ROLE OF BONE GRAFTS AND PRF/CGF IN DIFFERENT SPECIALITIES OF DENTISTRY - A SYSTEMATIC REVIEW

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***Abstract*: Bone grafts in dentistry are used to replace or recover bone volume that has been resorbed due to systemic pathologies, periodontal defects, tooth loss or other conditions. Bone grafts act as a filler and scaffold to facilitate bone formation and promote wound healing. These are bioresorbable grafts and have no antigen-antibody. Bone grafting is a surgical procedure that replaces missing bone with material from patient′s own body, an artificial, synthetic, or natural substitute. Bone grafting is possible because bone tissue has the ability to regenerate completely if provided the space into which it has to grow Bone grafts that are commonly used are autologous, allogeneic, xenografts and alloplasts. Their use has shown an effective amount of bone formation and proliferation in the defective sites and proves to be a beneficial choice in bringing back lost bone. Other bioactive surgical additives are also currently used along with autologous bone particles to induce bone regeneration and connective tissue attachment that shows excellent results such as PRF and CGF. PRF (Platelet rich-fibrin) and CGF (Concentrated growth Factor) regulates the inflammation and increase the speed of healing process. These contains various growth factors which enhances its action and promotes wound healing. These biomaterials seem to have several advantages and indications both for medicine and dentistry. It is also a minimally invasive technique with low risks and has satisfactory clinical results.**

***Keywords*: Bone grafts, bone regeneration, CGF, PRF, wound healing**

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INTRODUCTION

Modern medicine advances have led to increases in the availability of new biomaterials that can be used to enhance bone volume recovery. These biomaterials can be obtained from the patient's own body, other humans, animals, or can even be synthetically produced. [1] Bone grafting, in general is a surgical procedure which entails replacement of missing bone with material from either patient's own body, an artificial or natural substitute The reason behind bone grafting is because the bone tissue can regenerate completely into the space which it has to develop [2]. An ideal bone graft or scaffold should be made of biomaterials that imitate the structure and properties of natural bone extracellular matrix (ECM), including osteoprogenitor cells and should provide all the necessary environmental cues found in natural bone.[3] The scaffolds should also have chemical, physical, and mechanical properties similar as possible to that of a natural bone structure.[4] A good bone substituting scaffold should be settled by the resident bone cells or undifferentiated mesenchymal cells.[5,6,7]
In dentistry bone grafting is one of the therapeutic modality employed to fullfill the ideal goal of periodontal therapy i.e., reconstruction of periodontal tissues. It is also indicated in prosthodontic cases where minimal amount of bone requirement is a prerequisite, such as implant placement and denture fabrication. The types of bone grafts most frequently used in dentistry include,allografts, auotgrafts ,alloplastics and xenografts Till today, different types of these biomaterials have established their practical roles in dental clinics mainly due to their ease of application and predictable results. For several years different types of bone grafts have been studied and search is still continued for an ideal bone replacement material.[8]

Allografts are bone grafts taken from one individual for transplantation to another. Allografts used for bone repair often require sterilization and deactivation of proteins normally found in healthy bone. They contain bone growth factors, proteins, and other bioactive materials that is necessary for osteoinduction and successful bone healing the desired factors and proteins are removed from the mineralized tissue using a demineralizing agent such as hydrochloric acid. The advantages of allogeneic grafts include availability in adequate quantities, predictable results and the elimination of an additional donor site surgery. [16] The disadvantages of allografts include host incompatibility, potentially contaminated specimens resulting in recipient site infections and potential transmission of disease from donor to recipient of the allograft and impractical or biologically ineffective usefulness. Bone

allografts are being widely used in the field of dentistry[9,11], craniofacial surgery [12]and orthopaedics[13]. They are generally available used in two forms-freeze dried bone allograft (FDBA) and demineralized freeze dried bone allograft (DFDBA).

FDBA

Clincally FDBA have been implanted successfully by surgeons to treat fractures, to fill bone cysts. In addition they have been used in the oral surgery to treat tumors of jaw to facilitate bone formation after surgical repositioning of impacted adult cuspids to induce bone repair of periapical defects and to restore the deficient alveolar ridges prior to insertion of prosthesis. They are also used to reconstruct mandibular contour. FDBA used in combination with absorbable barrier membranes have been used as replacement for autograft blocks for ridge augmentation. The use of FDBA blocks for alveolar ridge grafting has shown presence of vital bone with a lamellar organization.

DFDBA

DFDBA was first used in dentistry and medicine in 1965 but for the treatment of periodontal defects in humans it was utilized in 1975 for the first time.[14] DFDBA also provides osteoconductive surface, and in addition, it also acts as a source of osteoinductive factors. DFDBA is used often and has shown to be effective in the reconstruction of both furcation and periodontal defects and has also demonstrated osteoinductive effects. When implanted in bone that is already well-vascularized, it has the ability to stimulate cell attachment, cell migration, and osteogenesis. DFDBA contains bone morphogenic protein (BMP) that causes new bone formation to take place during healing. It is therefore an effective option for bone regeneration. Some dental and oral surgery patients may require bone enhancing procedures prior to receiving an implant or other dental prosthesis. Due to the many benefits of DFDBA, it is a commonly used material for such bone enhancement and bone development processes. DFDBA can be used in certain scenario where early bone formation is desired such as immediate implant, sinus lift procedure either with immediate implant or delayed implant placement which can lead to functional rehabilitation.[15]They can also be used in cases where limited time is required between third molar extraction and performing sagittal split ramus osteotomy and also in socket preservation cases.

Autografts

autogenous bone grafting are obtained from same individual receiving the graft. Bone can be harvested from nonessential bones, such as from iliac crest, mandibular symphysis (chin area), and anterior mandibular ramus (coronoid process). When a block graft will be performed, autogeneous bone is the most preferred because there is less risk of graft rejection as the graft is originated from the patient′s body.[17]

It would be osteoinductive and osteogenic, as well as osteoconductive. Disadvantage of autologous grafts is that additional surgical site is required, another potential location for postoperative pain and complications.

Xenografts

Xenogratfs are bone grafts taken from a species other than human, such as bovine and are used as a calcified matrix. They have osteoconductive properties and also preserves the original bone mineral structure, The surgical removal of the xenograft materials may require advanced clinical skills because of the different configurations clinicians might encounter of the non-resorbed and migrated particles. Clinicians seeking to provide functional and esthetic outcomes should be aware of the complications of the bovine-derived graft materials. The long-term safety of xenografts and their potential association with disease are valid concerns. Bovine-derived substitutes have been by far the most commonly used xenografts in dentistry [16]

Alloplasts

Alloplastic grafts are readily available and eliminates the need for patient donor site.They may be made from hydroxyapatite, a naturally occurring mineral (main mineral component of bone), made from bioactive glass. Hydroxyapatite is a synthetic bone graft, which is the most used now due to its osteoconduction, hardness, and acceptability by bone. Some synthetic bone grafts are made of calcium carbonate, which start to decrease in usage because it is completely resorbable in short time and makes breaking of the bone easier.

The main requirements for bone grafts are osteoconduction (new bone growth on the graft), osteoinduction (cells differentiating into bone forming osteoblasts) and osteogenesis (bone/callus formation)and osteopromotion(enhancement of stegenesis)

OSTEOINDUCTION

It is defined as a chemical process by which molecules contained in the graft convert the neighboring cells into osteoblasts, which, in turn, form bone. It is a phenomenon regularly seen in any type of bone healing process. Osteoinduction implies the recruitment of immature cells and the stimulation of these cells to develop into preosteoblasts. In a bone healing situation such as a fracture, the majority of bone healing is dependent on osteoinduction.

OSTEOCONDUCTION

Occurs when bone graft material serves as a scaffold for new bone growth, which is perpetuated by the native bone. Osteoblasts from the margin of defect that is being grafted, utilize the bone graft material as a framework upon which to spread and generate new bone.[1] In the very least, a bone graft material should be osteoconductive.

OSTEOPROMOTION
Involves enhancement of osteoinduction without possession of osteoinductive properties. For example, enamel matrix derivative enhances the osteoinductive effect of demineralized freeze-dried bone allograft (DFDBA), but will not stimulate bone growth alone.[2]

OSTEOGENESIS
Osteogenesis occurs when vital osteoblasts originating from the bone graft material contribute to new bone growth along with bone growth generated via the other two mechanisms[18]

PRF is an autologous fibrin-based (membrane, matrix or scaffold), living biomaterial which is derived from human blood, (1) also referred to as an optimized blood clot.[30] In essence, PRF is a natural (autologous) composite biomaterial, consisting of fibrin, platelets, growth factors and various cell types including leukocytes and stem cells.The purpose of PRF technology is to extract from a patients' blood sample these key elements and to prepare it in a clinically usable form such as, a membrane or plug such as ,A-PRF, L-PRF or CGF or injectable liquid (i-PRF). The difference between natural blood clot and PRF is that the latter is more homogeneous and stable and easy to handle and place in the indicated local [29].PRF in general connects the various elements within the fibrin matrix with local tissues (bone and soft tissue) to accelerate neo-angiogenesis within the tissue and to enhance its healing and regeneration potential. The PRF technique continues to develop because it is very easy to prepare, inexpensive, and allows the quick production of natural fibrin membranes, enriched with platelets and leukocytes, that can be used immediately in any clinical situation. PRF membrane protects the surgical site and helps in wound healing [19] promoting soft tissue repair; when mixed with bone graft, it may act as a "biological connector", which attracts stem cell, favors the migration of osteoprogenitor cells to the center of the graft, and provides a neo-angiogenesis.

Advantages of using PRF

PRF preparation is a very simplified and efficient technique and has a Minimized blood manipulation .PRF does not require the addition of external thrombin because polymerization is a completely natural process, without any risk of suffering from an immunological reaction .It has a natural fibrin framework with growth factors within that may keep their activity for a relatively longer period and stimulate tissue regeneration effectively .It can be used solely or in combination with bone grafts, depending on the purpose [21] Increases the healing rate of the grafted bone .It is an economical and quick option compared with recombinant growth factors when used in conjunction with bone grafts .Used as a membrane, it avoids a donor site surgical procedure and results in a reduction in patient discomfort during the early wound-healing period [22].The studies of PRF present it to be more efficient and with less controversies on its final clinical results when compared to PRP [23].

Disadvantages of using PRF

PRF may present some disadvantages as follows:

The success of the PRF protocol depends directly on the handling, mainly, related to blood collection time and its transference for the centrifuge .Need of using a glass-coated tube to achieve clot polymerization.Possible refusal of treatment by the puncture required for blood collection. Only needs a minimal experience of clinician for PRF manipulation [13]. The realization of the PRF protocol depends directly on the handling of mainly the time the blood is collected and the transference for the centrifuge. The final amount available may be low because it is autologous blood. It only needs more than the minimal experience of the clinician for PRF manipulation. Patients with bleeding disorders or hematologic diseases do not qualify for this in-office procedure. You will need an experienced surgeon /physician to determine if PRP is right for you.

CGF (Concentrated Growth Factor) is different from platelet-rich plasma (PRP) and platelet-rich fibrin (PRF) in the methods for production since there are no additives added during its production. It is an advanced second generation platelet concentrate, obtained with differential continuous centrifugal technology, containing many kinds of growth factors and fibrins, and are able to facilitate the recovery of soft and hard tissues. They have comparatively higher adhesive strength, tensile strength, higher viscosity than the other platelet preparations (20) .CGF has a difference in centrifugation speed which permits the isolation of much larger and denser fibrin matrix richer in growth factors. CGF is a fibrin rich organic matrix which contains growth factors, platelets, leukocytes and CD34+ stem cells which help in the process of regeneration and also has immunological cells that are effective in regulating inflammation and minimizing the risk of infection. (CGF) is a biological inducing material which improves the quality of the formed bone, and facilitates the formation of bones and the healing of tissues.

DISCUSSION
The most common use of bone grafting is in application of dental implants, to restore edentulous area of a missing tooth. In general, bone grafts are either used in block (such as from chin or ascending ramus area of lower jaw) or particulated, to be able to adapt it better to a defect.When the transplanted bone is secured into its new location, it restores blood supply to the bone on which it has been attached. Besides the main use of bone grafting in dental implants, this procedure is used to fuse joints to prevent movement, repair broken bones that have bone loss, and repair broken bone that has not yet healed. The main drawback with these materials is the risk of transmission of bovine or porcine viruses or other infective agents. In vitro *and* in vivo *studies* have demonstrated safe and promising results, without contradictory findings, related to the use of PRF alone or in combination with other biomaterials. It

has several advantages and possible indications to be used both in medicine and dentistry. Currently, platelet-rich fibrin seems to be an accepted minimally invasive technique with low risks and satisfactory clinical results. Some studies [24] have demonstrated that PRF is a healing biomaterial with a great potential for bone and soft tissue regeneration, without inflammatory reactions and may be used alone or in combination with bone grafts, promoting hemostasis, bone growth, and maturation.

With the goal of providing an alternative to the autograft bone tissue engineers have focused on the development a bone graft substitute that mimics the bone tissue microenvironment. Autologous bone graft is designed to enhance bone repair and regeneration by incorporating bone progenitor cells and growth factors to stimulate cells into a scaffold made of various natural or synthetic biomaterials or their combination which provide the necessary support and with sufficient vascularization to allow access to nutrients to support this process. Studies have examined the ability of commercial DFDBA to induce new bone formation *in vivo* in order to assess if the broad variation in clinical response was due to differences in the preparations or to variations in host response. When a block graft will be performed, autogeneous bone is the most preferred because there is less risk of graft rejection as the graft is originated from the patient's body. It would be osteoinductive and osteogenic, as well as osteoconductive. Of the graft materials for obtaining bone union, autogenous bone is the gold standard. However, there have been many shortages of autogenous bone material, and such situations are currently on the rise.

Disadvantage of autologous grafts is that an additional surgical site is required, another potential location for postoperative pain and complications. Types of autograft include osseous coagulum bone blend cancellous bone marrow transplant, and bone swaging. In vitro and in vivo studies have demonstrated safe and promising results, without contradictory findings, related to the use of PRF alone or in combination with other biomaterials. It has several advantages and possible indications to be used both in medicine and dentistry. Currently, platelet-rich fibrin seems to be an accepted as a minimally invasive technique with low risks and satisfactory clinical results. When using human bone allografts in the practice of dentistry, practitioners should investigate carefully and be familiar with the institutions that they are patronizing. autologous bone and alloplastics were the most accepted bone grafts.

CGF also improves the quality of the formed bone, enhances tissue regeneration, promotes stabilization of grafts and is effective in regulating inflammation. The success of this therapy lies in the local delivery of a high concentration of growth factors and proteins. CGF act as a membrane support in recession coverage as it constantly releases growth factors to produce tissue regeneration. According to the study done by buzkart et al, CGF and CAF placed together enhances the healing of soft tissues.[28] This is similar to the physiologic wound healing, and supports reparative tissue process and local infiltration therapy, taking the surgical practice of regenerative techniques to a higher level.

The results of published studies indicate that following the use of bone grafts a significant bone filling can be expected against treatment by debridement, obtaining an average filling of the defect of between 60% and 65%. [31]The most common use of bone grafting is in application of dental implants, in order to restore edentulous area of a missing tooth. In general, bone grafts are either used in block (such as from chin or ascending ramus area of lower jaw) or particulated, in order to be able to adapt it better to a defect. Besides the main use of bone grafting in dental implants, this procedure is used to fuse joints to prevent movement, repair broken bones that have bone loss, and repair broken bone that has not yet healed.

Although bone allografts are being widely used in dentistry, many of clinicians sseems to be unfamiliar with their preparation and processing as well as their use as safe and effective graft materials Long-term clinical evaluations are needed to identify the biological complications of xenografts and alloplastics that are used extensively in dentistry.

CONCLUSION

Of all the graft materials for obtaining bone union, autogenous bone is considered ,the gold standard. There have been many shortages of autogenous bone material, and such situations are currently on the rise. Currently, there is no material to completely replace autogenous bone, and it is not easy to select the best bone substitute.An ideal bone graft material should be easy to use and should provide desirable results with minimal complications. Various bone graft materials have been used and tested in the field of medical science in the last few decades and many are still under trial, ensuring promising results and may put end to the search for a suitable bone graft material.CGF/PRF are solely used or in combination in periodontal diseases for bone regeneration. Esthetics is an inseparable part of today's dental treatment; however, consistency of results, reliability of treatment modalities, and long-term prognosis require scientific approaches to therapeutic procedures. The optimal dental solution recognizes the long-term.

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