral rehabilitation. One of the relatively frequent complications (15.0%) of the procedures is the rupture of the sinus membrane during displacement of the sinus membrane. The main complication of this rupture is related to graft containment [1]. In this context, small perforations with an extension of 1.0 to 2.0 mm are contoured with the folds of the membrane in its elevation, but when they reach lengths greater than these, the membranes must be added to close it, and larger slits than 10.0 mm. The surgery must be aborted and reinserted after a period of re-epithelialization of the antral cavity, that is, between 60 and 90 days [2]. Thus, the use of an autologous fibrin membrane, obtained by centrifuging the patient's venous blood, without adding anticoagulants, provides a quick and efficient repair of surgical wounds. Fibrin gel is the first scar matrix of injured sites [3]. I-PRF is the second generation of fibrin concentrates, succeeding i-PRF, which had the limitation of releasing growth factors and cytokines in a very short time [4].

Finally, the i-PRF has progressive polymerization and the incorporation of circulating cytokines increases in the fibrin mesh. Such a configuration implies a longer life for these cytokines, as they are released and used only in the remodeling of the initial scar matrix. Thus, cytokines are kept available in situ for a convenient

period, when cells begin to heal the matrix, that is, when they need to be stimulated to reconstruct the injured site. According to some authors, the i-PRF works to protect the growth factors of proteolysis, which, in this way, can maintain its activity for a longer period and stimulate tissue regeneration. The use of autogenous bone, especially the ability to osteoinduction, has been recommended for filling the antral cavity [2].

Bias and Limitations

No significant risks of bias were found among studies with small sample sizes, as indicated in Figure 2. The limitations found are related to the limited number of patients in each study, as well as the advances in phase II, III and IV clinical studies.

Conclusion

It was concluded that the use of small and large bovine xenograft particles for maxillary sinus augmentation provides comparable bone formation, ensuring stable graft dimensions combined with high implant success and healthy peri-implant conditions. However, the small particle size resulted in better bone-graft contact, providing greater osteoconductivity than with the larger particle size. Based on the literary findings, it was shown that the fibrin-rich plasma is favorable for bone formation processes for dental implants, especially when combined with xenografts.

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Informed Consent

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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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