REVIEW ARTICLE

Techniques for Extraction Socket Regeneration for Alveolar Ridge Preservation

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Abstract

Background: Alveolar bone undergoes volumetric changes after extraction due to physiologic bone remodeling. The amount of alveolar bone available during prosthodontic treatment can affect the esthetic outcome of the treatment and make implant placement challenging. Socket preservation techniques are advocated postextraction to maintain the bone's vertical and horizontal alveolar bone dimensions and prevent its atrophy.

Aim: This review is oriented toward a clinician, describing the different materials and techniques in practice today for socket preservation.

Review results: A variety of methods have been studied as a means to stop alveolar ridge resorption. While immediate implant placement was recommended as a socket preservation technique, clinical trials have not demonstrated favorable results. The main techniques favored by clinicians today involve bone grafts, bone substitutes, barrier membranes, and combinations thereof. As with periodontal defects, these materials show favorable outcomes in alveolar bone regeneration and ridge preservation. Tooth bone grafts, both autogenous and allogenous, have been recommended recently for ridge preservation as they are chemically similar to bone and can induce osteogenesis. The use of autologous platelet concentrates has yielded contradictory results in studies. Cutting-edge approaches entail using growth factors and tissue engineering concepts. While these strategies are still in the development stages, it has peerless potential in preserving and regenerating alveolar bone.

Conclusion: Alveolar ridge resorption is an unavoidable physiological process after extraction and leads to severe bone deficiencies, affecting esthetics. These changes in alveolar ridge dimensions make implant placement difficult and affect the longevity of the implant. Clinical intervention can prevent alveolar bone resorption and preserve the ridge. Bone grafts and substitutes including concentrates remain the best choices in ride preservation. The use of growth factors and tissue engineering concepts requires further clinical trials before widespread use in clinical practice.

Keywords: Alveolar ridge preservation, Autologous platelet concentrates, Barrier membranes, Bone grafts, Growth factors, Immediate implantation, Socket preservation, Tissue engineering, Tooth bone grafts.

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Introduction

The alveolar wall surrounding the tooth is unique. It has a double fibrillar orientation due to the insertion of Sharpey's fibers and is perforated by blood vessels and nerve fibers. The bone undergoes continuous remodeling due to constant biomechanical forces acting on the tooth.[1] The alveolar bone's shape and volume are determined by the inclination, axis of eruption, and form of the tooth. Following extraction, the alveolar socket inevitably undergoes various changes resulting in volumetric changes in the alveolar bone.[2] The amount of horizontal and vertical alveolar bone postextraction can make implant placement more challenging, affect osseointegration, and affect the esthetic result of the prosthodontic treatment, either through conventional prosthesis or through implant.[3] The systematic review published by Lang et al. calculated changes in soft tissue and hard tissue dimensions and determined the horizontal bone loss to be approximately 2.46–4.56 mm and the vertical bone loss be 0.8–1.5 mm 6 months after extraction. Buccal aspects, rather than lingual or palatal aspects, demonstrated more resorption, and buccolingual aspects demonstrated more resorption than mesiodistal aspects. The resorption rate was observed to be faster in the initial 3–6 months following the extraction and gradually slowed down after 6 months.[4]

Socket preservation procedures aim to preserve the volume of the alveolar ridge and neutralize early dimensional changes in the hard tissue at the extraction site. Hammerle et al. defined ridge preservation as preserving the ridge volume within the envelope existing at the time of extraction. The authors expounded the indications for ridge preservation to include situations wherein immediate or early implant placement is not recommended, if

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primary stability cannot be obtained, and if the prosthodontic rehabilitation requires ridge contouring.[5] As the popularity of implants skyrockets, socket preservation techniques may become a pre-requisite after any extraction. Socket preservation or alveolar ridge preservation maintains the integrity and volume of the hard and soft tissues at the extraction site, making it easier for future implant placement and supporting the esthetic and functional outcomes.[3]

This review aims to describe the techniques currently recommended for ridge preservation and provide clinicians with an evidence-based approach for alveolar ridge preservation.

Healing of the Extraction Socket

A keen understanding of the remodeling of the extraction socket is necessary to appreciate the techniques of socket regeneration and preservation. The first step in healing an extraction socket is the formation of a coagulum immediately after extraction, which is replaced with a provisional matrix. This is followed by the formation of woven bone forming a hard tissue bridge. Remodeling involves the removal of woven bone and the formation of lamellar bone. Additional layers of newly formed lamellar bone reinforce the hard tissue bridge. Finally, with the formation of the periosteum, the overlying mucosa attaches to the cortical bone. These resorptive and proliferative changes resulting in the formation of a cortical wall are referred to as corticalization. These events closely resemble fracture healing in a long bone.[6–8]

Socket Preservation Techniques

Various authors have advocated multiple materials and techniques for socket preservation. Advances in biomaterials and research unraveling the molecular mechanisms of alveolar bone changes have led to the exploration of new avenues to achieve the optimal treatment result. Alveolar ridge preservation techniques encompass procedures such as the flapless extraction technique recommended by Fickl et al.[9] to the cutting-edge treatments using autologous stem cells and growth factors.[10]

Immediate Implants as Socket Preservers

Conventionally, a dental implant is placed 6–12 months after tooth extraction to allow for complete healing of the alveolar socket. However, the dimensional changes occurring in the alveolar bone in that period may render implant placement difficult and affect the therapeutic outcome.[11] Paolantonio et al. recommended immediate implantation without other socket preservation techniques such as barrier membranes to avert alveolar bone changes.[12] However, other authors have observed contradictory results. Araujo et al. demonstrated that, with immediate implantation, approximately 2.6 mm of bone loss was observed after 3 months of healing.[13] Another study by the same researchers found that bone-to-implant contact was made at the end of 1 month after extraction. However, the buccal wall of the alveolar bone underwent resorption and the bone-to-implant contact was partly lost after 3 months of healing.[14] These results have been confirmed by clinical studies of Botticelli et al.[15] Immediate loading after immediate implantation did not alter the amount of buccal bone resorption that took place.[16] These studies demonstrated that immediate implants with or without immediate loading did not particularly alter the bone resorption pattern after tooth extraction.

Bone Grafts and Bone Substitutes

Bone grafts and bone substitutes, either alone or in combination with other biomaterials such as barrier membranes, are extensively used to treat periodontal bone defects. They have also been recommended as a socket filling material to prevent loss of alveolar bone during healing.[17]

Bone grafts generally refer to autogenous bone grafts and allogenous grafts. Autogenous grafts are harvested from the patient's body and are the "gold standard" material. Common donor sites include maxillary tuberosity, edentulous ridges, mandibular ramus, and mandibular symphysis intra-orally or the iliac crest, tibia extra-orally. Autogenous bone grafts are osteoconductive and osteoinductive and can induce osteogenesis. They are also biocompatible and nonimmunogenic. They can be of three main types: corticocancellous, cancellous, and cortical.

Allogenous grafts or allografts refer to grafts obtained from different individuals of the same species. Depending on their processing technique, they can be demineralized freeze-dried, freeze-dried, or fresh frozen. Demineralized bone allograft has osteoinductive properties as the demineralization process exposes bone morphogenetic protein (BMP). However, there is an increased risk of disease transmission and risks of immunogenic reaction with allografts.[18,19]

Bone substitutes include xenogenic grafts (=xenografts, =alloplastic grafts, =alloplasts). Xenografts are obtained from different species and then transplanted into humans. They are bovine, porcine, equine, or coralline in origin. Xenografts carry a higher risk of disease transmission and immunogenicity. Alloplasts are synthetic bone substitutes and primarily function as defect fillers. They include natural and synthetic polymers and bioceramics like hydroxyapatite. Since they are manufactured under controlled conditions, their properties like degradation rate and pore size can be controlled.[19–21]

Boix et al. examined the use of an injectable alloplast on socket preservation. The alloplast was a composite of biphasic calcium phosphate (BCP) bioceramic and polymer solution. Alveolar bone resorption was significantly less in extraction sites filled with the composite material.[22] Wood and Mealey compared the effects of demineralized freeze-dried bone allograft (DFDBA) and mineralized freeze-dried bone allograft (FDBA) on the healing of extraction sockets and the changes in alveolar ridge dimension width. Clinically, no significant difference was observed in dimensional changes in the alveolar ridge with either DFDBA or FDBA. However, histological analysis revealed that DFDBA grafted sites had more vital bone and fewer residual graft particles.[23] Araujo et al. used Bio-Oss collagen, a combination of bovine-derived xenograft and porcine collagen, for socket preservation and observed that while Bio-Oss did serve as a scaffold material, it did not increase bone formation. However, they noted that alveolar ridge preservation was better than nongrafted sites.[24] Rothamel et al. applied nanocrystalline hydroxyapatite paste (NHA) into fresh extraction sockets of dogs to evaluate its effect on the alveolar ridge and reported that NHA was not effective in socket preservation.[25] Froum et al. compared socket preservation with DBBM and bioactive glass. More vital bone was observed in sites where the bioactive glass was used rather than DBBM.[26] Medical grade calcium sulfate hemihydrate (MGCSH) was investigated as a socket graft in a study by Guarnieri et al. The authors placed MGCSH in 10 fresh extraction sockets and re-evaluated the patients at 3 months. At 3 months, histologically, lamellar arrangements were seen in

the newly formed bone, and MGCSH particles were not observed. This indicates that MGCSH had completely resorbed in the healing period and can be considered an ideal graft material in socket preservation techniques.[27]

Barrier Membranes in Socket Preservation

Melcher hypothesized that colonization of wounds by nonosteogenic cells, cells from gingival connective tissue, can prevent the migration of osteogenic cells and affect the bone formation in the site.[28] Based on this hypothesis, Nyman et al. in 1982 used cellulose acetate filter paper as a barrier membrane to study new attachment on the diseased root surface. They noted that by preventing the gingival epithelial and connective tissue cells from coming into contact with the diseased root surface, periodontal ligament cells could populate the defect area, leading to the formation of new cementum and periodontal fibers.[29] The term "guided tissue regeneration (GTR)" was then coined by Gottlow (1986). Guided bone regeneration, commonly referred to as GBR, was expounded from the principles of GTR. It involves using a membrane to isolate the defect, thereby allowing space for osteoprogenitor cells to proliferate and differentiate along osteoblastic cells lineage. This increases the osteogenic activity in the defect area resulting in new bone formation.[30]

Barrier membranes are classified based on degradation characteristics into nonabsorbable and absorbable membranes. Nonabsorbable membranes include extended polytetrafluoroethylene (ePTFE) membrane and titanium mesh. Absorbable membranes can be naturally derived materials like cross-linked collagen or synthetic polymers like poly-D,L-lactide-co-glycolide.[31,32]

Lekovic et al. used ePTFE membrane, a nonresorbable membrane, to cover the extraction socket of 10 patients. After 6 months of healing, ePTFE membranes were removed, and changes in the dimensions of the alveolar ridge were studied. Upon evaluation, it was determined that experimental sites with ePTFE membranes covering the socket showed better results with more socket fill and a lesser amount of loss of alveolar ridge. However, sites with membrane exposure showed results comparable to control sites wherein no membrane was used.[33] In another study, a bioabsorbable membrane made of glycolide and lactide polymers was used to cover the extraction socket. This study also showed positive results, and the experimental sites had more bone formation and less resorption of the alveolar ridge. Here, there was no exposure of the placed membrane, reducing the chances of postoperative infection.[34]

Combination of Bone Graft and Membranes

Studies have also analyzed the efficacy of bone grafts in combination with barrier membranes to treat bone defects.[35] Pinho et al. studied the effect of titanium mesh in conjunction with autologous bone graft on alveolar socket preservation. They found no significant difference between patients who received titanium mesh with autologous bone graft and patients who received just the titanium membrane concerning measured parameters like bone fill and loss of alveolar ridge. However, membrane exposure was observed in 5 out of 10 patients.[36] Luczyszyn et al. investigated acellular dermal matrix with resorbable hydroxyapatite to prevent loss of alveolar ridge dimensions. Here, the acellular dermal matrix acted as a cell occlusive membrane, and hydroxyapatite was used as a socket filler. The results showed that while the ridge dimensions were preserved in patients whom acellular dermal matrix was used along with hydroxyapatite and in patients whom only acellular dermal matrix was used, the changes were significantly better when both were used in conjunction.[37]

Iasella et al. compared socket preservation with tetracycline hydrated mineralized FDBA and collagen membrane with extraction alone. As with other studies using FDBA and collagen membrane, it helped maintain the alveolar ridge levels and prevent resorption of alveolar bone.[38] Fugazzotto et al. compared a resorbable membrane with titanium-reinforced membrane, both in conjunction with Bio-Oss. It was observed histologically in both groups that Bio-Oss particles had completely resorbed with approximately 69% of new bone filling seen in the socket. Clinically, titanium-reinforced membranes showed better results than resorbable membranes. This was attributed to the fact that titanium membranes were stable once placed, and it was also possible to suitably adapt the titanium-reinforced membrane onto the socket.[39,40] Zubillaga et al. investigated the use of membrane stabilization on ridge preservation. Ten patients with eleven extraction sites were treated with DFDBA and a bioresorbable membrane. The membrane was stabilized with a bioabsorbable tack system in seven patients and was not tacked in the other six patients (seven sites). There was less loss of alveolar bone observed in the tacked group when compared to the nontacked group. Therefore, the authors concluded that membrane stabilization is beneficial when membranes are used in socket preservation.[41]

Tooth Bone Graft

An autogenous bone graft, considered the gold standard in graft, requires obtaining bone from a donor site. This may lead to an increase in patient morbidity and risk of infection in the donor site. Recently, extracted teeth have proven to be a new avenue for graft tissue. Though extracted teeth have generally been discarded as biowaste, the dentin within shows promise as a graft material. Dentin is chemically very similar to bone and has osteoconductive and osteoinductive properties.[42,43] Currently, three different processing techniques are recommended for autogenous tooth bone grafts. These result in undemineralized dentin (UDD), partially demineralized dentin matrix (PDDM), and demineralized dentin matrix (DDM).[44] DDM does not induce immunogenic reactions and is biocompatible as it is entirely acellular and avascular. It is acid insoluble and contains 95% highly cross-linked type I collagen in a collagenous matrix. The matrix also contains other proteins and growth factors like bone morphogenetic protein (BMP), fibroblast growth factor (FGF), transforming growth factors, and insulin-like growth factors.[45–47] Koga et al. demonstrated that DDM and PDDM showed better bone regeneration than UDM and PDDM with larger particle sizes, approximately 1000 µm, showed more potential at bone regeneration.[48]

Minamizato et al. studied the clinical efficacy of autogenous PDDM mixed with PRP when used as a socket preservation material. After 4–6 months of healing, it was observed that this combination helped preserve the width and height of the alveolar bone. In this study, PRP was added to PDDM for easier handling, but PRP itself can promote bone formation and may have accelerated bone regeneration.[49] Um et al. compared DDM with DDM loaded with recombinant bone morphogenetic protein-2 (DDM/rhBMP-2). In this

study, DDM acted as a carrier for rhBMP-2. The reduction in height and width of alveolar bone observed was significantly smaller for DDM/rhBMP-2 than with DDM alone. A synergistic effect is seen here with exogenous rhBMP-2 and endogenous growth factors in DDM.[50]

However, it is challenging to obtain autogenous tooth bone grafts in the required volume in edentulous patients or patients with grossly decayed teeth. Therefore, allogenous dentin bone grafts obtained from orthodontically extracted teeth or wisdom teeth of other individuals have been recommended. Kim et al. used allogenic DDM in socket preservation and observed that it gives comparable results to autogenous DDM. Further, he reported no complications or immune responses with allogenic DDM.[51,52]

Autologous Platelet Concentrates (APCs)

Autologous platelet concentrates are products derived from autologous blood. It contains a fibrin mesh and extracellular matrix, which binds various biologically active substances, including different growth factors. Based on leukocyte and fibrin content, they are categorized into pure platelet-rich plasma (P-PRP), leukocyte- and platelet-rich plasma (L-PRP), pure platelet-rich fibrin (P-PRF), leukocyte- and platelet-rich fibrin (L-PRF). Autologous fibrin glue can also be combined with bone graft to form "sticky bone." This sticky bone has copious amounts of growth factors and can accelerate bone formation.[53,54]

Though platelet concentrates have found a variety of applications in regenerative therapies,[55] the use of APCs in socket preservation is controversial, and reports in the literature offer contradictory findings. Two systematic reviews investigating platelet concentrates concluded that while sufficient evidence is available regarding the effect of platelet concentrates on soft tissue healing, evidence on the effect of platelet concentrates on preserving hard tissue volume is minimal and contradictory.[56,57] Alissa et al. investigated the effect of PRP in soft tissue healing and new bone formation following tooth extraction. It was observed that both soft tissue healing and bone formation were better with PRP than with the control group.[58] Hauser et al. used PRF as a socket filler after extraction and evaluated its effect on alveolar bone formation and preservation of the alveolar crest. They observed that the use of PRF accelerated bone healing and also preserved the alveolar crest to a more significant extent.[59] Farina et al. used plasma rich in growth factor (PRGF) and evaluated its effect on early bone formation. However, the authors did not find any significant radiographic or histomorphometric change in the PRGF group compared to the control group.[60] Another study by Suttapreyasri et al. also obtained similar results when PRF was used. While PRF accelerated soft tissue healing, they observed that it did not accelerate or enhance new bone formation.[61]

Growth Factors

Growth factors are a specific category of cytokines that can induce specific biological responses, including survival, migration, proliferation, and differentiation of various cells. While there are a variety of growth factors, the most explored factors include bone morphogenetic protein (BMP), transforming growth factor (TGF), platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), and insulin-like growth factor (IGF).[62,63] To reduce the dose of growth factor required and improve outcomes, it is used in combination with other materials like DDM, allografts, and xenografts.[64] BMP belongs to the family of transforming growth factors and includes factors like BMP-2, BMP-4, and BMP-7, all of which have strong bone-inducing capacity. It can act on undifferentiated mesenchymal cells and commit them to an osteoblastic pathway. PDGF is produced by platelets, endothelial cells, and osteoblasts and exists in three isoforms—PDGF-AA, PDGF-BB, and PDGF-AB. Even though PDGF can stimulate mesenchymal cells and osteoblasts, its bone inducing capacity is less than BMP.[65]

Coomes et al. investigated the effect of rhBMP-2 in an absorbable collagen sponge (ACS) carrier on bone augmentation. rhBMP-2 was found to be effective in regenerating buccal plates in this study.[66] Huh et al. used *Escherichia coli*-derived rhBMP-2 coated β-tricalcium phosphate (β-TCP) to fill the socket. At the end of 3-month healing period, it was observed that rhBMP-2-coated β-TCP was more effective in maintaining the alveolar ridge volume than β-TCP alone.[67] Geurs et al. combined rhPDGF-BB with FDBA, β-TCP, and collagen plug and compared this to a combination of PRP with FDBA, β-TCP, and collagen plug, a combination of FDBA, β-TCP and collagen plug, and collagen plug alone. Significant new bone formation was observed in all the groups 8 weeks after extraction. However, less bone graft material was observed in the socket when PRP and rhPDGF-BB were used.[68]

Stem Cells and Tissue Engineering

The National Science Foundation workshop in 1988 defined tissue engineering as "the application of principles and methods of engineering and life sciences toward the fundamental understanding of structure-function relationships in normal and pathological mammalian tissues and the development of biological substitutes to restore, maintain or improve tissue function." It comprises three components—stem cells, scaffolds, and signaling molecules.[69]

Stem cells are undifferentiated cells with the capacity for self-renewal and multilineage differentiation. They can be pluripotent, multipotent, or totipotent. Adult stem cells, also known as somatic stem cells or postnatal stem cells, can be obtained from sites like periodontal ligament, gingiva, tooth pulp, and oral epithelium in the orofacial region.[70] Yamada et al. fabricated injectable tissue-engineered bone precursors by combining bone marrow mesenchymal stem cells (BMMSCs) with PRF. The BMMSCs were observed to participate in osteogenesis and slowly differentiate into osteoblastic lineage cells with osteoblasts and osteocytes seen in the defect area. Radiographic analysis showed new bone formation with no resorption in the follow-up period.[71] Mashimo et al. transplanted BMMSCs into the extraction sockets of mice. At the end of 6 weeks, radiographic and histological analyses showed accelerated healing and new bone formation.[72] However, much more *in vitro* and *in vivo* research is required about the long-term safety and efficacy of stem cells before being recommended for clinical practice.

The future of alveolar ridge preservation involves growth factors and stem cells. Stem cells with their ability to differentiate into different cell types and growth factors with their ability to recruit different cells and aid in cell differentiation and osteogenesis may prove to be ideal materials to regenerate alveolar bone.

Conclusion

Alveolar ridge resorption is a physiological process after extraction and is unavoidable. However, it can lead to severe bone deficiencies in the extraction site, affecting the esthetic result of further

treatment. These volumetric changes in alveolar ridge dimensions also make it harder to place an implant and may affect the success of the placed implant. Clinical intervention is therefore needed to prevent alveolar bone resorption and ridge preservation. While many materials and techniques have been studied to prevent postextraction resorption, none of the currently used techniques provides complete efficacy. The use of growth factors and tissue engineering concepts is still in its nascent stage and, while promising, requires more clinical trials before it can be utilized in clinical practice.

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