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Major approaches and clinical outcomes of bone regeneration for dental implants: a systematic review

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Abstract

Introduction: In the last decades, the number of dental implant procedures has increased in the world, with about 1.0 million dental implants per year. When a tooth is lost in the posterior region of the maxilla, there is a natural resorption of the alveolar process. There are several surgical techniques that can be used to reconstruct the atrophic alveolar ridge. **Objective:** A systematic review was carried out to present the key considerations of bone regeneration and bone, cellular and molecular grafts for adequate bone formation for successful dental implants. **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 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:** The total of 132 articles were found. A total of 74 articles were fully evaluated and 31 were included in this study. Normal bone formation and tissue repair involve coordinated interaction between bone-forming cells and biological signals. 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 into the osteoblastic lineage. 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. The combination of FRP and Bio-Oss® has been studied with good clinical results, reducing healing time from 180 days to approximately 106 days. The use of bone grafts significantly improves the residual alveolar ridge regardless of the membrane used. Furthermore, implants placed in fresh extraction sockets with and without elevation of the mucoperiosteal flap can be successfully performed with augmentation procedures.

Keywords: Dental implants. Bone regeneration. Bone graft. Cells. Cytokines.

Introduction

In the last decades, the number of dental implant procedures has increased in the world, with about 1.0 million dental implants per year [1]. In Brazil, there was a rapid evolution with significant success rates [2-4]. In this context, the development of biomaterials for use in dental clinics represents a powerful therapeutic tool in the correction of bone defects [4].

In this aspect, the maxillary sinus is the largest of the paranasal sinuses and its function is to contribute to the resonance of phonation and to equalize pressures in the nasal cavity, which is covered by Schneider's membrane. This membrane is constituted by a pseudostratified cylindrical ciliary epithelium with goblet 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 [1].

In this scenario, 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, increasing its volume towards the place where the roots existed and this many times. will sometimes make it difficult or impossible to restore implants in place. Thus, the maxillary sinus floor elevation procedure should be performed, or short implants when possible [1,2].

Also, when graft procedures are needed, the focus is often on the type of biomaterial to be used. It is also necessary to consider the type of defect to be treated. In this way, morphology has an impact because the defects have different vascularization capacities, different capacities to recruit osteogenic cells, have different capacities for natural stabilization of grafts, therefore, the characteristics of biomaterials for clinical use must be considered, as well as the bed and therapeutic target bone defect characteristics [5].

In this context, several surgical techniques can be used to reconstruct the atrophic alveolar ridge, isolated techniques, or associated with autogenous, allogeneic, xenogeneic 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 self-regenerative potential [4]. As a disadvantage to autogenous bone graft, the need for second surgical access in the donor area stands out, resulting in longer surgical time, morbidity, and consequent greater patient resistance to the proposed treatment.

Thus, allogeneic, xenogeneic, and alloplastic bone grafts present themselves as an alternative for the treatment of bone deficiencies in the jaws, since they avoid the need for second surgical access [7]. But due to the need for processing to eliminate antigenic components, these grafts are uniquely osteoconductive with a lower bone formation potential compared to autogenous bone grafts [8,9]. To increase the bone formation potential of these grafts, combinations have been proposed to obtain better regenerative conditions through volume preservation (osteoconduction) and the induction of differentiation and cell migration (osteoinduction) [10].

In addition, platelet concentrates stand out as regenerative materials in bone regeneration and construction procedures, alongside bone grafts, such as PRP (platelet-rich plasma) and FRP (fibrin-rich plasma). FRP is a second-generation concentrate, that is, no anticoagulant is used for its acquisition. Leukocytes and platelets synthesize and release a variety of cytokines and growth factors that act in chemotaxis, angiogenesis, differentiation, and cell inhibition [9,11].

Added to this, 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, especially deproteinized sterilized bovine bone marrow, which has been extensively researched and shown to have similarities with human marrow bone, such as Bio-Oss® [12]. Deproteinized sterilized bovine bone marrow is an excellent osteoconduction, providing a favorable framework for bone formation. Its slow reabsorption contributes a lot to maintaining the volume of the graft, favoring contact with the blood clot. A study with deproteinized sterilized bovine bone marrow used alone or mixed with autogenous bone at various percentages in maxillary sinus floor elevation demonstrated bone formation similar to that of autogenous bone after 9 months [13].

Therefore, the present study performed a systematic review to present the key considerations of bone regeneration and bone, cellular and molecular grafts for adequate bone formation for successful dental implants.

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 April 2022.

Descriptors (MeSH Terms) And Search Strategy

The main descriptors (MeSH Terms) used were "Implantes dentários. Regeneração óssea. Enxerto ósseo. Células. Citocinas". For greater specification, the description "bone regeneration para implantes dentários" for refinement was added during the searches, following the rules of the word PICOS (Patient; Intervention; Control; Outcomes; Study Design).

Selection, Risk of Bias and Quality of Studies

Two independent reviewers 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. The quality of the studies was based on the GRADE instrument and the risk of bias was analyzed according to the Cochrane instrument.

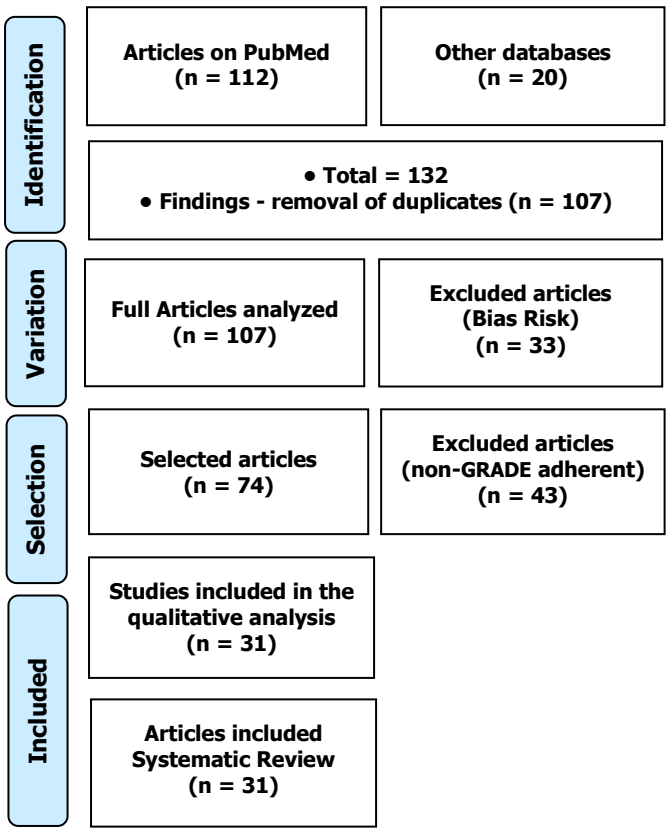
Results and Discussion

Article Series and Eligibility

The total of 132 articles were found. Initially, the duplication of articles was excluded. After this process, the abstracts were evaluated and a new exclusion was performed, removing the articles that did not include implantes dentários e bone regeneration, A total of 74 articles were fully evaluated and 31 were included in this study (**Figure 1**).

Considering the Cochrane tool for risk of bias, the overall assessment resulted in 30 studies with high risk of bias (studies with small sample size) and 3 studies with uncertain risk (studies with results without statistical significance). Also, 43 studies were excluded because they did not meet the GRADE.

Figure 1. Flowchart showing the article selection process.



Normal bone formation and tissue repair involve coordinated interaction between bone-forming cells and biological signals [5,14]. Osteoblasts can produce new bone along with biomaterials and can initiate the release of biological signals that guide bone formation and remodeling. 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, bone-forming cells migrate to the application area [15-17].

Furthermore, 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 [18,19].

In this context, dental implants are being increasingly used due to high success rates. However, a large number of patients do not have sufficient minimum bone conditions for the installation of implants, requiring previous bone reconstructive surgery [20]. Bone integration of the implant into the recipient bone tissue is necessary [21].

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 [22]. Some researchers recommend avoiding tissue exposure to leukocyte-containing FRP, arguing that an inflammatory reaction may occur [23]. 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 [23].

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 [23].

The need to rehabilitate edentulous areas that have undergone significant resorption is a current need and the maxillary sinus lift maneuver is a viable way to implant anchorage for implant-supported oral rehabilitation [24]. One of the complications that occur in around 15.0% of the procedures is the rupture of the sinus membrane, which is related to graft containment [25].

Thus, the use of an autologous fibrin membrane, obtained by centrifugation of the patient's venous blood, without the addition of anticoagulants, provides a fast and efficient repair of surgical wounds. The fibrin gel constitutes the first scar matrix of the injured sites [26].

In addition, FRP presents 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. Cytokines are thus kept available in situ for a convenient period, when the cells begin to heal the matrix, that is, when they need to be stimulated to rebuild the injured site [26].

In this scenario, some authors postulate that FRP acts to protect growth factors from proteolysis, which, in this way, can maintain their activity for a longer period and stimulate tissue regeneration. The use of autogenous bone, especially the capacity for osseoinduction, has been recommended for filling the antral cavity. However, the use of autogenous bone alone has a fast resorption time, resulting in a lower quality neoformed bone, compared to that used in association with hydroxyapatite [25-28].

Thus, bovine hydroxyapatite (Bio-Oss®) is considered a suitable bone substitute. The combination of FRP and Bio-Oss® has been studied with good clinical results, reducing healing time from 180 days to approximately 106 days. Another study, with a 6-year clinical follow-up, used FRP as the only filling material during maxillary sinus elevation and implant placement, promoting bone regeneration [29].

In this regard, a randomized clinical trial evaluated the results of guided bone regeneration (GBR) with and without a bioabsorbable membrane in the placement of dental implants. 20 patients were divided into two groups (n = 10). The first was Group I- GBR with bioabsorbable collagen membrane (BioGide™) and the second was Group II- GBR without membrane. For Group I, baseline bone levels were not significant. Likewise, non-significant values were observed in both groups at 3 months with bone level values of 0.25 ± 0.17 and 0.38 ± 0.24 for Group I and Group II, respectively. Changes in bone levels were 2.45 ± 0.349 and 2.58 ± 0.304 in Groups I and II, respectively. The percentage of intergroup bone gain at the end of 3 months was 89.15% ±0.678 for Group I and 88.68% ±0.503%. Therefore, the use of bone grafts significantly improves the residual alveolar ridge regardless of the membrane used [30].

Finally, another randomized clinical trial evaluated and clinically compared the clinical success and relative bone healing of implants that are placed using a flapless procedure and compare it with those placed by the conventional flap technique. Ten patients were randomly divided into two groups. Group A included patients with implants placed immediately after extraction with flap elevation. Group B included patients with implants placed immediately after extraction without any flap elevation. There was an improvement in the plate score from baseline to 1 month and from baseline to abutment placement (6 months), which was statistically significant, but the plate score from 3 months to abutment placement (6 months) was statistically non-significant in both groups. There was an increase in the modified gingival score from baseline to 3 months, from baseline to abutment placement (6 months) and 3 months to abutment placement (6 months), which was statistically significant in both the groups. Therefore, implants placed in fresh extraction sockets with and without elevation of the mucoperiosteal flap can be successfully performed with augmentation procedures. Short-term survival rates and clinical outcomes for both groups were similar [31].

Conclusion

Based on the objective and results of the present study, it was concluded that 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. The combination of FRP and Bio-Oss® has been studied with good clinical results. The use of bone grafts significantly improves the residual alveolar ridge regardless of the membrane used. Furthermore, implants placed in fresh extraction sockets with and without elevation of the mucoperiosteal flap can be successfully performed with augmentation procedures.

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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.

Similarity check

It was applied by Ithenticate@.

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