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RESEARCH ARTICLE

PLATELET RICH FIBRIN A BAY OR BOON IN REGENERATIVE PROCEDURES: A REVIEW

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ABSTRACT

Platelet rich fibrin is a second-generation platelet concentrate and a natural source of growth factors. Platelet rich fibrin (PRF) is a leukocyte and platelet rich fibrin biomaterial that acts as a binding site for both platelets and growth factors. Through increasing the local concentration of growth factors at specific tissues, PRF promotes tissue regeneration. Placement of PRF is less technique sensitive than GTR and bone graft placement for the periodontal therapy. This review will attempt to summarize the relevant literature regarding the recent studies in regeneration procedures done with PRF.

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INTRODUCTION

Wound healing is a complex biological process where many cellular events taking place simultaneously leading to the repair or regeneration of damaged tissues. Manyattempts have been made in the field of tissue regeneration with the aim of predictably repairing, regenerating, or restoringdamaged and diseased tissues.[1,2,3,4] These include strategies with foreign materialsoften derived from allografts, xenografts, or synthetically produced alloplasts to regenerate host tissues. In the last few decades a variety of biomaterials have been introduced in dentistry that can fill in osseous defects and accelerate wound healing. Materials like hydroxyapatite, freeze dried bone graft, tricalcium phosphate, bioactive glass etc. have been widely used and tested for their contribution in healing and regeneration of soft and hard tissues. It was first described by Dr. Joseph Choukroun in France to promote wound healing in implants. Currently, the studies have been focussed on the use of an autogenous material called Platelet Rich Fibrin (PRF) that provides an osteoconductive scaffold along with growth factors to stimulate patient's own cells towards a regenerative response.[1,2,3,4] Platelet-rich fibrin is a second-generation platelet concentrate and is defined as an autologous leucocyte- and platelet-rich fibrin biomaterial.[5] Platelet rich fibrin affects cellular activities at genetic and cellular levels.[6,7] PRF membrane consists of a fibrin 3-D polymerized matrix in a specific structure, with the incorporation of almost all the platelets and more than half of leucocytes along with growth factors and circulating stem cells. Ross *et al* were amongst the pioneers who first described a growth factor.[8] Growth factors are released after activation from the platelets trapped within fibrin matrix and have been shown to stimulate the mitogenic response in the periosteum for bone repair during normal wound healing.[9] Fibrin is the activated form of a plasmatic molecule called fibrinogen. PRF is better than other platelet concentrates like Platelet Rich Plasma (PRP) due to its ease and inexpensive method of preparation and also it does not need any addition of exogenous compounds like bovine thrombin and calcium chloride. Thus, PRF has emerged as one of the promising regenerative materials in the field of dentistry.[10]In this review, we will discuss about the platelet concentrate PRF, its preparation, clinical applications, advantages and disadvantages over other biomaterials.

Preparation of PRF: The technique for PRF preparation was invented by Dr. Joseph Choukroun in 2000. It is the current PRF technique authorized by the French Health Ministry in which PRF is prepared without using an anticoagulant during blood harvesting or bovine thrombin during gelling.[11] The protocol was developed using a simpler centrifugation protocol requiring only 1 cycle of 12 minutes at 2700rpm(750g). The original objective was to spin at high centrifugation speeds in order to phase separate the layers between the red corpuscle base and the overlaying clear liquid containing leukocytes and plasma. As no anti-coagulants were utilized, the resultant formulation came with a three-dimensional fibrin scaffold termed PRF. Also, PRF membrane can be obtained by squeezing out the liquids present in the fibrin clot. Liquid removal from the PRF fraction can be done through

mechanical pressure between gauze layers resulting in a fairly solid, gel-like material that can be used in various clinical applications as a filling material or as a suturing membrane.[12] PRF membrane can also be prepared by compressing PRF clot in special tools like "PRF Box" resulting in standardized membranes of constant thickness and size along with PRF exudate. PRF exudate contains good amount of growth factors (TGF-b1, PDGF-AB, VEGF etc.), matrix glycoproteins (fibronectin, vitronectin etc.) and proteins specialized in increasing cell attachment to biomaterials and titanium and therefore can be used for biomaterial impregnation, rinsing surgical sites, hydration of graft materials and for storage of autologous grafts.[13]

Advantages of PRF

- Simple and cost-effective method of preparation of PRF
- Eliminates the use of bovine thrombin and thereby reduces the chances of cross infection. It has been discovered that the use of bovine thrombin may be associated with the development of antibodies to the factors V, XI and thrombin, resulting in the risk of life-threatening coagulopathies.[14]
- Slow natural polymerization of PRF on contact with glass particles of the test tube results in physiologic thrombin concentration.[15]
- Fine and flexible 3-D structure of PRF more favourable to cytokine enmeshment and cellular migration.3-D network-connected tri-molecularequilateral junctions in PRF allows the establishment of a fine and flexible fibrin network able to support cytokines enmeshment and cellular migration.[15]
- PRF has supportive effect on immune system.[16]
- PRF helps in hemostasis.[16]
- An in-vitro study showed that PRF is superior results to PRP, considering the expression of alkaline phosphatase and induction of mineralization, caused markedly by release of TGF-β1and PDGF-AB.[17]

Table 1. Advantages of Leucocyte and Platelet Rich Fibrin (L-PRF) over Platelet Rich Plasma(PRP)

Blood Products	PRF	PRP
Preparation Protocol	Simple	Complex
Speed	Fast	Slow
Reproducibility	No bias	Possibility of bias
Anticoagulants	Not required	Required
Production outcome	Low	Good
Cost of preparation	Low	Comparatively high
Molecular/microscopic framework	Trimolecular	Tetramolecular
Lucocyte Content	60-65%	0-50%
Angeogenesis Properties	High	Very Low
Scaffolding Properties	High	Poor

Disadvantages of using PRF

- The final amount available is low because it is autologous blood.[18]
- The success of the PRF protocol depends directly on the handling, mainly, related to blood collection time and its transference for the centrifuge.[19]
- Need of using a glass-coated tube to achieve coat polymerization.[20]
- Possible refusal of treatment by the puncture required for blood collection.
- Only needs a minimal experience of clinician for PRF manipulation.[21,22]

Clinical applications of PRF in dentistry

Oral Maxillofacial Surgery

- PRF can be used as filling material in extraction sockets. As a filling material in extraction sockets, PRF will act as a stable blood clot for neovascularization and accelerated tissue regeneration. This can be used to improve wound healing in immunocompromised and diabetic patients. Also, as PRF stimulates coagulation (with thrombospondin) and wound closure, it can be used as an adjuvant in patients on anticoagulant therapy.[23]
- PRF has been extensively used in sinus lift procedures. Some studies show the use of PRF as the sole filling material during sinus lift and implantation. Some studies show the use of PRF in combination with other bone graft materials in various direct and indirect sinus lift techniques like bone-added sinus floor elevation, osteotome-mediated sinus floor elevation, minimally invasive antral membrane balloon elevation etc.[21]
- The filling of avulsion sockets with PRF leads to very favourable results when bony walls are intact. A combination of PRF with bone substitutes and other adjuncts may be necessary in residual defects where one or several walls are missing or damaged in order to provide an adequate reconstruction of bone volume. PRF increases the cohesion between the graft materials as fibrin act as physiological glue between the wound tissues.[23] Natural blood coagulation leads to formation of a fibrin matrix that biologically links wounded tissue together along with cell proliferation, cell migration, neomatrix apposition and remodelling. Therefore, the combination of PRF with other graft materials should improve the integration of graft material, since PRF is an optimized blood clot.
- In cases of wide sockets and lesions where primary closure is difficult, PRF membrane can be used as a covering and protective membrane that promotes re-epithelialization of the site and accelerates the merging of the wound margins. The elasticity and strength of PRF fibrin membrane makes it easy to suture. As a membrane for guided bone regeneration (GBR), the PRF dense matrix architecture covers, protects and stabilizes bone graft material and operative site in general.[24]

Periodontology & Oral Implantology

- PRF has been used to treat gingival recession, intra-bony defects and periapical lesions. Some case reports show the use of a combination of PRF gel, hydroxyapatite graft and guided tissue regeneration (GTR) membrane to treat IBD.[25]
- Some studies show the use of PRF gel and PRF membrane in combination with a bone graft for treating a tooth with a combined periodontic- endodontic lesion.[26] Some studies show use of two layers of PRF membrane with to cover the defect. The membranes are very thin and inhomogeneous and leucocytes and platelet aggregates are believed to be concentrated in end of the membrane. Therefore, two layers of membrane in opposite sense can be used to prevent the resorption of the thin membrane and to allow the entire surgical area to be exposed to same components (leucocytes and platelet aggregates).[26] Platelet rich fibrin as a potential novel root coverage approach has been reported by Anil kumar *et al*. for covering localised gingival recession in mandibular anterior teeth using combined laterally positioned flap technique and PRF membrane.

Table 2. Literature/Studies on PRF

Author	Year/Month	Type of study	Conclusion
Choukroun *et al*.[39]	2006	In-Vitro	PRF as a healing biomaterial
Lundquist *et al*.[38]	2008/Jan	Review	PRF provides sustained release and protection against proteolytic degradation of endogenous fibrogenic factors important for wound healing
Diss *et al*.[37]	2008/May	In-Vivo	The bone-added osteotome sinus floor elevation (BAOSFE) procedure with PRF as grafting material can lead to an endosinus bone gain
Anil Kumar *et al*.[40]	2009/May	Case Report	The beneficial outcomes of PRF, including reduction of bleeding and rapid healing, holds promising reults in several procedures and also described laterally displaced flap technique with PRF membrane technique as a navel root coverage approach for gingival recession of the mandibular anterior teeth
Aroca *et al*.[41]	2009/Feb	In vivo	The addition of a PRF membrane positioned under the Modified coronally advanced flap provided inferior root coverage, but an additional gain in gingival/mucosal thickness (GTH) at 6 months compared to conventional therapy
Magremanne *et al*.[42]	2009/Apr	Case report	PRF may induce healing at the site of non-reossified cystic cavity by supplying local growth factors
Simonpieri *et al*.[43]	2009/Apr	In vivo	PRF membranes promotes soft tissue healing, protects the surgical site and when its fragments mixed with other graft material it functions as a “biological connector”
Simon *et al*.[44]	2009/May	Animal study	PRFM alone can be the best grafting material for ridge preservation procedures
Simonpieri *et al*.[45]	2009/Jun	In vivo	PRF membranes are helpful for periosteum during healing and maturation.
Su *et al*.[50]	2009/Jul	In vitro	We should use PRF membrane immediately after formation to maximize release of GF to surgical site. The remaining fluid of PRF membrane can be used as an additional source of GF for grafting.
Gassling *et al*.[51]	2009/Jul	In vitro	Application of PRF in cell cultures leads to release of growth factors but PRP showed higher levels of growth factors.
Dohan Ehrenfest *et al*.[49]	2009/Sep	In vitro	This study showed the effects of PRF on several very different cell types. During stimulation,the proliferation of these cells, the effects on the osteoblastic differentiation are highly significant.The role of leucocytes in these cocultures also seems to be important.
Kfir *et al*.[48]	2009/Oct	In vivo	Minimally invasive antral membrane balloon elevation with Inj. PRF can be applied to all patients in need of posterior maxilla bone augmentation with high procedural success, low complication rate, and satisfactory bone augmentation and implant survival.
He *et al*.[47]	2009/Nov	Animal study	PRF releases autologous growth factors gradually and expresses stronger and more durable effect on proliferation and differentiation of rat osteoblasts than PRP in vitro
Sclafani*et al*.[46]	2009/Nov	Review	By using of an autologous platelet derivative (Selphyl; Aesthetic Factors, Princeton, NJ), it allows rapid and inexpensive generation of a PRFM that enhances the healing after facial procedures as well as rejuvenate the face without tissue manipulation
Mazor *et al*.[52]	2009/Dec	In vivo	6 months after surgery, the use of PRF as sole filling material during a simultaneous sinus lift and implantation, stabilized a high volume of natural regenerated bone in subsinus cavity up to the tip of implants.
Aleksić *et al*.[56]	2010/Jan/Feb	In vivo	PRF utilization resulted in a decreased postoperative discomfort and advanced tissue healing
Picardi *et al*.[55]	2010/Feb	In vivo	Platelet gel is a safe and effective therapeutic tool for the management of skin and mucosal ulcers related to graft versus host disease.
Dohan Ehrenfest *et al*.[54]	2010/Mar	In vitro	Combination of both human oral bone mesenchymal stem cells (BMSC) and PRF offers many potential clinical and biotechnological applications, and deserves new studies
Gürbüzer *et al*.[53]	2010/May	In vivo case study	PRF does not seem to increase detectable enhanced bone healing within the extraction sockets of soft tissue impacted mandibular third molars 4 weeks after surgery. Further studies are needed to evaluate the impact of PRF or its combinations with bone grafts on the remodelling phase of the bone healing process.
Gassling *et al*.[57]	2010/May	In vitro	PRF appears to be superior to Bio-Gide as a scaffold for human periosteal cell proliferation.
Jang *et al*.[76]	2010/Jun	Animal study	A peri-implant defect can be successfully repaired with the application of Choukroun PRF and silk fibroin powder
Huang *et al*.[75]	2010/Oct	In vitro	PRF was demonstrated to stimulate cell proliferation and differentiation of dental pulp cells (DPCs) by upregulating OPG and ALP expression. These findings might serve as a basis for preclinical studies that address the role of PRF in reparative dentin formation
Ari *et al*.[74]	2010	Case report	PRF can perform well in treating intra-bony defects combined with endodontic lesion
Chang *et al*.[73]	2010/Oct	In vitro	PRF is capable in stimulation of osteoblastic proliferation. The application of PRF may provide benefit for bone regeneration
Toffler *et al*.[72]	2010/Oct	In vivo	The PRF membrane or plug, can provide protection to sinus membrane during the use of osteotome; and during perforation, the fibrin matrix can aid in wound closure.

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Kathuria *et al.*[71]	2011	Case report	The combined use of Mineral Trioxide and PRF as an apical barrier, showed faster results in peri-radicular healing and complete resolution of symptoms.
Liao *et al.*[70]	2011/Jan	Animal study	Autologous PRFG plus osteo-induced mesenchymal stem cells have good potential for bone regeneration. When combined with MEDPOR as GTR, bone regeneration is enhanced by preventing soft tissue in growth hindering bone regeneration
Peck *et al.*[69]	2011	Case report	Using L-PRF in an alveolar ridge preservation (ARP) procedure, wound healing is improved and stimulation of bone formation is also there to facilitate implant placement in a compromised extraction socket
Kang *et al.*[68]	2011/Feb	In vitro	PRF can be used as a bio-scaffold and reservoir of growth factors for tissue regeneration
Simonpieri A *et al.*[67]	2011/Feb	In vivo	L-PRF can be used as a sole filling material during simultaneous sinus-lift and implantation and is a reliable surgical option promoting natural bone regeneration
Prakash *et al.*[66]	2011/Mar	Review	PRF as a biomaterial appears to accelerate physiologic healing, but still, numerous perspectives of PRF has to be clinically tested
Simon *et al.*[65]	2011/Jun	In vivo	Advantages of PRFM alone includes less surgical time, less technique sensitive and healing difficulties associated with membranes, and less resorption during healing; over guided bone regeneration procedures
Lee *et al.*[64]	2011/Jul	Animal study	In this study peri-implant defect sized 3.0×5.0 mm was successfully repaired by the application of PRF alone
Kim *et al.*[63]	2011/Aug	Animal study	The PRF-mixed Tricalcium Phosphate (TCP) showed more rapid bone healing than the rhBMP-2-coated TCP or the TCP-only control.
Ruga *et al.*[62]	2011/Sep	In vivo	Combined action of PRF and piezoelectric surgery can be considered as a safe technique for surgery of third molar and alveolar socket healing
Sharma *et al.*[61]	2011/Oct	Randomized controlled clinical trial	PRF implies its role as a regenerative material in treatment of furcation defects
Thorat *et al.*[60]	2011/Oct	Controlled clinical trial	Greater reduction in PD, more clinical attachment level (CAL) gain, and greater intra-bony defect fill at sites treated with PRF than the open flap debridement alone
Roy *et al.*[59]	2011/Nov	In vitro and in vivo wound studies	A slow and steady release of growth factors from PRFM was observed because of the use of non-thrombin activation approach. The VEGF released from PRFM was primarily responsible for endothelial mitogenic response via ERK activation pathway and the preparation effectively induced endothelial cell proliferation in wounds and improved wound angiogenesis in ischemic wounds
Sharma *et al.*[58]	2011/ Dec	Randomized controlled clinical trial	Greater PD reduction and periodontal attachment level (PAL) gain, and bone fill at sites treated with PRF with conventional open-flap debridement compared to conventional open-flap debridement alone.
Tatullo *et al.*[78]	2012	In vivo	PRF and piezo surgery reduced the healing time when compared to 150 days described in literature, favouring optimal bone regeneration.
Clipet *et al.*[77]	2012/Feb	In vitro	Expression of osteopontin and osteocalcin and late osteogenic markers was observed and confirmed PRF is useful in stimulating tissue healing and bone regeneration
Peck *et al.* [81]	2012/Mar	Case report	L-PRF has been used in number of surgical procedures to optimize wound healing and was used to stimulate bone formation to facilitate ideal placement of implants
Anitua *et al.*[80]	2012/Mar	In vivo	Plasma rich in growth factors (PRGF) presents a role in reducing tissue inflammation after surgery, increasing new bone formation, and promoting vascularization of bone tissue
Pradeep *et al.*[79]	2012/Mar	Randomized control clinical trial	Porous hydroxyapatite (HA) combined with PRF, increases the regenerative effects observed with PRF in treatment of human three wall intra-bony defects

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Jankovic *et al.*[82]	2012/Apr	Randomized controlled clinical study	PRF membrane in gingival recession treatment provides acceptable clinical results, followed by enhanced wound healing and decreased subjective patient discomfort compared to connective tissue graft (CTG)-treated gingival recessions
Zhang *et al.*[83]	2012/Jun	In vivo	The results demonstrated neither an advantage nor disadvantage of the application of PRF in combination with deproteinized bovine bone mineral in sinus augmentation after a healing period of 6 months
Del Corso *et al.*[84]	2012/Jun	Review	Use of L-PRF also defines new therapeutic principles like Natural tissue regeneration (NTR) for the treatment of periodontal intra-bony lesions and natural bone regeneration (NBR) for the reconstruction of alveolar ridges
Bielecki *et al.*[86]	2012/Jun	Review	Leukocyte PRP (L-PRP) and L-PRF are found in significant amount in two families of platelet concentrates. Presence of leukocytes has a great impact on biology of these products, not only because of their immune and antibacterial properties, but also because they are improving the wound healing process and the local factor regulation
Wu *et al.*[85]	2012/Jun	In vitro	PRF promotes the increase in osteoblast attachment, proliferation, and simultaneously upregulating collagen-related protein production and in combination these factors would effectively promote bone regeneration
Bains *et al.*[87]	2012/Sep	Case report	Histological events and reaction of mineral trioxide aggregate (MTA) with PRF is not studied so far, however, the autologous and biocompatible nature of components used for present treatment modalities seems to be beneficial for long-term clinical results
Shivashankar *et al.*[88]	2012/Oct	Case report	Necrotic-infected immature tooth can be revitalized under conditions of total canal disinfection and PRF is an ideal biomaterial for pulp-dentin complex regeneration
Keyhan *et al.*[89]	2013/Mar	Double-blinded prospective clinical trial	PRF and fat when combinedly used, found more effective than the combination of fat and PRP in the context of facial lipostructure surgery
Gassling *et al.*[90]	2013/Mar	In vitro	PRF eluates support human osteoblast cell proliferation in vitro. Furthermore, it was shown that PRF is a suit-able scaffold for cultivating human osteo-blastsin vitro. Nevertheless both systems,PRF and collagen (BioGide®), seem to be suit-able as scaffold materials for seeding byosteoblast cells in vitro
Agarwal M *et al.*[103]	2014/Jun	Review	PRF as an adjunct in wound healing and periodontal regeneration has shown promising results. It has been successfully used for correction of osseous defects in periodontics, oral and maxillofacial surgery and implant dentistry. In addition to these, PRF has shown good results in regeneration of pulp-dentin complex for endodontic procedures.
Raaj V *et al.*[102]	2015/Mar-Apr	Review	The ease of PRF formation and its application has various beneficial outcomes, which also includes reduction in bleeding, graft stabilization and bone growth. Apart from its application in dentistry PRF is also been used all over the world in various surgeries including orthopaedic surgery and plastic surgery. Still numerous prospective of this new generation platelet concentrate have to be obtained and searched for
Borie E *et al.*[101]	2015/May	Review	Platelet-rich fibrin seems to be an accepted minimally invasive technique with low risks and satisfactory clinical results.
Kobayashi E *et al.*[95]	2016/Jan	Case Report	PRP release significantly higher proteins at earlier time points whereas PRF displayed a continual and steady release of growth factors over a 10-day period. Furthermore, in general, it was observed that the new formulation of PRF (A-PRF) released significantly higher total quantities of growth factors when compared to traditional PRF
Anantula K *et al.*[92]	2016/Sep	Case report	PRF can be considered as a healing biomaterial and it features all the necessary parameters permitting optimal healing, but numerous perspectives of PRF have still to be clinically tested.
Tunali M *et al.*[94]	2016/Sep	Preliminary Study	The study defined 10 min MT-PRF as a new autogenous product with superior fibrin network and results showed that, fibrin formation was made more organised and denser with 2-way direction centrifugation
Crisci A *et al*[97]	2017/Nov	Case report	L-PRF production will improve our understanding about wound healing, particularly in the regenerative therapy of chronic skin lesions in humans. The data collected show that the best preparation method is the 2 min compression of the clot after 0 min of blood sampling, using the 9 mL vacutainer system and not a 9 mL syringe
Titirinli K er al.[96]	2017/Jun	Animal study	PRF and its variations have positive effects on the new bone tissue and cell number, and may lead to more rapid ossification compared to the unprocessed bone defects.
Reddy S *et al.*[91]	2018/Jan	Case report	T-PRF is efficacious clinically and radiographically in the treatment of a periodontal intrabony defects. It is an autologous preparation and found to be clinically effective and economical than any other available regenerative materials including PRP.
Ozer K *et al.*[99]	2019	Case report	L-PRF treatments protect and maintain bare soft tissue structures viable, facilitate the formation of granulation tissue and epithelization, and remarkably reduce the need for additional soft tissue surgeries in small-to-medium-sized complex wounds
Grecu AF *et al*[98]	2019/May	Review	PRF is considered as a beneficial adjuvant for a range of chronic muscle, tendon, bone or other soft tissue injuries. Further clinical trials to confirm these benefits require consistency in PRF preparation and the classification of a successful clinical outcome to fully harness its potential.
Crisci A *et al.*[93]	2019/Mar	Review	The results indicate that A-PRF™ shows, however, an antimicrobial activity against Staphylococcus aureus, Streptococcus mutans, Enterococcus faecalis and Candida Albicans. Furthermore, the spectrum and potency as an antimicrobial agent are far lower than those of an established surgical antimicrobial (specific antibiotic).
Mohan SP *et al.*[100]	2019/Nov	Review	PRF is considered as a new generation of platelet concentrate, is a novel step in regenerative periodontal treatment with simplified processing and without biochemical modification. Apart from its application in dentistry, PRF is also been used in various medical fields: orthopedic and plastic surgery.

- PRF can promote the healing of osseous defects by the following mechanisms. According to Chang *et al*. PRF promotes the expression of phosphorylated extracellular signal-regulated protein kinase (p-ERK) and stimulates the production of osteoprotegerin (OPG) which in turn causes proliferation of osteoblasts. Another study by Huang *et al*. reported that PRF stimulates the osteogenic differentiation of the human dental pulp cells by up regulating osteoprotegerin and alkaline phosphatise expression. PRF also releases growth factors such as platelet-derived growth factor and transforming growth factor which promote periodontal lregeneration.[27,28]

Endodontics

- PRF can be used as a scaffolding material in an infected necrotic immature tooth for pulpal regeneration and tooth revitalization.[26]
- The combination of PRF membrane as a matrix and MTA in apexification procedures prove to be an effective alternative for creating artificial root-end barriers and to induce faster periapical healing in cases with large periapical lesions.[29]
- Use of PRF in regenerative pulpotomy procedures have also been documented where coronal pulp is removed and the pulp wound is covered by PRF followed by sealing it with MTA and GIC [6]. PRF has also been used to fill in the bony defects after periapical surgeries like root end resection etc.[29]
- PRF might serve as a potentially ideal scaffold in revascularization of immature permanent teeth with necrotic pulps as it is rich in growth factors, enhances cellular proliferation and differentiation, and acts as a matrix for tissue ingrowth. The potential theory behind the success of the use of PRF for regeneration of open apex could be attributed to a study conducted by Huang *et al*, who concluded that the PRF causes proliferation of human Dental Pulp Cells and increases the protein expression of these Dental Pulp Cells differentiate into odontoblasts like cells. OPG and ALP expression are generally regarded as markers of odontoblastic differentiation.[26]

Pedodontics

- Platelet Rich Plasma could be an effective material used for direct pulp capping due to its excellent wound healing, tissue regeneration & osteogenic properties.Many researchers have proven that pulp tissue contains highly proliferative and clonogenic population of progenitor/stem cells which can differentiate into hard tissue forming cells on injury.[30] Pulp Capping in carious teeth can be unpredictable, therefore case selection can be an important criterion (Bashutski and Wong, 2008).[31] Important criterion for successful outcomes is type and location of injury, age of the tooth, the treatment modality and integrity of cavity restoration.[32]
- Cytotoxicity and mutagenic effects have always been major disadvantages discovered with the use of formocresol, as a pulpotomy agent. Platelet Rich Plasma with its low toxic effects and increased tissue regeneration showed excellent clinical results.A study conducted by Damle *et al*[34], in 2004 compared PRP and Calcium Hydroxide and found 100% success rate with Platelet Rich Plasma. Another study with Nagasaki *et al*.[33] in 2007 compared PRP vs Hydroxiapetite crystals, and found PRP to be much superior.
- Hellig *et al*[35] in 1984, and Waterhouse11 in 2000 gave the criterion for tooth selection in pulpotomy using Platelet Rich Plasma. Other than the usual criterion like symptoms indicative of advanced pulpal inflammation, or symptoms suggesting a non-vital tooth, pulp necrosis, periapical pathology, internal resorption, they also suggested that an important criterion could be that hemorrhage stops within 5 minutes from amputated pulp stumps, using a sterile pledget of moist cotton.
- 3.Apexogenesis is mainly performed to preserve the pulp vitality, as pulp has the reserve of cells which have regenerative properties. As explained earlier, PRP is an autologous source of many growth factors, which can induce stem cells and thus can lead in the regeneration of the tissues.[36]

Tissue Engineering: In a study by Gassling *et al*. reported that PRF appears to be superior to collagen as a scaffold for human periosteal cell proliferation and PRF membranes can be used for in vitro cultivation of periosteal cells for bone tissue engineering. Thus, PRF is a potential tool in tissue engineering but clinical aspects of PRF in this field requires further investigation.[24]

CONCLUSION

PRF is a 2nd generation of platelet concentrates and the slow polymerization mode confers to PRF membrane as a particularly favourable physiologic architecture to support the healing process. The use of PRF as an adjunct in wound healing and periodontal regeneration has shown promising results. It is essential that the research using PRF as an adjunct to soft tissue and hard tissue regenerative therapies develop appropriate studies with the necessary controls to further evaluate the maximum regenerative potential of PRF for the healing of soft and hard tissue wounds.

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