



Dental Implants and Plasma Rich in Fibrine: A Wide Literary Review

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Abstract: Introduction: 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 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. For this reason, the procedure for elevating the floor of the maxillary sinus or short implants should be performed when possible. 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. 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, PRP and FRP are found to act as autogenous platelet aggregates with osteoinductive properties. **Objective:** The present study aimed to conduct a wide literature review on maxillary sinus surgery using fibrin-rich plasma. **Methods:** Experimental and clinical studies (case reports, retrospective, prospective and randomized) with qualitative and/or quantitative analysis were included. **Results:** The total of 48 articles were found involving Maxillary sinus surgery, Fibrin-rich plasma, and Biomaterials, of which 22 were selected to compose the present study. **Conclusion:** Based on the literary findings, it was shown that the FRP is favorable for bone formation processes for dental implants, especially when combined with xenografts.

Keywords: Maxillary sinus surgery, Fibrin-rich plasma, Biomaterials, Dental implants.

1. Introduction

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].

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. [2].

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 [3]. 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 [3].

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 [4].

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 [3]. 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].

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 [5]. 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 [5].

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, PRP and FRP 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.

The present study aimed to conduct a review of the literature on maxillary sinus surgery using fibrin-rich plasma.

2. Methods

An exploratory and narrative review of world literature was developed. Experimental and clinical studies were selected, involving retrospective, prospective and randomized studies. Initially, keywords were determined by searching the DeCS tool (Descriptors in Health Sciences, BIREME base) and then verified and validated by the MeSH system (Medical Subject Headings, the US National Library of Medicine) to achieve a consistent search.

2.1. Descriptors

The main descriptors (MeSH Terms) used were "Maxillary sinus surgery", "Fibrin-rich plasma", "Biomaterials". For further specification, the "regeneration" description for refinement was added during searches. The bibliographic search was carried out through online databases: PubMed, Scopus, Periodicos.com, and Google Scholar.

2.2. Eligibility

The total of 48 articles were found involving maxillary sinus surgery using fibrin-rich plasma. Initially, the existing title was excluded and duplicated according to the interest described in this work. After this process, the abstracts were evaluated and a new exclusion was performed. A total of 32 articles were evaluated in full and 22 were included and discussed in this study (Figure 1).

3. Literature Review and Development

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 [3]. Trauma in the face region can affect both soft and hard tissues so that these injuries can affect the victim's quality of life and health [3].

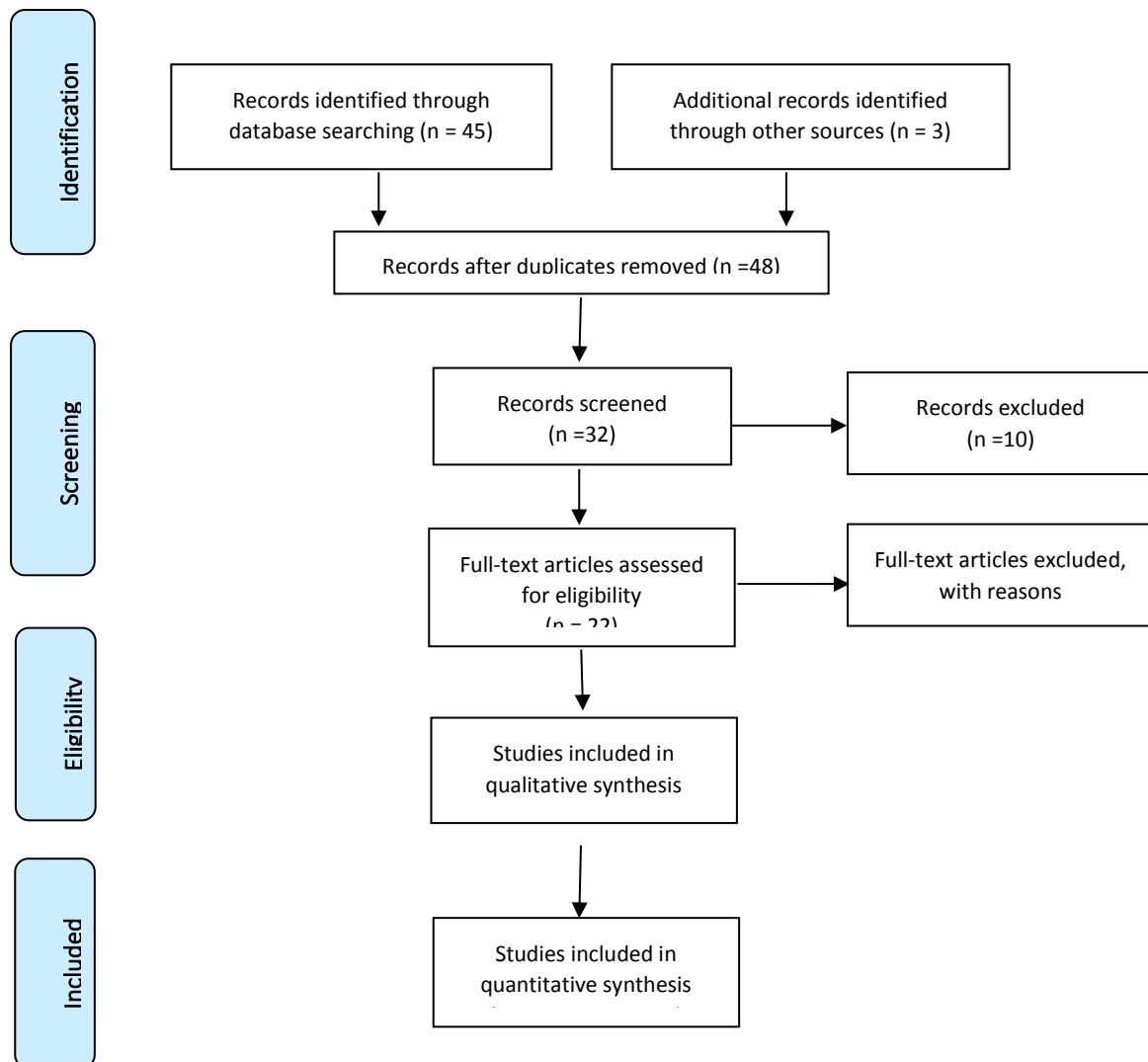


Figure 1. Flow Chart

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 in the Unified Health System (NHS) [4]. 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 [5].

In this context, fibrin-rich plasma (FRP) 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 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 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 FRP 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 [8-10]. In this context, with the 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 [12]. Cytokines are thus kept available in situ for a convenient period when cells begin remodeling the matrix [13].

Also, FRP is based on the protection of proteolysis growth factors that can maintain its 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 maxillary sinus lateral wall is its detachment [15]. 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 lack of bone support to raise curettes, exerting excessive pressure on the membrane, and the presence of septa [16-19].

If perforations of the sinus membrane are present, this must be quantified [20], 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 [21]. Another study indicated the use of fibrin membranes obtained from the FRP 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 [22].

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 [22]. 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 PRP creates a good relationship between hard and soft tissue, in addition to the advantage of the psychological relationship with the patient [1].

Migration and cell proliferation on the surface of the implants are fundamental to initiate 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 [2-5].

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 bone marrow (OBMED), which has been extensively researched and shown to have similarities with human bone marrow. OBMED is a great postcondition, 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 the 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 [16].

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 mineral 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 [19].

Therefore, although the results do not seem to confirm that the 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. Also, 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 procedure costs [20].

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].

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].

Thus, FRP 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 three-dimensional 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 [17].

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 surgeries for severe maxilla atrophy after breast elevation procedures in 106-120-180 days, to determine whether the use of FRP is able to 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, in fact, the use of FRP has optimized bone formation [17].

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 composite FRP / Bio-Oss® was grafted and the composite Tisseel® / Bio-Oss® was grafted into the other sinus cavity. After a 6-month healing period, 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, the bone formation at the graft sites is significantly greater than when Tisseel® is used [19].

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 load conditions. In addition, it is necessary to have a bone layer of the host that is healthy, compatible and that allows primary stability [20].

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 neoformation, bone remodeling, and soft tissue epithelization [20]. During this process, the alveolar ridge undergoes relevant changes, both in height and in thickness, which influence the possibility of installing the implants. 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 greater success rate and patient comfort [20].

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. In this sense, filling biomaterials can be FRP, Bio-Oss®, hydroxyapatite, lyophilized and ground demineralized bone marrow, autogenous bone, which is considered the gold standard, among others [20].

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 FRP 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. [21].

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 [22]. The FRP has gained prominence in the scientific community for not requiring the addition of an activator or anticoagulant, making the product more autologous, 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 [22].

In this sense, the bioactivation of the dental implant surface with FRP 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 [22].

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 [1]. 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 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]. FRP is the second generation of fibrin concentrates, succeeding FRP, which had the limitation of releasing growth factors and cytokines in a very short time [4].

The FRP 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 [5].

According to some authors, the FRP 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 [6].

4. Conclusion

Based on the literary findings, it was shown that the FRP is favorable for bone formation processes for dental implants, especially when combined with xenografts.

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No additional data are available

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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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