

An autologous indigenous armour -- Platelet Rich Plasma

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Abstract

A major goal of periodontal therapy is regeneration of the attachment structures such as alveolar bone, periodontal ligament and cementum. Open flap debridement results in the formation of long junctional epithelium, which is more susceptible to microbial invasion and is thought to be a less stable attachment. However regeneration is thought to partially mimic developmental mechanisms, which require a coordinated orchestration of cellular events such as proliferation, migration and differentiation. Polypeptide growth factors are naturally occurring biological modifiers that have the potential to alter the host tissue to stimulate or regulate the wound healing process. They can regulate key cellular events in tissue regeneration, including cell proliferation, chemotaxis, differentiation, and matrix synthesis via binding to specific cell surface receptors. Platelet rich plasma is exactly what its name suggests. The substance is a by-product of blood (plasma) that is rich in platelets. It contains platelets, coagulation factors and plasma proteins. PRP permits the body to take advantage of the normal healing pathways at a greatly accelerated rate, which play an important role in regeneration of periodontal tissue. Scientific proof of bone and soft tissue healing has been shown using platelet concentrate with viable platelet levels increased 300% to 600% above baseline levels. The more growth factors that can be delivered to the injury site, the greater the potential to enhance the healing process.

Keywords: Platelets, Periodontal regeneration, Wound healing, Platelet rich plasma, Growth factors.

Introduction

Periodontal therapy aims at protecting and maintaining the natural dentition over his or her lifetime for optimal comfort, function and aesthetic purpose.⁽¹⁾ After a periodontal therapy, repair and regeneration generally precede the healing phase. Repair is healing of a wound by tissue formation which does not fully restore the architecture or function of the affected site, whereas regeneration is reproduction or reconstitution of a lost or injured part.⁽²⁾ Periodontal flap surgery, which provides good amount of access to the root and helps in reduction of probing pocket depth as repair occurs by the formation of healthy, long junctional epithelial attachment.

The main aim of regenerative procedures is to induce regeneration at the alveolar bone, cementum and is to develop a new functional periodontal ligament.⁽³⁾ The use of barrier membranes and graft materials helps in the reduction of the probing depths, supports the formation of new periodontal ligament which favours functional reconstruction.⁽⁴⁾

Tissue regeneration occurs in four prominent phases. The Inflammatory Phase, Proliferative phase, Maturation and Remodelling phase and Re-epithelialization phase. Formation of an inflammatory reaction is initial step, which is followed by a series of cascading events that constitute the entire healing process. Inflammation further releases considerable amount of growth factors, which cause the migration and division of inflammatory cells that are needed for the phagocytosis of cellular debris, hence setting the stage for the next phase.⁽⁵⁾

After periodontal surgery, platelets aggregate to form a stable blood clot, by releasing a variety of growth factors that induce and support healing and tissue formation. Administration of these growth factors along with tissue regeneration techniques may help in the repair of intra-bony defects, furcations and cyst cavities.⁽⁶⁾

Platelet-rich plasma is an autologous source of platelet-derived growth factors that enhance surgical soft- and hard-tissue wound healing. These growth factors are concentrated to about 300 times more than that of the levels normally present in plasma. These growth factors stimulate the progenitor cells to produce new host tissue as quickly as possible, that is the reason why platelet rich plasma is so effective in the post-treatment healing process.⁽⁷⁾

The use of platelet rich plasma (PRP) to enhance bone regeneration and soft tissue maturation has increased dramatically in the fields of orthopaedics, urology, plastic surgery, maxillofacial surgery and periodontics over the last decade.⁽⁸⁾ Platelet-rich plasma is used to deliver high concentrations of growth factors to sites requiring bone healing and regeneration and therefore considerable interest has emerged of the potential benefits, in addition to those of bone healing and regeneration.⁽⁹⁾

Growth factors are primarily present in bone matrix and released during remodelling or after trauma. These are bone inductive mediators which are powerful modifiers of the healing process. Incorporation of osteo-inductive mediators into bone graft material or other carriers can be applied to sites in conjunction with conventional bone augmentation procedures to enhance

the outcome. They act on the local osteo-progenitor differentiated cells and constitute a separate group of proteins because of their mode of action.⁽¹⁰⁾

History

Platelet rich plasma was developed in the early 1970's as a by-product of multi-component plasmapheresis. In 1974, Ross et al⁽¹¹⁾ determined that the addition of either intact platelets and calcium, or the supernatant derived from thrombin activated platelets, resulted in significant improvements in the mitogenic capacity of plasma serum. It was equal to that of the serum derived from whole blood and concluded that platelets must be the major source of the proliferative effect provided by serum. The term, "platelet derived growth factor" (PDGF) was coined by Witte et al⁽¹²⁾ in 1978 and later in 1979 Kaplan et al⁽¹³⁾ used the subcellular fractionation to determine the presence of PDGF within the alpha granules of platelets. The presence of transforming growth factor- β was identified within the alpha granules of platelets by Assoian et al.⁽¹⁴⁾ Later the insulin like growth factor (IGF-I) was identified by Karey and Sirbasku⁽¹⁵⁾ in 1989. Growth factors such as basic fibroblast growth factor (bFGF) and vascular endothelial growth factor (VEGF) were identified by Brunner et al⁽¹⁶⁾ in 1993 and banks et al⁽¹⁷⁾ in 1998 respectively.

However, the credit of introducing platelet-rich plasma into contemporary oral surgery goes to Whitman et al, in 1997.⁽¹⁸⁾ He was the pioneer to use PRP in oral surgical procedures. But the first clinical dental results with PRP were reported by Marx and others in 1998.⁽¹⁹⁾ He used PRP to improve graft incorporation in mandibular reconstructions in patients who had received cancellous bone marrow grafts after tumour removal. They concluded that the addition of PRP to bone grafts accelerated the rate and degree of bone formation and was significant both radiographically and histologically.

Platelet rich plasma and its constituents: Platelets are small, discoid, anucleate cells formed from the fragmentation of long pro-platelet extensions of the megakaryocyte. These extensions become interwoven through endothelial pores of the bone marrow sinusoids and are fragmented by shear forces, releasing a heterogeneous population of nascent platelets into the bloodstream.⁽²⁰⁾ They have a circulating lifespan of 5–9 days and their predominant mechanism of clearance is via Kupffer cells and hepatocytes, based upon lectin receptor recognition of altered glycan structures on their surface.⁽²¹⁾ The functional responsiveness of platelets is variable and known to be affected by size and age of the cell, with younger and larger platelets demonstrating greater haemostatic function than smaller or older cells.

Though they lack a nucleus, platelets possess an extensive cytoskeleton, mitochondria, lysosomes, ribosomes, and a modified version of smooth

endoplasmic reticulum, as well as a number of unique organelles and membrane features. There are 3 types of platelet granules: alpha, dense and lysosomes. Alpha granules are the most numerous organelles in the platelet and contain over 300 different proteins⁽²²⁾ the majority of which are synthesized or endocytosed by the parent megakaryocyte.⁽²³⁾

PRP works via the degranulation of the alpha granules in platelets, which consists synthesized and pre-packed growth factors. The growth factors which are released from activated platelets are PDGF, VEGF, TGF- β 1, β 2, bFGF, IGF, PAF-4. The secretion of these growth factors initiates the clotting process of blood. More than 95% of pre synthesized growth factors are secreted within one hour. Therefore, PRP must be developed in an anticoagulant state and should be used on the graft, flap (or) wound, within 10 minutes of clot initiation.⁽¹⁹⁾

Growth Factors in PRP: Growth factors are generally polypeptide dimers, consists of 2 antiparallel monomers that are arranged in a "cystine knot" configuration which consists of 8 cysteine residues within each monomer chain. These cysteines have the ability for disulfide bonding both between and within the monomer chains, which formulates into similar three-dimensional structures among the various growth factors. One intra-chain disulfide bonded loop is nested within another, in a sort of "C-in-a-C" arrangement, referred to as the "cystine knot".⁽²⁴⁾

The growth factors which are released from activated platelets are:

1. Platelet derived growth factor (PDGF)
2. Transforming growth factors beta 1 and beta 2 (TGF β -1 & 2)
3. Vascular Endothelial Growth Factor (VEGF)
4. Insulin like growth factor – 1 (IGF-1)
5. Platelet derived epidermal growth factor (EGF)
6. Basic fibroblast growth factor (bFGF)
7. Platelet-derived angiogenesis factor (PDAF)
8. Platelet activating factor -4 (PAF-4)

Along with these growth factors PRP also contains blood proteins known to act as cell adhesion molecules for osteoconduction. The blood proteins are fibrin, fibronectin, Osteocalcin, and Thrombospondins.⁽²⁵⁾ Periodontal and oral surgical techniques may involve use of these factors for the healing of both soft and mineralized tissues.⁽²⁶⁾

Platelet derieved Growth Factor (PDGF)

Platelet-derived growth factor was the original growth factor discovered in alpha granules, after observation of its potent mitogenic effect on cultured cells.¹¹ It is a basic dimeric glycoprotein with 2 disulphide bonded polypeptides, referred to as A and B chains. Five isoforms of PDGF are present: AA, BB, CC, DD and the heterodimeric isoform AB.⁽²⁴⁾ Based upon the combination of α and β chains into homo or heterodimer, 2 pdgf receptors have been identified. As

the platelets adhere to an injured site, all isoforms of PDGF are released from the alpha granules.

PDGF has long been identified as a product of many other cell types, but platelets are said to be its primary source. The other sources are from monocytes, macrophages, fibroblasts, endothelial cells and bone matrix. The PDGF is a well characterized regulatory protein with an isoelectric point of 9.8 and a molecular weight of approximately 30,000 Da.⁽²⁷⁾

PDGF generally stimulates fibroblasts, glial, smooth muscle and bone cells which are of mesenchymal in origin.⁽²⁸⁾ The PDGF-AB heterodimer and the PDGF-BB homodimer have similar mitogenic activity and potency, however the PDGF-AA homodimer appears to have a different spectrum of activity with less potency.⁽²⁹⁾ This variation in activity is due to the differences in the number of PDGF receptors expressed in cell types. PDGF-AA, AB and BB are secreted as active molecules, whereas PDGF-CC and DD are secreted as inactive proteins and are cleaved either by plasmin, tissue plasminogen activator, or urokinase plasminogen activator. PDGF-BB is recognized as an universal isoform of PDGF.⁽³⁰⁾ The AA and BB isoforms are believed to enhance the proliferation of bone cells by increasing the production of PDGF-AA in osteoblast cultures by an autocrine process. PDGF, stimulates certain cells to produce their own progression growth factors. PDGF is the most thoroughly described growth factor in terms of its effects on the periodontium in vitro and in vivo. In vitro, all isoforms have proliferative activity on periodontal ligament fibroblasts. PDGF has chemotactic effect on the fibroblasts, which enhances the collagen and protein synthesis.⁽³¹⁾ When fibroblasts are exposed to platelets, a sustained and rapid signal is observed. These signalling cascades results is migration, proliferation and matrix synthesis, which is considered to be a triad of cellular events. PDGF is released by platelets in the wound bed which creates a chemotactic concentration gradient for fibroblasts, neutrophils and macrophages. It also activates macrophages to produce more growth factors which helps in the debridement of the damaged tissues. PDGF induces mitosis in fibroblasts and smooth muscle cells, and also stimulates these cells to produce proteoglycans, hyaluronic acid, fibronectin⁽³²⁾ and to a lesser extent, collagen. The diversity of PDGF is regulated by the integrin phenotype of the target cell, which varies over time according to the extra-cellular matrix composition.

Recently, there is a renewed interest in PDGF which can act as an adjunct therapy for fracture healing and periodontal alveolar reconstruction. It has been suggested that by mobilizing pericytes (mesenchymal stem cells) from the vasculature surrounding a fracture, PDGF helps in the formation of new vessels within the site and also acts as a progenitor cell with high osteogenic potential.⁽³⁰⁾

Transforming Growth Factor

The TGFs are a family of functionally and structurally unrelated proteins that have been isolated from normal and neoplastic tissues.⁽³³⁾ The two best characterized polypeptides from this group of growth factors are TGF- α and TGF- β . TGF- α is a 50-aminoacid single-chain protein with a molecular weight of approximately 5600 Da.⁽³⁴⁾ TGF- α exhibits 42% homology with EGF, competes for the EGF receptor and stimulates epithelial and endothelial cells TGF- β is the name given to a group of homodimeric proteins involved in the formation and development of many tissues. TGF- β is a highly conserved dimeric polypeptide with a molecular weight of 25,000 Da and consists of 2 amino acid chains linked together by disulfide bonds.⁽¹⁴⁾ TGF- β appears to be a major regulator of cell replication and differentiation. TGF- β is bifunctional or pleiotropic and can, therefore, stimulate or inhibit cell growth. Furthermore, TGF- β can modulate other growth factors, such as PDGF, TGF α , EGF and FGF, possibly by altering their cellular response or by inducing their expression.⁽³⁵⁾

Most cells secrete TGF β as a large latent complex, which then binds to the ECM to provide a “controlled release” of the growth factor to its target cells. When compared to other cellular sources of this growth factor, the TGF β contained by platelets is secreted in active form upon release from the alpha granules⁽³⁶⁾ and this characteristic may have implications for TGF β as delivered by PRP treatment. TGF β 1 is strongly associated with pathologic fibrosis because of its strong induction of collagen synthesis in both health and disease. It is specifically anti-proliferative for many immune cells and tumour cells, by inducing the synthesis of the 2 main cyclin-dependent kinase inhibitors (P15 & P21). So TGF- β is considered to be a tumour suppressor early in neoplastic processes, though it can facilitate metastasis and invasion in the advanced stages of malignancy. TGF- β exerts multiple and varied cellular effects. It inhibits epithelial cell proliferation and stimulates fibroblast chemotaxis and proliferation and also induces extracellular matrix production. TGF- β has both stimulatory and inhibitory effects on osteoblast proliferation.⁽³⁷⁾

Several in vivo investigations support the role of TGF- β in wound healing. The application of TGF- β increased the formation of granulation tissue.

Lynch et al⁽³⁸⁾ stated that the topical application of TGF- β to epidermal wounds in pigs inhibited re-epithelialization and increased connective tissue volume, collagen synthesis and angiogenesis. The use of implanted chambers or tubes filled with TGF- β alone or in combination helps in the increase of the protein and collagen content and enhances the growth of fibroblasts and capillaries.⁽³⁹⁾ By the addition of TGF- β 1 alone or in combination with PDGF-BB the proliferative activity of periodontal ligament fibroblasts are stimulated.⁽⁴⁰⁾ TGF- β helps in the enhancement of

collagen gel in vitro, and its effects are influenced by the addition of PDGF and IGF.⁽⁴¹⁾ TGF- β has a direct influence on the biosynthesis of type I collagen and fibronectin and helps in the bone matrix deposition.⁽⁴²⁾

Vascular Endothelial Growth Factor (VEGF)

The VEGF family has five isoforms of VEGF (VEGF-A, VEGF-B, VEGF-C, VEGF-D, VEGF-E) and placenta growth factor (PLGF).⁽⁴³⁾ The VEGF isoforms are generated as a result of alternative splicing from a single VEGF gene.⁽⁴⁴⁾ They exert their biological functions by binding to three different transmembrane tyrosine kinase receptors, designated VEGFR-1, VEGFR-2, and VEGFR-3. VEGF-A is a major regulator of vasculogenesis and angiogenesis during development, and it plays a key role in the regulation of angiogenesis during wound-healing. The expression of VEGF is regulated by the hypoxia-inducible factor alpha (Hif1 alpha) as HIF alpha promotes angiogenesis and osteogenesis by elevating the levels of VEGF in osteoblasts. Because of its angiogenic activity, VEGF plays an important role in bone tissue regeneration.⁽⁴⁵⁾

Insulin like Growth Factor

IGFs are a family of single-chain serum proteins that share 49% homology in sequence with proinsulin.⁽⁴⁶⁾ IGF has 2 forms, I & II each of which has 2 single chain peptides. The IGF-1 & IGF-2 are 2 polypeptides from this group that have been well described. IGF-1 is a 70-aminoacid protein with a molecular weight of 7649 Da and an isoelectric point of 8.4. IGF-2 is a 67-aminoacid neutral peptide with a molecular weight of 7471 Da.⁽⁴⁷⁾ Both growth factors have 62% homology with each other. They are synthesized by multiple tissues, including liver, smooth muscle and placenta and are carried in plasma as complex with a specific binding protein.⁽⁴⁸⁾ IGF-1 & 2 are similar to the somatomedins C & B respectively. In general IGFs have a similar spectrum of activities to that of insulin.⁽⁴⁹⁾ This is due to the homology in amino acid sequence and by the structural similarity in receptors between IGFs and insulin. IGF-1 acts as a progression factor in the cell cycle. IGF shows a similar affinity and binds to the same receptors as insulin does and helps in the development of many tissues, including the teeth.⁽⁵⁰⁾ Both the forms of IGFs have the potential for the survival of haemopoietic cells, fibroblasts and the nervous system. Both these forms are present in bone but IGF-2 ranks as the most abundant growth factor which are present in bone matrix.⁽⁵¹⁾ IGF shows chemotactic effects for periodontal ligament cells, and has strong affinity for periodontal ligament fibroblasts and protein synthesis. IGF-1 is synthesized and secreted by osteoblasts and its action is bone formation by proliferation and differentiation.⁽⁵²⁾ A dose dependent chemotactic action is seen on osteoblasts. IGF's play a crucial role in bone formation as it increases the DNA synthesis in osteoblasts and induces the formation of

bone matrix in organ culture. IGFs are the only growth factors which have the potentivity to enhance DNA synthesis and proliferation of chondrocytes.⁽⁵³⁾

Fibroblast Growth Factor

The FGFs are a family of polypeptides that are potent mitogens and chemoattractants for endothelial cells as well as for a variety of mesenchymal cells, including fibroblasts, osteoblasts, chondrocytes, smooth muscle cells and skeletal myoblasts.⁽⁵⁴⁾ These factors have also been shown to stimulate the formation of new blood vessels (i.e. angiogenesis and neovascularization) in vivo. The two most studied proteins from this family are acidic FGF (aFGF) and basic (bFGF). Both the factors were initially isolated from neural tissue but have been subsequently found in numerous other tissues.⁽⁵⁵⁾ aFGF has an isoelectric point range of 5.6-6.0 and a molecular weight range of 15,000Da. bFGF has an isoelectric point of 9.6 and a molecular weight range of 16,000-18,000 Da.⁽⁵⁶⁾ aFGF and bFGF have a similar spectrum of biological activities and exhibit 55% homology in their amino acid sequence. The basic form is 300-100 fold more potent than the acidic form in vitro. However, in the presence of heparin, aFGF and bFGF exhibit similar mitogenic activity.⁽⁵⁷⁾ The FGFs acts as competence growth factors as it stimulates the resting cells in G0 to enter the cell cycle in G1. As these resting cells enter the cell cycle, presence of growth factors are needed to stimulate their transit through G1 into the S phase or synthetic phase. It's here where FGFs plays a key role by initiating a cascade of cellular. However this event is incomplete without the required synergistic action of progression growth factors to maximize DNA synthesis and cell growth.

Epidermal Growth Factor

EGF is a single chain, amino-acid protein and has a broad spectrum of activity. The human derived form has molecular weight of approximately 5400Da.⁽⁵⁸⁾ EGF and TGF α are structurally related and therefore possess similar properties.⁽⁵⁹⁾ The major source of EGF are urine and salivary glands, although it has also been isolated from brunner's glands and platelets. Cerebrospinal and amniotic fluids are also a good source of EGF.⁽⁶⁰⁾ In vitro, EGF stimulates DNA synthesis and cell growth in a large variety of cells, including those of epithelial, endothelial and mesodermal origin. EGF however, stimulates prostaglandin production and induces bone resorption in cultures of neonatal mouse calvaria.⁽⁶¹⁾ Investigations using different animal models have reported that the topical application of EGF for abraded corneas, partial thickness wounds, full thickness wounds, and superficial burns significantly enhances re-epithelialization and wound healing.⁽⁶²⁾ Slow release of EGF from sponges implanted subcutaneously stimulated fibroblasts proliferation and angiogenesis as well as granulation tissue formation.⁽⁶³⁾

Platelet-Derived Angiogenesis Factor (PDAF)

PDAF induces vascularization in vivo. It helps in the stimulation of vascular endothelial cells by direct or indirect actions, as it plays a key role in the formation of new blood vessels by invading the de-vascularized tissue.⁽⁶⁴⁾ It also helps in the up-regulation of several cytokines and growth factors such as PDAF, IGF-1, TGF α and β , PDGF, basic fibroblast growth factor (bFGF), PDEGF, and interleukin 1 β (IL-1 β).

Platelet Factor –4

PF-4 is a chemo attractant for neutrophils released from alpha granules, which may be partially responsible for the initial influx of neutrophils into wounds.⁽⁶⁵⁾

Fibronectin

It is a high molecular weight glycoprotein first isolated from whole plasma and is also produced by fibroblasts, epithelial cells and endothelial cells.⁽⁶⁶⁾ Fibronectin has been identified on the surface of cells in connective tissue matrices and in cellular fluids. Fibronectin plays a major role in wound healing and is associated with the attachment of cells to other cells and to extracellular matrix. Fibronectin promotes increased cellular spreading over collagen coated tissue media and has been isolated from areas in contact with collagen.⁽⁶⁷⁾

Preparation of Platelet Rich Plasma

PRP is prepared in the laboratory or a surgical or dental suite from blood collected in the immediate preoperative period. Pure platelet concentrates for topical use were first developed as an application for the classical transfusion platelet units which was first reported for maxillofacial surgery.⁽¹⁹⁾ PRP can be obtained either by automated or manual methods.

Mechanism of Action: PRP has been found to work via 3 mechanisms⁽⁶⁸⁾

1. PRP works via the degranulation of the alpha granules in platelets, which contain the synthesized and pre-packed growth factors. The growth factors which are released from activated platelets are PDGF, VEGF, TGF- β 1, β 2, bFGF, IGF, PAF-4. Therefore, PRP must be developed in an anticoagulant state and should be used on the graft, flap (or) wound, within 10 minutes of clot initiation. The secreted growth factors immediately bind to the external surface of membranes of cell in the graft, flap (or) wound via transmembrane receptors. These transmembrane receptors in turn induce an activation of an endogenous internal signal protein, which cause the expression of (or) unlocks a normal gene sequence of the cells such as cellular proliferation, matrix formation, osteoid production, etc. The PRP growth factors act through the stimulation of the normal healing, at much faster rate.

2. **Increase in local cell division (production of more cells):** According to Nathan E Carlson⁽⁶⁹⁾ after an injury, platelets start to aggregate so as to expose the collagen proteins and adenosine diphosphate are released from the granules, serotonin and thromboxane, all of which help in the haemostatic mechanism and in the formation of clotting cascade.
3. Inhibition of excess inflammation is managed by decreasing the early macrophage proliferation.

Properties of platelet rich plasma

- It increases the tissue vascularity through increased angiogenesis
- Enhances the collagen synthesis
- Enhances osteogenetic potential
- Increase the rate of epithelial and granulation tissue turn over
- It promotes antimicrobial effect
- PRP does not react (or) interfere with any other restorative material such as glass ionomer cements or composite resin used as a filling material.
- It is very much biocompatible and can be used in humans or animals as it is non-toxic. PRP offers a biologically active substance as it releases growth factors.
- PRP allows good regeneration of tissue as it contains considerable amount of growth factors.

Role of PRP in the process of wound healing

The wound healing process is a complex mechanism characterized by four distinct, yet overlapping phases.⁽⁷⁰⁾

- Haemostasis Phase
- Inflammation Phase
- Proliferation Phase
- Remodeling Phase

The process of wound healing can be divided into 3 different stages:⁽⁶⁸⁾

- Biomechanical activation
- Cellular activation
- Cellular response

PRP has been shown to remain sterile and the concentrated platelets are viable for upto 8 hours once developed in the anti-coagulated state.⁽⁷¹⁾ Thus, Activated autologous platelet releases growth factor that increases collagen content, accelerate epithelial and epidermal regeneration promotes angiogenesis, enhances wound strength, hasten haemostasis, improves tissue regeneration, hasten remodelling, reduces pain and reduces infection which ultimately leads to regeneration.

Role of PRP in periodontal regeneration

The main rationale of periodontal therapy is “regeneration of the periodontal attachment”, including

cementum, a functionally oriented periodontal ligament, and an alveolar bone. Platelets contain various growth factors which directly or indirectly play an important role in tissue regeneration. Growth factors along with cell adhesion molecules have beneficial effects on bone cementum and components of periodontium through cellular proliferation, migration and differentiation.⁽⁵³⁾ The main reason for adding PRP to bone grafts is to increase the number of activated platelets in a wound, which will increase the local concentration of secreted GF and subsequently enhance tissue repair and regeneration. PRP increases the vascularity in the first 20 days with an increase of osteoblast and immature osteoid tissue formation within 3-6 weeks, improving the quality and quantity of newly formed bone tissues. PRP also minimizes the use of autologous bone necessary during regenerative surgery, thus decreasing the need for extra oral tissues. The main advantage of using PRP in regenerative procedures is, its autologous nature which eliminates concern regarding the potential for disease transmission or immunological reactions.

Role of PRP in Implants

The breakthrough in oral rehabilitation was initiated by the discovery of dental implants, made of pure titanium which achieves anchorage in the jaw by direct bone-to-implant contact. This functional ankylosis is often referred to as osseointegration and was first described by Branemark and Schroeder.⁽⁷²⁾ The important factor for the success of implant is good initial stability. Plasma rich in growth factors (PRGF) has been recently proposed as an aid to enhance regeneration of osseous and epithelial tissues. Platelet-derived growth factors can trigger stimulation of osseous and soft tissue regeneration, as well as reduce inflammation, pain and unwanted side effects. The growth factors present in PRP can stimulate several biologic functions such as chemotaxis, angiogenesis, proliferation, differentiation and modulation, thereby representing an effective therapeutic cause for more rapid and effective regeneration of hard and soft tissues.⁽⁷³⁾

Three predominant biologic factors emerge in consideration of osseointegration and immediate loading such as factors affecting interfacial bone formation (osteogenesis), peri-implant bone resorption (osteolysis) and micromotion effects on peri-implant osteogenesis. Success of implant depends on maintaining implant stability during initial healing. Strategies for improving the success of immediate loading may be directed at enhancing osteogenesis limiting functional loads, micromotions and controlling the resorption that reduces stability during the healing period.⁽⁷⁴⁾ PRP when applied to implant surface adheres to the metal and creates a new dynamic surface that could potentially slow biologic activity. This protein layer consists of a fibrin net embedded with growth

factors that covers the implant surface and transforms the initial interactions of the implant surface with the surrounding tissues. It also induces cellular attachment, proliferation differentiation and bone matrix deposition.⁽⁷⁵⁾

Conclusion

PRP is a new application of tissue engineering and a developing area for clinicians and researchers. It is a storage vehicle for growth factors, especially PDGF and TGF- β , both of which influence bone regeneration and tissue repair. The most important fact is that PRP is an autologous preparation introduced at the time of surgery, which eliminates concerns about disease transmission and immunogenic reactions, which are associated with allogeneic or xenogeneic preparations, and also avoids the possibility of mislabelling a sample, which might occur through a laboratory system.

The delivery of PRP versus isolated growth factors has many advantages, including controlled and sustained delivery, the potential for additive and synergistic interactions between the released growth factors and the therapeutic benefits of the fibrin matrix. Due to many beneficial components of PRP, it is reported as advantages on wound and bone repair, for its ease of availability, low risk, and low cost methods for its preparation. The bone science recognizes the key role of growth factors in clinical bone grafting success. PRP is seen as an available and practical tool for enhancing the rate of bone formation and enhances the final quality of bone formed. Much is still unknown about PRP and an adequate body of research and controlled studies are needed to provide a solid evidence of PRP's capacity for its role in wound healing, soft-tissue reconstruction and augmentation procedures. So that it can be used as an adjunctive material in both oral and periodontal surgeries.

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