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Role of Platelet Concentrates in the field of Oral Implantology: An Update

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ABSTRACT

Dental implants have gradually become the standard of care for the treatment of missing teeth. Today the potential for osseointegration is no longer considered a question, but rather a certainty in implant dentistry. As with all successful techniques, the focus has now shifted to the finer details of treatment protocols and techniques. Platelet concentrates like Platelet Rich Plasma, Platelet Rich Fibrin, Injectable-PRF, etc were used as an adjunct with dental implant procedures to accelerate the speed and quality of osseointegration, improve the bone type to enhance primary stability, long-term aesthetic stability, and periodontal biotype has received much attention. This review article mainly focuses on the soft tissue and bone improvement around dental implants with the use of platelet concentrates.

Keywords: Platelet concentrates, PRF, Implant, Sinus lift, GLAM Technique

INTRODUCTION

Implant dentistry would be remiss without mentioning the importance of bone and soft tissues surrounding the implant for long-term success. Today, the symbiotic relationship between bone and soft tissues to maintain the integrity of the implant is increasingly being understood. Past and current trends have focused on bone and its augmentation to implant success, however, it is the symbiotic relationship between the bone and soft tissue that maintains long-term health and aesthetics. The bone supports the soft tissue and in return, the soft tissue reinforces bone stability. For this reason, it is essential to ensure that implant sites are developed appropriately to ensure optimum bone and soft tissues.

Stable bone is key to the long-term success of implants and the difficulty in predictably regenerating this bone when lost remains a major challenge. A minimum of 2 to 4 mm of bone around the implant is essential to maintain the stability of the soft tissue. Vice versa, it is essential that a minimum of 2 to 3 mm of attached soft-tissue thickness in both the vertical and horizontal dimensions be present to protect bone from resorption. Far too often, one or the other of these components is neglected which leads to potential long-term breakdown.[1] Hence this review article emphasizes on enchancing bone and soft tissue around the dental implants with the use of platelet concentrates.

ROLE OF PRP IN IMPLANTS

The successful osseointegration of an implant depends on the initial cascade of events and PRP is crucial in enhancing this outcome. PRP when coated on the surface of an implant releases an array of growth factors that enhance the early wound healing providing an initial stabilization for the implant.

Various studies suggest that implants coated with PRP before placement into the alveolus had a better osseointegration capability. (Anitua et al.2006, Anand et al.2012)

Because PRP enhances osteoprogenitor cells in the host bone and bone graft, it has been found to have clinical applications in fully autogenous bone grafts and composites of autogenous bone grafts with a variety of bone substitutes with as little as 20% autogenous bone. PRP has improved results in continuity defects, sinus lift augmentation grafting, horizontal and vertical ridge augmentations, ridge preservation grafting, and periodontal/peri-implant defects.

PRP is used to allow earlier implant loading and improved osseointegration, in compromised bone such as osteoporotic bone and bone after radiotherapy. Because PRP also enhances soft tissue mucosal and skin healing, it is used in connective tissue grafts, palatal grafts, gingival grafts, for root coverage, skin graft donor and recipient sites, dermal fat grafts, facelifts, blepharoplasty, laser resurfacing surgery, etc.

OSSEOINTEGRATION

The term osseointegration was introduced by Branemark following his work in the early 1950s and at first, was considered a "functional ankylosis," but was further revised as "a direct structural and functional connection between ordered, living bone and the surface of a load-bearing implant".[2]

In essence, the placement of biologically inert material such as titanium or zirconium will lead to the apposition of bone around the implant, which is strong enough to withstand the forces of occlusion. This demonstrates the normal physiology of bone in function, with both deposition and resorption concerning the load of the implant following integration. The phases of osseointegration are synonymous with routine inflammation and wound healing seen in traumatic bone injury.[3]

Trauma by the osteotomy drill cuts and orderly fractures the bone and ruptures its supplying blood vessels in the process. This surgical intervention initiates a cascade of complex but orderly wound healing events, highlighted by hemostasis, inflammation, proliferation, and tissue maturation. The implant osteotomy fills with blood that coats the implant as it is inserted. Initially, its support is derived entirely from friction with the bone and is defined as primary stability. Later, secondary stability is achieved as the blood and cellular products produce healing that apposes newly formed bone on the implant surface. Following insertion, platelets are activated and aggregate, forming a clot that seals the ruptured vessels at the osteotomy. The platelets degranulate and release a variety of growth factors and cytokines that stimulate per vascular cells during neoangiogenesis.[4]

Thereafter, activated fibrin within the forming clot provides a provisional matrix within the wound micro spaces surrounding the implant surface. Inflammatory cells are then recruited from the vessels and into the wound to participate in clearing debris. This ingress of leukocytes also contributes to the overall increase in the release of inflammatory cytokines that recruit future cells, kill bacteria, clean the wound and promote healing.

The inflammatory cytokines recruit macrophages that migrate to the area to remove tissue debris and mediate the inflammatory process. Macrophages also secrete growth factors that recruit fibroblasts to synthesize collagen to reinforce the wound matrix. Osteoclasts initially resorb the microscopic fractured bone and in turn release growth factors from bone that stimulate osteoblasts. The perivascular cells also migrate to the healing bone and implant surface and differentiate into osteoblasts. These cells then produce a matrix that mineralizes, producing woven bone within the first and second weeks. With time the bone is remodeled and ordered into trabeculae via osteoblast and osteoclast interactions. Since these highly complex interactions between cells and their products of inflammation are the basis of osseointegration, it is therefore biologically feasible to apply PRF in the osteotomy to promote these processes.[5]

Although the scientific data is sparse for PRF and implants, there is an enormous amount of data that can be extrapolated to contribute to educated clinical decision-making.

USE OF PRF AT OSTEOTOMY SITE

The high predictability of osseointegration has prompted clinicians and researchers to push the boundary to accelerate healing and expedite the completion of treatment. Developments in micro-roughened implant surface technology have largely facilitated this and have successfully shown to increase ISQ (implant stability quotient) at shorter time intervals.[6]

This means a restoration present in the mouth earlier for the patient and patient functioning earlier than previously possible. The downside, however, is that micro-roughened implant surfaces may be more susceptible to bacterial

colonization and peri-implantitis. Numerous studies over the years have investigated implant surfaces enhanced with growth factors with varying results.[7]

Some studies utilizing cell adhesion molecules or bone morphogenic proteins (BMPs) can increase osteoblastic differentiation and functional integration and have shown increases in BIC values. PRF delivers platelets and leukocytes to the wound or osteotomy and releases growth factors locally (namely platelet-derived growth factor [PDGF], transforming growth factor-β, insulin-like growth factor (IGF) and vascular endothelial growth factor (VEGF)) that accelerate the healing process by attracting undifferentiated endothelial cells and mesenchymal cells to the injured site.

A recent study reported increased ISQ values during the early healing period when PRF was applied inside the osteotomy during insertion and the implant itself coated in plasma extruded from the PRF. However, these studies have shown statistically significant improvement in type 2 bone, while limited data exists supporting other types of bone, especially type 3 and 4 of poorer density that presents clinical challenges. The significance of PRF and implants seems to be limited to the early stages of osseointegration. This is an interesting development in PRF's uses and deserves further research.[8]

Glam Technique (2017) (*Guided Bone Regeneration with L-PRF in the Atrophic Maxilla):* Patients with maxillary atrophy and loss of lip support are often a challenge in terms of prosthodontic rehabilitation and surgical approach due to the aesthetic changes and bone availability for implant placement.

In edentulous patients, with severe maxillary atrophy and marked loss of lip support, the anterior maxilla commonly exhibits a thin buccal bone plate that requires horizontal bone augmentation, with several authors mentioning a minimum of 2 mm of facial bone to prevent vertical bone resorption. The scientific literature presents several options for these cases (such as collagen or titanium membranes, non-resorbable pins, use of xenografts, allografts, or autogenous bone) but still, none is considered as the gold standard.

The simultaneous approach, where implant placement is coincident with graft procedures, is preferred by both patients and clinicians since it reduces treatment time and cost. However, it can't be applied in every case, due to the need for proper implant stability.

Significant clinical interest has grown regarding the use of L-PRF for regeneration, solely or in combination with xenografts, given its ease of protocol preparation, economic advantages, less invasive technique (no need for donor sites), and biological properties. Also, L-PRF has been used in immediately placed implants to restore the anatomy loss and to speed up soft tissue wound healing. However, the use of enough L-PRF membranes seems to be crucial to obtain an optimal effect. For this reason, the use of guided bone regeneration with L-PRF in the Atrophic Maxilla (GLAM) technique is suggested as a surgical approach in patients with maxillary atrophy and evident loss of lip support, where Guided bone regeneration is performed with the use of L-PRF membranes and xenograft to restore the buccal bone volume of the Atrophic Maxilla, simultaneously to implant placement.[9]

DV-PIMS TECHNIQUE 2019 *(Deepak Vikhe - Pravara Institute of Medical Sciences Technique):* There are various techniques of using PRF. These techniques need skill and practice to use PRF. This (DV-PIMS) method aimed to explain a new implant design that dispersed an I-PRF solution from the inside out. The screw section of the new implant was made of a reservoir running vertically down inside. That reservoir was filled with (injectable) PRF, and then a cover screw was placed. The solution begins to slowly diffuse out, through the vents in the implant, keeping biofilms from forming or avoiding at the screw–bone interface and accelerating the healing process. This technique helped clinicians to use bioactive surgical additives (I-PRF) with more ease and efficacy. It improved implant design for better attachment of gum tissues, grafting I-PRF around the implant. This implant can also be filled with an antimicrobial mouthwash, which gets dispersed and can stop Streptococcus mutans biofilms from forming and kill the ones that had grown on the implant beforehand at the initial healing stage.[10]

PRF AND SOFT-TISSUE HEALING AT IMPLANTS

Thick soft tissue favors coronal peri-implant bone stability. A symbiotic relationship between bone and soft tissue is necessary to maintain the stability and integrity of the implant. Bone and its augmentation in numerous reconstruction techniques traditionally have been a keen topic in implant dentistry. Current understanding now stresses the importance of bone to maintain the soft tissue and the soft tissue to reinforce bone stability. The lack of adequate soft- and hard-tissues development could be one of the reasons why high levels of peri-implantitis are observed in the current works of literature. This raises the question, "could PRF contribute to soft-tissue healing and augmentation when placed within soft-tissue flaps raised during implant placement?" The concept certainly seems biologically plausible by locally applying an autogenous biomaterial rich in growth factors that stimulates neoangiogenesis and collagen formation within the soft-tissue flap, atop an implant. Moreover, PRF when

compressed into membranes can maintain the integrity of an augmentation procedure, enhancing site protection when used in conjunction with other barrier membranes, and contributing to the healing of the overlying flap.[11]

While to date, approximately 164 publications regarding PRF and its effects on soft-tissue regeneration and healing have been published, only one study has been reported on PRF and soft-tissue healing at placed implants. Hehn and coworkers had experimented with the insertion of PRF within a split-flap at implant placement and reported this to reduce soft-tissue thickness. These findings here suggest that splitting the flap may unnecessarily strain the soft-tissue healing in addition to a full mucoperiosteal flap raised for implant insertion.[12]

An ideal procedure would be to place the PRF beneath the flap without additionally dividing the tissue.

PRF IN SINUS FLOOR AUGMENTATION

The resorption of the upper jaw bone after tooth loss is a frequent problem faced in posterior maxillary implant placement due to the lack of required bone mass for anchorage. Common maxillary sinus augmentation techniques provide a solution via increasing the available bone height at the expense of sacrificing the volume of the maxillary sinus. Traditionally, autologous bone grafts and resorbable membranes are used to promote osteogenesis and avoid soft tissue in-growth into the surgical site. However, donor site morbidity and size restrictions, the latter resorption of the graft, and the high cost of membranes are the main disadvantages. In this context, PRF appears to provide a promising alternative to overcome such limitations.

Two Randomised controlled trials evaluating the use of PRF in lateral window sinus augmentation were found. Applications were performed either as:

(a) Grafting material (PRF/Bio-Oss® constructs versus Bio-Oss®) or
(b) Absorbable covering membrane for the lateral osteotomy window (PRF versus Geistlich Bio-Gide®).

In both studies, included subjects were systemically healthy adults with maxillary atrophy (defined as <5 mm residual bone crest height measured in OPG/orthopantomogram). Smoking status was not assessed.

The addition of PRF to Bio-Oss® bone substitute revealed neither advantages nor disadvantages over Bio-Oss®-alone controls. After six months, clinical and radiographic examinations revealed both groups exhibiting similar amounts and density of mineralized tissues, with no signs of material resorption.

Histological evaluations also showed non-significant differences regarding:
(a) Newly generated bone percentage.
(b) Residual Bio-Oss® percentage.
(c) Bone-to-bone-substitute contact.
(d) Post-treatment inflammatory reactions.

Regarding coverage of the lateral osteotomy sinus window, PRF use resulted in a comparable amount of residual bone substitute and vital bone formation (%) when faced against Bio-Gide® controls (PRF: 17.0% and 15.9%, Bio-Gide®: 17.2% and 17.3%, differences were not statistically significant). Overall, despite a slightly superior to no coverage at all (12.1%), it can be stated that results were similar to those reported using other conventional membranes (collagen: 17.6%; e-PTFE (expanded polytetrafluoroethylene): 16.9%). Within the presented limitations in both randomized controlled clinical trials, evidence suggests that PRFs are safe, simple to use and handle, and a cost-effective alternative to traditional bone grafts and absorbable membranes for low-income patients pursuing maxillary sinus augmentation procedures. Some studies regarding sinus elevation procedures are:

Diss et al. 2008
Osteotome sinus floor elevation using Choukroun's platelet-rich fibrin as grafting material: a 1-year prospective pilot study with micro threaded implants.

Mazor et al. 2009
Sinus floor augmentation with simultaneous implant placement using Choukroun's platelet-rich fibrin as the sole grafting material: a radiologic and histologic study at 6 months.

Sohn et al. 2009
CGF in intermaxillary sinus elevation, infrabony pocket, and for GBR in an implant placement surgery. The results showed a well-augmented ridge and reduction in Pocket depth.

Simonperi et al. 2011
Simultaneous sinus-lift and implantation using micro threaded implants and leukocyte- and platelet-rich fibrin as sole grafting material: a 6-year experience.

Tajima et al. 2013
Evaluation of sinus floor augmentation with simultaneous implant placement using platelet-rich fibrin as sole grafting material.

Jeong et al. 2014
Simultaneous sinus lift and implantation using platelet-rich fibrin as sole grafting material.

Zaho et al. 2015
Clinical application of platelet-rich fibrin as the sole grafting material in the maxillary sinus augmentation.

Sohn et al. 2015
Comparison between CGF membrane and collagen membrane in a case of horizontal bone defects. After a 6-month healing period, favorable ridge augmentation was seen at both sites.

Comparison between sticky bone with/without titanium mesh for ridge augmentation in implant placement surgery. After 4 months of healing, favorable horizontal ridge augmentation was observed on both sites. Sticky bone in the treatment of labially fenestrated ridge in implant surgery. It results in stable bone augmentation.

Aoki et al. 2016
Sinus augmentation by platelet-rich fibrin alone: a report of two cases with histological examinations.

Kanyama et al. 2016
Crestal approach to sinus floor elevation for atrophic maxilla using platelet-rich fibrin as the only grafting material: a 1-year prospective study.

PRF TREATMENT OF PERI-IMPLANT DEFECTS

The two peri-implant defect types receiving the most attention are coronal bone loss seen in peri-implantitis and the buccal gap at immediate implant placement. It is widely known that immediate implant placement dictates a more palatal or lingual approach and a deeper placement to establish primary stability. The so-called buccal gap is observed as the implant is placed away from the buccal plate (Figure 1).[13]

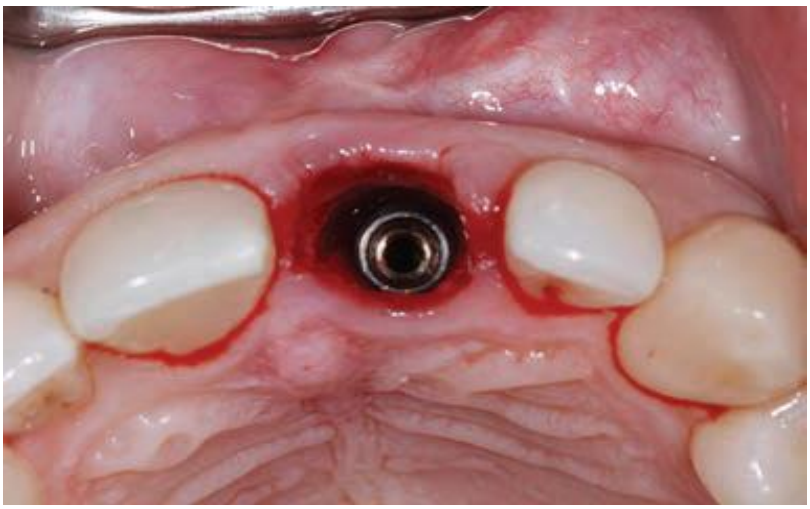

Figure 1: Implant placement slightly lingually; a buccal gap is created between the implant surface and the buccal bone wall.

PRF may contribute its leukocyte cytokines and growth factors to this process that may have a positive influence on the healing of this bony defect (Figure 2). Lee and coworkers created buccal gap defects during implant placement to experimentally simulate this in an animal model. Positive results were demonstrated with an increase in bone volume in the defect area and the interthread spaces when augmented with PRF.[14] Additional studies have also shown that PRF alone or with particulate bone material in non-infective peri-implant defects showed high bone to implant contact (BIC) of 61% and 73% respectively.[15,16]

As such the use of PRF is beneficial during the filling within this buccal gap during immediate placement, or in combination with a bone biomaterial.

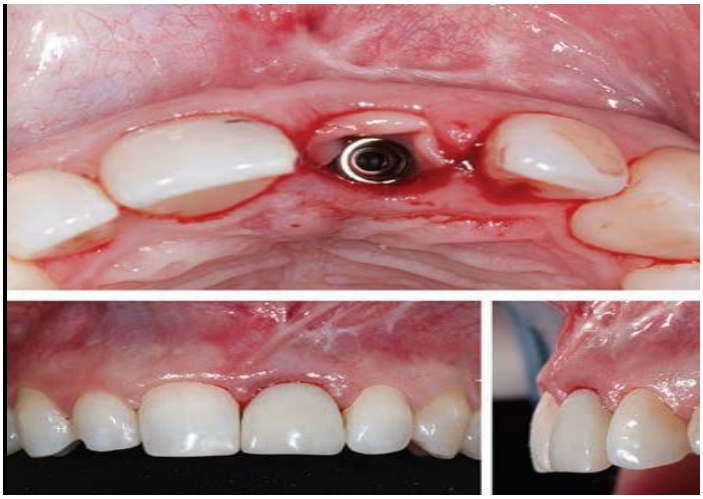

Figure 2: The buccal gap filled with PRF.

Contrary to the augmentation of the buccal gap, treating peri-implant defects as a result of peri-implantitis is far more complex.[17] This topic remains largely unresolved and its exact etiology with reliable treatment options is poorly understood.[18] Various reports have now investigated the use of PRF in human studies. In such a study, the implants had full-thickness flaps raised and decontaminated. The experimental group additionally utilized PRF placed within the bone defect before the flap was closed. When healing occurred with PRF, a minor difference in probing depth reduction was seen.[19]

Furthermore, clinical attachment levels seemed to benefit and an increase in keratinized mucosa was reported. These results suggest that PRF may be beneficial for the treatment of peri-implantitis defects; however much further research remains necessary to validate these preliminary findings. Again, the clinician should be aware that the treatment of peri-implantitis is at present unpredictable, with great variations in bone defects and diverse responses to treatment.[20]

Simultaneous Sinus Floor Elevation and Implant Placement using L-PRF as a Sole Graft Material: L-PRF as a sole graft material during simultaneous Sinus Floor Elevation and implant placement has proven to be a practical, safe, and economical subsinus graft material, resulting in natural bone formation.

An Injectable-PRF (I-PRF) for Adequate Graft Stability and Compaction:
Since the development of an injectable PRF (I-PRF) in 2014, many possibilities now exist since I-PRF is harvested in a liquid formulation that quickly coagulates following contact with bone-grafting materials. `Therefore, its use has vastly improved the potential of these surgeries with no unnatural additives being utilized.

Bahruddin Thalib et al. 2017 studied the post-placement Bone Dental implant Contact (BIC) value of dental implant coated and not coated with PRP. Evaluation of Bone Area (BA) and Bone-Dental Implant Contact (BIC) was done. There was a 20% increase in BIC values in implants coated with PRP.[21]

Franz JS et al. 2018 gave a systematic review which suggested that:
1. PRF might reduce alveolar width resorption and might enchance implant stability during the early phase of osseointegration.
2. PRF combined with grafting materials does not affect sinus floor elevation.
3. There is a lack of adequate studies for implant placement, peri-implantitis defects, soft tissue healing, and postoperative pain although the preliminary data seems promising.[22]

Renu Gupta et al. 2019 evaluated the effects of PRF on short implants both clinically and radiographically. They concluded that the use of PRF along with short implants is an important adjunct in oral implantology as it accelerates the soft and hard tissue healing around the implant without performing any extensive surgery in deficient bone height patients and it also contributes to the overall success of implants.[23]

Bhavana Vasudev Lokwani et al. 2020 gave a systematic review which reported that:
1. Concentrated Growth Factors (CGF) might aid in obtaining vertical bone gain around implants when used alone or in combination with allogenous and xenogenous grafts.
2. The quality of new bone formed around implants is significantly improved with the use of CGF.
3. There is a lack of adequate studies evaluating the effect of CGF on implant stability, sinus floor augmentation, soft tissue healing, and implant survival per se, although the preliminary data seems promising.[24]

CONCLUSION AND FUTURE DIRECTIONS

A consistent theme in discussions regarding platelet concentrates is that experts on the topic are recommending more research to substantiate the exciting possibilities it presents. The potential for PRF in conjunction with implant therapy is limitless. While some studies have investigated PRF's value in accelerating osseointegration, some evidence has been provided, and even more, will be needed to fully determine its evidence-based validity. Likely, a great opportunity presents in inquiring about PRF's potential when combined with particulate bone material in guided bone regeneration (GBR) procedures with implants. Similarly, the question of whether PRF can augment soft tissue thickness at implants and contribute to coronal bone stability remains unanswered. These are exciting times in implant dentistry and much awaits to be discovered regarding the use of platelet concentrates in conjunction with placed dental implants.

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