An overview of bone augmentation techniques

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Abstract

The purpose of this review is to present several techniques available for augmenting and regenerating the deficient alveolar bone mainly for implant placement and restoring the lost bone for functional and esthetic purposes. These include, but are not limited to, the use of barrier membranes for guided bone regeneration, particulate grafting materials, block grafting techniques, distraction osteogenesis, ridge split techniques, the current applications of growth factors to accelerate the rate of bone formation, and enhance the quality of bone formed especially in severe defects, and finally, to discuss the combination staged approach of these techniques.

Particulate bone grafting technique

Particulate bone grafting is performed to repair a deficiency in contour and/or volume in dental arches. There is a wide variety of suggestions upon experts in the field regarding what particulate materials should be used for typical clinical applications, the rationale for their use, as well as combing one or more materials together, and the percentages of each material used in combination [1,2]. Bone grafts fall into main four categories, which are; autografts, allografts, xenografts, and alloplasts. The use of these materials in regenerative procedures is based on the assumption that they possess osteogenic potential by triggering the activation of bone-forming cells in the area to form new vital bone, or osteoinductive by containing bone inducing substances, or simply are osteoconductive by serving as a scaffold for bone formation, or having a combination action of all the previous [3]. It has been approved that autogenous bone harvested from intraoral or extraoral sites is the most predictable osteogenic organic graft for osseous tissue regeneration and hard tissue formation [4].

Main extraoral sites utilized in harvesting procedures include iliac crest which provides adequate quantity of graft material with excellent osteogenic, osteoinductive, and osteoconductive properties, however, high morbidity related to the second surgical site as well as root resorption were reported as side effects to this surgical procedure [5]. Therefore, in cases when availability of intraoral sites for harvesting graft material is limited, or donor site morbidities, or inadequate quantity of the harvested bone, the use of other grafting materials has been proposed whenever possible.

The autograft, allograft, alloplast, and xenograft materials all have reported success, alone or in combination with either growth factors, membranes or both. Autografts are considered to be the gold standard for most craniofacial and periodontal bone grafting for years, including the treatment of dental implant–related defects [6]. Several studies demonstrated the effectiveness of particulate autograft [7-9]. However, autografts have recognized several limitations including donor site morbidity, inadequate quantity and volume of graft material needed, potential resorption, and mismatch of particulate size desired [6,9].

Allografts are grafts transferred between members of the same species, which are genetically dissimilar. They have the advantage of being available in higher quantities and eliminate the morbidity associated with a second surgical site related to autografts. Allografts has been used as a substitute for autografts or in combination with autografts to enhance the quality of augmentation procedure [10]. Allograft are primarily used in the particulate form, although, other forms are available for usage such putty, gel, collagen sponge, sheets, as well as cortical or cancellous blocks also are used. Several studies regarding allografts showed that growth and differentiation factors are present in demineralized freezed dried bone allograft (DFDBA) preparations [11]. However, some reports revealed unpredictable or poor bone formation with some commercially available DFDBA [12]. The use of particulate allograft bone replacement substitute has been reported for numerous applications, including sinus augmentation [13], ridge augmentation [14], and in extraction socket preservation procedures [1]. In a comparative study between the use of mineralized freezed dried bone allograft (FDBA) and DFDBA for localized ridge and sinus augmentation, histologic observations showed regeneration of 42% new bone area with no statistical difference between the two materials. In regards to the risk for disease transmission among allografts, several studies have been conducted to examine the effectiveness of these materials' infection control processing and reported that disease transmission is approximately non-existent. However, concerns still exist for some patients and estimates for the risk were reported [15,16] as the probability that DFDBA might contain HIV has been calculated to be one in 2.8 billion [17]. This has, in part, encouraged the attempts to identify alternative bone graft substitutes, such as those made from synthetic materials to overcome these patients' concerns.

Evolution in the field of dental biomaterials related to hard tissue

regeneration and engineering and further observation of limitations associated with the use of autografts and allografts have directed attention toward the invention and investigation of alloplastic graft materials [18]. These synthetic bone graft materials are osteoconductive with no osteogenesis or induction properties. Osteoconduction provides the ingrowth of capillaries, perivascular tissues, and osteoprogenitor cells from the adjacent recipient bed toward the area targeted for bone formation [19]. Main advantages of Alloplasts includes the absence of any restriction to the available quantity of graft, and the risk for disease transmission and need for harvesting bone tissue are eliminated. Further investigation have proved their success in dental surgical approaches such as alveolar ridge preservation, augmentation [20], and sinus grafting procedures [21,22]. As time passed by, these synthetic graft materials have been a well established alternative for autograft and allograft in surgical therapy for [23] two of the most used Alloplasts are Calcium sulfate (CS) and calcium phosphate (CP) compounds due to their biocompatibility, handling characteristics, porosity, different rates of dissolution, chemical and physical resemblance to bone mineral, and potentially unlimited supply at a modest cost [24-27]. Granular porous Hydroxy Apetite (HA) has been also considered a unique alloplast which is formed by the hydrothermal chemical conversion of sea coral from biogenic carbonate to HA [28]. Ridge augmentation with HA particulate, with and without autografts or plaster, was reported with success [29]. Sinus augmentation with HA showed also success and excellence in terms of dimensional stability when material was placed in the sinus. The second generation of CP bone cements has shown promise in hard tissue reconstruction in both craniofacial and orthopedic surgical fields, which also encouraged its use in implant related hard tissue reconstruction in the periodontal and maxillofacial fields [30].

Xenografts are derived from another species and are introduced to hard tissue reconstruction procedures since 1889 [31]. They showed to be biocompatible and osteoconductive. Xenografts are derived from a variety of animal sources, including bovine, porcine, equine, and coralline. They are found generally to be biocompatible and structurally similar to human bone. Many of these xenograft materials have the potential to resorb and be replaced with host bone over time [32,33].

Block grafting approaches

Clinical studies stated that a considerable amount of horizontal augmentation can be added predictably to the defected bony area by the use of autogenous block graft in augmentation procedure [34,36]. In terms of failure rate, a study composed of 115 autogenous block grafts reported only one complete failure where the block was removed [36]. However, it is important to note that this surgical technique is highly technical sensitive. The stabilization and intimate contact of these blocks to well prepared recipient bed must be established with care to gain successful outcomes with this procedure [37,38]. Blocks' stabilization can be achieved with the use of bone fixation screws, which should not be less than two to prevent rotational movement of the block [39] or the simultaneous multiple implant placement simultaneously [40,41]. In addition, it is beneficial to keep the harvested block vascularized during the healing period, to increase the blood supply as well as the flow of esteoprogenitor cells to the area. This can be achieved by performing decortication during recipient bed preparation by intra-marrow penetration. It also has been shown that harvested block re-shaping and obtaining round edges can improve intimate contact of block and the remodeling process [42-44]. The healing of autogenous block grafts has been observed through having a formed viable bone to replace the necrotic bone within the block. This phenomena is called "creeping

substitution". Autologous block graft techniques have been used frequently in different areas intra-orally in both maxilla and mandible where severe horizontal and vertical resorption of edentulous ridge is present. It showed a high success rate through time in both the maxilla and mandible. In contrast several complications can still be present with this procedure such as graft resorption, soft tissue dehiscence, and paresthesia which can make the decision of implant placement in the grafted area a challenge [45,46].

The primary locations for harvesting intraoral block grafts include the external oblique ridge of the posterior mandible, ramus to obtain a block containing purely cortical bone, and symphysis to obtain a block which contains both cortical and cancellous bone. The revascularization of cortico-cancellous block grafts takes place in a much faster rate when compared to cortical bone block autografts. However, it's resorption rate tends to be much slower than particulate autografts. Revascularization of block grafts enables maintenance of their vitality, and, hence, reduces chances of graft infection and necrosis [37]. Intra oral block grafts harvest is found to be a preferable approach compared to the well-known extra-oral autogenous bone which is usually harvested from the iliac crest, cranium, or tibia due to ease of intraoral harvest and because of the fact that intra-oral bones are derived from intramembranous bone which have less resorption than endochondral bone that is the precursor of extra-oral bones [47].

In terms of post-operative resorption rates of autogenous block grafts, it is found to be in a range of 0% to 25% at the time of implant placement and up to 60% at the time of abutment connection placement. This associated resorption rate can be reduced by the used of a barrier membrane to cover the block at the time of the surgery [48,49]. A human study showed a percentage of 17% of resorption related to mandibular block grafts used in combination with particulate autograft and xenograft for vertical ridge augmentation, with an average gain of 5 mm and revealed a retained vitality of bock autografts used in this study [50]. Although autogenous bone grafts (as block or particulate form) remain the gold standard for ridge augmentation, donor site morbidity associated with block graft harvest has turned attention to the use of allogenic block graft materials. Case reports demonstrated success with FDBA and DFDBA block grafts for application in horizontal and vertical ridge augmentation procedures. However, further comparative studies with long periods of follow up are needed to evaluate the healing of these allogenic blocks from clincial and histological points of view [49].

Combination approaches

With reference to the aforementioned GBR techniques, combining on or more of the previously described approaches can be utilized in cases where severe bone defects are present in order to optimize GBR outcomes. In many situations, a membrane may not be required, and the graft material alone can be effective. However, it is found that the use of barrier membranes to cover the grafting material can further improve the quality of regeneration by holding grafting material in proper location which particulate grafts are used, acting as space maintenance and minimizing alveolar bone resorption. Barrier membranes can be non-resorbable, such as expanded polytetrafluoroethylene (ePTFE) and titanium, or resorbable, such as polypeptides (collagen) and synthetic polymers (polylactide and polyglycolide). These membranes may be used in combination with block grafts and/or particulate graft materials [50,51]. Membranes required for grafting of severe bony defect has to have a space maintenance property, which make them rigid enough to be shaped to the desired contour, height and width of future bone

needed. This can be achieved by using commercially available non-resorbable titanium based and titanium reinforced membranes or the adjunct use of tenting screws and simultaneous placement of implants to prevent barrier membranes collapse into the space of the bony defects by the overlying soft tissue during healing [51]. In some reports where autografts were utilized for GBR purposes, resorption tended to be higher with when no membrane was used [38,52]. A clinical study reported a significantly less resorption of the block grafts was found when e-PTFE membranes were used to protect the graft. A histologic study that used autograft and barrier membranes in humans revealed a bone–implant contact of 22% in the 4 mm of vertically regenerated bone, compared to the 44% found in native bone. A 5-year analysis of the vertical augmentation with this approach demonstrated stable vertical gains [53]. Finally, combination approaches may be considered when the grafting procedure is performed at the time of implant surgery to optimize gaining enough bone surrounding the implant, reduce the healing period and decrease the number of surgeries required as well as the morbidity and cost to the patient [54].

Ridge expansion/ ridge splitting techniques

Ridge splitting is an alternative to the various techniques described for horizontal ridge augmentation, such as distraction osteogenesis. It was proven that both pervious mentioned procedures have a similar healing pattern and end results. In an area with a narrow ridge measuring 3 mm in bucco-lingual width or more, splitting of the alveolar is started by using either chisels, osteotomes, or piezosurgical devices to increase the horizontal ridge width. Buccal and lingual cortical plates or targeted sites should not be fused and some intervening cancellous bone between those cortical plates should be present to prevent a complete bone fracture and separation. This technique has showed to be successful and comparable to alternative techniques in increasing horizontal ridge width providing that adequate vascularity and stabilization of the mobile bone segment is achieved along with sufficient inter-positional bone grafting and soft tissue protection. A long term clinical study evaluating more than 400 implants placed in expanded maxillary ridges by the previous mentioned technique showed that success rate of ridge split technique reached 97%, which is consistent with placement in native bone in similar defects. As a modification of the ridge expansion of splitting technique, a two-phase approach to the ridge split technique was introduced to minimize the risk for unfavorable fractures of the segment in less flexible bone, and to maintain the segment vascularity during its expansion [12]. In the first surgery, a full-thickness mucoperiosteal flap is elevated on the buccal aspect of the ridge. A chesil, bur, or piezosurgical device is used to perform the apical horizontal, proximal, and distal vertical corticotomies. The crestal corticotomy can be made at the primary or secondary operation. A month later, the second surgery is performed by splitting and expansion of the ridge using osteotomes. At this stage, split-thickness buccal mucoperiosteal flap is elevated to preserve the vascularity of the buccal cortical plate. Implants can be placed in the space created between the buccal and lingual plates, with or without inter-positional grafting. The primary advantages of the ridge split technique using particulate, or GBR, compared to the mentioned lateral augmentation techniques, are to reduced treatment time and morbidity resulting from avoiding a separate donor site as well to avoid extra cost accompanied with the use of other grafting materials [37].

Distraction osteogenesis

Distraction osteogenesis is a procedure that is based on the long-standing biologic phenomenon that new bone fills a gap that is created between two separated pieces of bone. This separation should be done in slow rate and under tension. Distraction of the segment can be achieved in a vertical and/or a horizontal direction. The basic principles involved in distraction osteogenesis include a latency period of 7 days for initial post-surgical soft tissue regeneration and wound healing. A distraction phase during which the two pieces of bone undergo gradual incremental separation at a rate of 1 mm per day, and a consolidation phase that allows bone regeneration in the created space. Several studies showed a reliable success rate especially in gaining lost alveolar bone height with the use of variety of alveolar bone distractors [55,56]. Distractor devices can be either intraosseous or extraosseous. When the clinical requirement for significant vertical ridge augmentation exists, distraction osteogenesis can be used successfully with a variety of devices. Thorough assessment and treatment planning is crucial to achieve success with this procedure. For optimal bone augmentation of defects using distraction osteogenesis, are a minimum of 6 to 7 mm of bone height must be present above vital structures, such as inferior alveolar nerve in the mandible or maxillary sinus in the maxilla. The defect size is an another important factor when treatment is proposed using distraction osteogeneis, the vertical ridge defect size should not be less than of 3 to 4 mm and should be a span of three or more missing teeth [57]. The height of bone on adjacent teeth acts as reference points for the extent of vertical gain that can be achieved. Improvement of attachment levels on teeth with distraction has not been successful in animal models. Therefore, compromised dentition with considerable bone loss may need to be extracted to create a true vertical component of 4 mm within the defect span. Smaller ridge defects of a span of one or two missing teeth in width were associated with higher rates of complications when treated with the distraction technique [58,59]. In such cases, conventional ridge augmentation techniques should be considered to prevent associated complications. In terms of vertical gain using this approach, up to 9 mm of vertical bone gain was reported using implant like distractor in human case reports. Another device, with a small-diameter intraosseous approach, was used successfully with reporting the same amount of vertical gain. In contrast to these intraosseos distractos, an extraosseous distraction system with all moving components external to the cortical plate was developed and used successfully. The use of a prosthetic restorable distractor also was described showing a range of 4 to 6mm of vertical height gain. Data on implant success in distracted bone out 3 to 5 years showed favorable results comparable to other grafting approaches which lead periodontists and surgeons to consider this approach as a valid option in regeneration proceders [60-62].

Bone augmentation approaches using growth factors

Incorporation of growth factors during regenerative therapy provides the opportunity to accelerate new bone formation and enhance soft tissue healing. Growth factors are the signaling molecules that modulate cell growth and development. They play a role in cell proliferation, migration, and extracellular matrix formation. Some of the most important growth factors involved in bone homeostasis include platelet-derived growth factor (PDGF), transforming growth factor-β, fibroblast growth factor, insulin-like growth factor, vascular endothelial growth factor, parathyroid hormone, and bone morphogenetic proteins (BMPs) [63]. The molecular approach using BMPs has received the most attention over the past decade. BMPs are differentiation factors that are part of the transforming growth factor super family. They have multiple effects, including the ability to differentiate osteoprogenitor cells into mineral-forming osteoblasts. Two of these proteins, BMP-2 and -7 (or osteogenic protein-1), have

been investigated, studied extensively, and show promise for intraoral applications. Multiple human studies have been conducted to study the safety of BMPS and concluded that BMP-2 can be safely used intra-orally in surgical procedures such as ridge preservation and sinus augmentation [64,65]. Although BMP-2 has been approved by the Fodd and Drug Administration in the unites states of America (FDA) for human intraoral applications, the carriers and dosage of BMP-2 and -7 are still under regular review and investigation [66]. Another growth factor that receive the most attention in intra-oral application is PDGF. This growth factor has shown to be an important controller of osteogenesis in repair and regeneration circumstances. In an animal model, an attempt was done to test the effect of PDGF in forming new bone by the application of PDGF along with ePTFE membranes around immediate implants, this study revealed that PDGF lead to more rapid bone formation compared to the negative control. In another animal study evaluating recombinant human PDGF-BB (rhPDGF-BB) and inorganic bone blocks for vertical bone augmentation application, test sites with rhPDGF-BB showed statistically significantly more vertical bone growth than controls [67]. In terms of commercial availability, tri-calcium phosphate is used as a carrier for rh-PDGF with a concentration of 0.3 mg/ml. This concentration was approved to be useful when used for bone regeneration. As with the differentiation factors, the optimal carriers and growth factor dosages are still under investigation and regulatory review for intraoral bone augmentation use. However, the field of growth and differentiation factors is still in a dynamic change and are regularly under investigation; therefore, to optimize the clinical outcome with different concentrations, types of carriers and release evaluations, further long term human clinical studies need to be performed [68].

Another growth factor approach is to use the patient's autogenous blood, extraction of the platelet-rich plasma (PRP) as well as platelet-rich fibrin (PRF) after a specific preparation protocol and adding this concentrated group of autogenous growth factors to the grafting material by mixing or placing it on top of the grafting material. The addition of PRP to autogenous grafts showed a more rapid and dense bone formation compared to autogenous grafts used alone for bone augmentation. An improvement in bone formation when PRP is added to other graft materials has not been demonstrated clearly [69]. On the other hand, PRF has been proved to accelerate soft tissue healing however, its effect on bone regeneration is still in the process of investigation [70].

Future approaches can be used for augmentaion

Gene therapy is a relatively new therapeutic modality based on the potential for delivery of altered genetic material to the cell. The main aim of localized gene therapy is to increase the concentration of desired growth or differentiation factors in order to enhance the regenerative response and by that improving the regeneration process in the targeted area [70]. The gene therapy is initially introduced as the process of facilitating the body to deliver high doses of autogenous BMP to promote bone regeneration. This current method of delivering higher concentrations of growth factors to local bone augmentation site over longer periods of time shows promise but still need further investigation to obtain acceptable clinical results and most importantly, to assure its safety. A cellular tissue engineering strategy that exploits the regenerative capacity of bone may include the in vitro amplification of osteoblast cells or osteoprogenitor cells grown within three-dimensional constructs [71]. Approaches specifically targeting intraoral bone augmentation demonstrated in vitro osteoblast amplification in different constructs. Alternatively, the use of mesenchymal stem cells

for construct seeding or development of an immortalized osteoblast line showed promise for bone regeneration. These amplification approaches, in combination with gene therapy and molecular stimulation, may lead to improved approaches for multifactorial tissue engineering strategies aimed at alveolar bone augmentation. Other tissue engineering approaches include cell culture to create cell sheets from fibroblasts, or scaffolds rich in cells that can form membranes, as well as the use of stem cells and immortalized dental follicle cells is still being studied to be used for bone formation and regeneration purposes [72].

Conclusions

Several techniques have been found to aid in approaching a successful bone augmentation to facilitate reaching a proper bone dimensions and correct placement of dental implants. Suitable technique must be selected after careful evaluation of defected area and consider related factors such as the extent of the defect, patient preference, surgeon expertise, available materials and instruments, cost, and ease of specific procedures to be performed. It is important to review all applied successful techniques and available materials to enhance proper selection of method to reach best outcomes and high success rates. It is advisable to use an evidenced-based approach when a treatment plan is being developed for bone augmentation cases to predict final outcomes and to set accurate expectations of the final results of the augmentation procedure. This can enhance the quality of final implant being placed and facilitate improve patient's satisfaction.

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