Review article

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Platelet-rich fibrin to manage different periodontal defects combine with Flap surgery and other uses in dentistry. A descriptive review

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ABSTRACT:

In these days, periodontal diseases are very much common in Asian subcontinent especially in Bangladesh, due to some relevant factors that is more prevalent in this country. Most of the time patient neglect their condition and ultimately loss their teeth. Even after doing phase 1 therapy that is scaling, polishing with antimicrobial agents, it could not heal the periodontal condition with advanced bone destruction or clinical attachment loss. Therefore, after proper oral hygiene maintenance therapy, different flap surgery should consider. . In recent study, it is found that platelet rich fibrin (PRF) PREPARED From the patient's Own blood and then placement within defect could enhance the early healing procedure. This PRF membrane is also used in a variety of discipline in dentistry, including regenerative surgery. This PRF membrane is now used in a variety of disciplines in dentistry, including regenerative surgery and enhancing early healing. The goal of this study is to critically analyze and appraise the currently available research with an emphasis on the use of PRF in regenerative periodontal surgery.

An electronic search was conducted (PubMed/MEDLINE, Google Scholar, BanglaJOL, Cochrane library). Various combinations of the following keywords were used: 'prf', 'prf membrane', 'periodontal regenerative surgery', 'prf in dentistry', 'systemic diseases and periodontitis', 'drawback of prf', 'platelet-derived growth factors', 'prf in oms', 'prf in orthodontics'. Articles were searched until August 2021

All of these studies reveal that the PRF membrane enhances the healing of various defects in a variety of periodontal diseases and in several fields of dentistry. Studies are going on pulp regeneration and socket healing after extraction with PRF in dentistry. More emphasis should have to give to the prevention of periodontal diseases as well as more concern should have to give on PRF with flap surgery to enhance healing and improve the social health of the general population by preventing tooth loss and for different research purposes on PRF in different other fields of dentistry in Bangladesh.

KEYWORDS: platelet-rich fibrin, prf membrane, prf preparation, periodontal disease, flap surgery

INTRODUCTION:

Bangladesh is one of the densely populated countries in this world. Total population around 165 million in 2020 (1) and ranked position 8th in the world. (2) People are suffering from multiple systemic diseases as well as dental diseases here. Because of poor oral hygiene practices, betel quid chewing & complication of different systemic diseases, periodontal diseases become more prevalent among all dental problems in Bangladesh. (3–5) This type of patient is commonly treated here by phase-1 nonsurgical therapy mainly by scaling, polishing, and oral hygiene instructions and given antimicrobial therapy. (6) flap surgery is indicated if the periodontal condition is not improved by non-surgical periodontal therapy. Different grafts like Xenogenic collagen matrix , autologous connective tissue graft or enamel matrix derivatives etc. as an adjunct to different advanced flaps surgery are utilized to enhance the healing. (7–12)Platelet-rich fibrin (PRF) is a second-generation autologous platelet concentration that is obtained from the patient's blood in a simple and cost-effective manner. (13) Platelet-rich fibrin (PRF), as described by Choukroun et al, was initially used in clinical practice in Southern Europe in oral maxillofacial and

implant surgery. (14) It was created as a less expensive, but more biocompatible and effective, alternative to platelet-rich plasma (PRP) for bone and soft tissue regeneration. PRF is less soluble after administration than PRP needs less biochemical blood processing, and offers a longer-lasting release of platelet cytokines and growth factors. (15)

BACKGROUND HISTORY OF PRF:

Platelets have been used as useful tools for periodontal regeneration for over two decades due to their important role in the wound healing process. Although the use of fibrin adhesives has been well documented over the last 30 years(16,17), their use remains controversial due to the difficulty in preparation and the risk of cross-infection. Following that, a less complex production protocol was used to create concentrated platelet-rich plasma (cPRP). It is made from the patient's blood and is activated with thrombin and calcium. The structure is made up of a three-dimensional biocompatible fibrin scaffold and a small volume of platelet-enriched plasma. Growth factors and proteins are released into the immediate environment when PRP is activated,(18) facilitating postoperative wound healing and tissue regeneration. However, the downside of employing PRP is that its qualities can vary based on platelet concentration, leukocyte count, activator type, and time of fibrin scaffold insertion after clotting. (19) However, there are some hazards linked with PRP use. The presence of bovine thrombin in PRP can lead to the formation of antibodies to the clotting factors V, XI, and thrombin, which can cause the coagulation process to be disrupted. Furthermore, when challenged with a foreign protein, bovine thrombin preparations contain clotting factor V, which might cause immune system activation. Other disadvantages of PRP use include permissible requirements on handling blood, as well as literary disagreements concerning the benefits and clinical outcomes of PRP use.

All of this has resulted in the development of platelet-rich fibrin, a novel type of platelet concentrate that solves many of the drawbacks of PRP. PRF is a powerful autologous regenerative substance that has a wide range of clinical applications in periodontics, as it promotes both soft and hard tissue regeneration.(20). Other than PRF there are certain growth factors also used in Dentisrry like: Enamel Matrix Derivatives, Platelet-Derived Growth factor, Bone Morphogenic Proteins, Platelet rich plasma but Platelet rich Fibrin proven success in variety of Dental procedures and easily obtainable. (21)

PRF PREPARATION:

Dr. Choukroun(22) invented the traditional PRF preparation technique in 2000. It is the current PRF technique approved by the French Ministry of Health, in which PRF is prepared without the use of an anticoagulant during blood collection or bovine thrombin during gelling. (23)

To obtain the proper quantity and quality of fibrin matrix, leukocytes, platelets, and growth factors, a standard protocol for PRF preparation should be followed. A PC-02 table centrifuge(24) and a blood collection kit consisting of a 24 gauge butterfly needle and 9 ml blood collection tubes are required for PRF preparation. A blood sample is collected from the patient without anticoagulant in 10 ml(24) tubes and immediately centrifuged at 3000 rpm for 10 minutes. (20)(25) or for 12minutes (24,26,27) The typical PRF preparation is centrifuged for 12 minutes at 2700 rpm, while the advanced platelet-rich fibrin (A-PRF) is centrifuged for 14 minutes at 1500 rpm, according to some reports.(28)

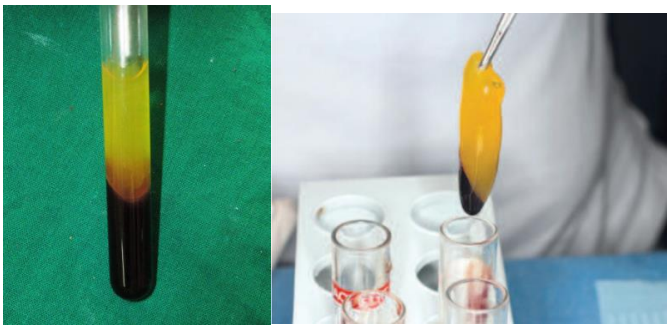

Figure 1: Test tube showing Platelet-rich fibrin after centrifugation of blood, PRF membrane being withdrawn from the blood tube.

When blood comes into touch with the test tube wall during centrifugation, platelets get activated, causing the coagulation cascade to begin. The final product is made up of three layers after centrifugation. (14)

Acellular PPP (platelet-poor plasma) is on top, followed by a PRF clot in the middle, and RBCs at the bottom of the test tube. After centrifugation, the fibrin clot is removed from the tube, and the associated red blood cells are scraped off and discarded. By squeezing out the fluids in the fibrin clot, PRF can also be made in the form of a membrane.

Mito Kobayashi et al (29) have been suggested the stainless steel PRF compression device, created for PRF membrane preparation is made up of two spoon-shaped pieces. Many pinholes were included in the stage where the PRF clot was put for fastening the clot and draining excess fluid from the serum when the clot was compressed. The clearance between the spoon pieces was increased to 1 mm. As a result, a standard 1-mm thick PRF membrane was consistently prepared when the PRF clots were squeezed with this equipment. (Figure-2)

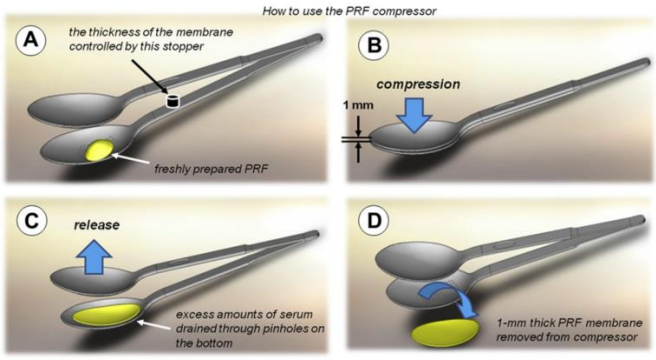

Figure-2: Appearance of the PRF compressor and the protocol for operation. The PRF clot is placed on the lower spoon, which possesses many pinholes (A), and is compressed by pushing the handles together (B). In this step, excess amounts of exudates would be removed. The compression force is then released (C), and the resulting 1-mm thick PRF membrane is removed (D). (This figure has been collected from an article By Mito Kobayashi et al (29) was published in the journal of Biologicals, Volume 40, Issue 4, September 2012, Pages 323-329 under open access policy with **Creative Commons Attribution-NonCommercial-No Derivs (CC BY-NC-ND) & CC BY Licence. (30)**

Some author suggest The L-PRF Wound Box for the preparation and standardization of PRF in clots and membranes. The membrane in the clots is compressed using the PRF Wound Box in a slow and homogeneous minor compression, ensuring that the final membrane is always uniformly moist and soaked in serum. (31)

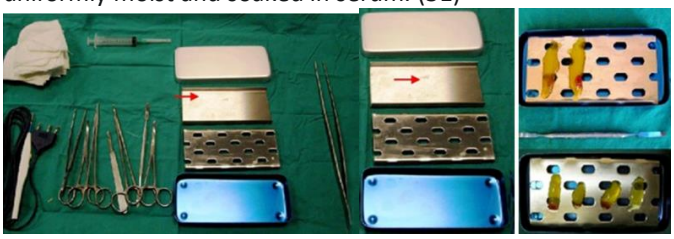

Figure: 3 : L-PRF Wound Box. (This figure has been collected from an original article By by*Alessandro Crisci* et al(31)was published in the Journal of Unexplored Medical Data published on 22 Nov 2017, under open access policy with **Creative Commons Attribution (CC BY-4) License.(32)**

The amount of time between blood collection and the centrifugation process is an essential factor in the procedure's success and clinical outcome. Because blood is handled slowly throughout the centrifugation process, diffuse polymerization of fibrin occurs, resulting in the creation of a tiny blood clot with uneven consistency. As a result, a PRF technique that is repeatable has been developed.

MECHANISM OF ENHANCING HEALING:

Platelets taken from the blood serve as an autologous resource of growth factors. Platelet concentrate generated from blood can be used in general medical practice to prevent and manage bleeding caused by disorders such as severe thrombocytopenia, severe oral hemorrhage associated with medullary aplasia, acute leukemia, and so on. (33)Platelet concentration as a bioactive surgical addition is being developed with the help of fibrin adhesives. Since 1990, certain blood components have been identified as being a part of the natural healing process and having the ability to speed wound healing when administered to wounded tissues or surgical sites. The first description of fibrin glue, which is made by polymerizing fibrinogen with thrombin and calcium, was in 1970. It was made with donor plasma, but due to the low concentration of fibrinogen in plasma, the durability and quality of the fibrin glue were poor. (34) These fibrin adhesives can be obtained either autologously from the patient or commercially, however, the latter carries a slight risk of disease transmission.

Platelet-rich fibrin (PRF), a second-generation platelet-rich aggregation, is easy to make and releases cytokines gradually as it degrades. (35) As a result, PRF has a high capacity for wound healing and tissue regeneration. (36,37) PRF greatly enhances the osteogenic potential of BMSC membranes in nude mice, and a rabbit skull defect model revealed a synergistic effect of PRF and osteoblastic bone marrow mesenchymal stem cells (BMSC) membranes on bone defect repair. (38) The cytokine stimulation and fibrin scaffolding effects of PRF on tissue repair are principally responsible. TGF-1, insulin-like growth factors (IGFs), vascular endothelial growth factor (VEGF), and platelet-derived growth factors (PDGFs) are the most common cytokines found in PRF. They effectively recruit cells that are important for tissue repair to defect sites and then promote and regulate the tissue repair process. (35,39) Furthermore, PRF fibrin offers a three-dimensional framework that encourages recruited cells to proliferate and differentiate. (40) PRF has been effectively utilized to treat bone and cartilage defects, dental implants, and severe periodontitis, with significant treatment outcomes. (41,42)

CLINICAL APPLICATION OF PRF IN DENTISRY :

PRF membrane can be utilized for a variety of applications in dentistry.

A. PRF IN PERIODONTAL DISEASES:

It can be used for correction of different types of gingival recession (43,44), The most predictive plastic surgery is a coronally advanced flap procedure with subepithelial connective tissue. PRF has recently been utilized in conjunction with traditional order to improve the efficacy of root coverage treatments while lowering morbidity.(45) According to Aroca et al. (46) when compared to the modified coronally advanced flap alone, the use of PRF membrane resulted in an increase in the width of keratinized gingiva at the test sites after 6 months.

Gabriel Merizalde et al. has showed one successful surgical case with utilization of PRF in in 33, 34 teeth and improvement of clinical attachment loss from 5mm to 3mm within next 3

months (Figure-4) (25), Anilkumar et al.(45) also demonstrated that six months after using a laterally repositioned flap in conjunction with PRF to cover a localized recession on the buccal side of a mandibular incisor, complete root coverage was achieved with excellent tissue contour and color, demonstrating that this fibrin biomaterial has potential for use in periodontal surgeries.

Figure -4: Gingival recession located 33 and 34 buccal surfaces, -PRF membranes placed on gingival recession Clinical appearence six months after surgery (This figure has been collected from an article By byGabriel Merizalde et al(25). was published in the International journal of odontostomatologyVolume 13, no-1 , March 2019, under open access policy with Creative Commons Attribution (CC BY-NC) License.(63)

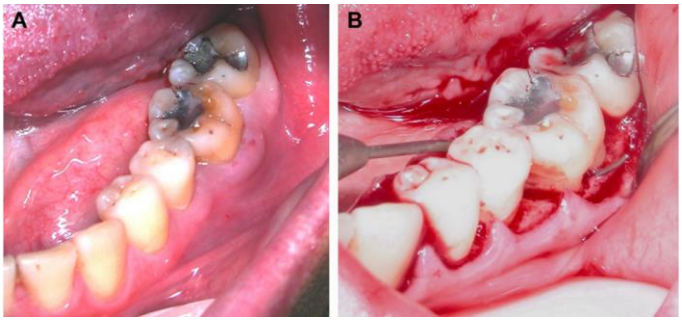

Figure-5: The clinical pictures of left mandibular sextant. (A) Before surgery. (B) After flap reflection, mesial infrabony defect and a through-and-through furcation invasion were noted at #36. (This figure has been collected from a case report By Yu-Chao Chang et al. (24) was published in the Journal of Dental Sciences, Volume 6, Issue 3, September 2011, Pages 181-188 under open access policy with **Creative Commons Attribution-NonCommercial-NoDerivs (CC BY-NC-ND) license. (**https://www.elsevier.com/journals/journal-of-dental-sciences/1991-7902/open-access-journal**) (64)**

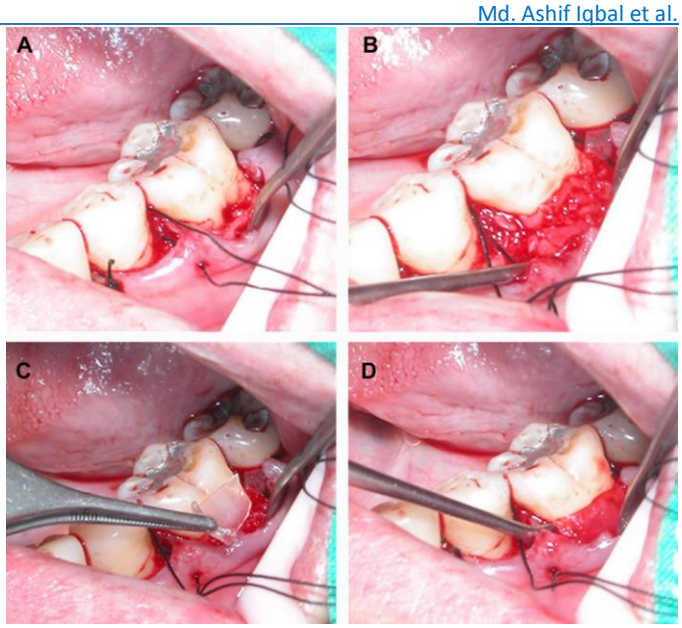

Figure: 6- Clinical application of platelet-rich fibrin (PRF) on the buccal aspect of #36. (A) Minced PRF was applied to the defect walls and root surfaces. (B) Minced PRF was tightly packed in the furcation area. (C) PRF membrane was trimmed to cover the osseous defects. (D) PRF membrane was adapted over the grafted defect and above the cementoenamel junction by Yu-Chao Chang et al. (This figure has been collected from a case report By Yu-Chao Chang et al. (24) was published in the Journal of Dental Sciences, Volume 6, Issue 3, September 2011, Pages 181-188 under open access policy with **Creative Commons Attribution-NonCommercial-NoDerivs (CC BY-NC-ND) license. (**https://www.elsevier.com/journals/journal-of-dental-sciences/1991-7902/open-access-journal**) (64)**

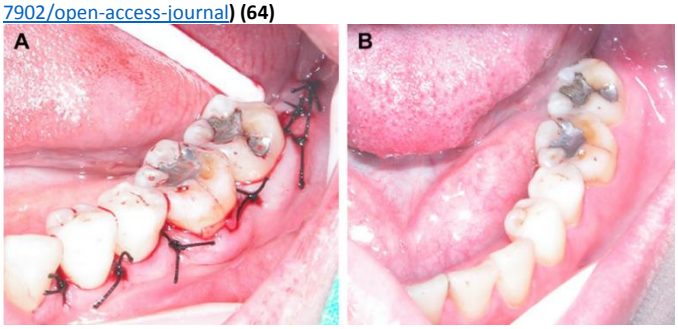

Figure: 7 : The clinical pictures after platelet-rich fibrin application. (A) The flaps were repositioned to their presurgical levels and sutured with silk utilizing an interrupted technique. (B) The clinical picture of #36 3 months after operation. (This figure has been collected from a case report By Yu-Chao Chang et al. (24) was published in the Journal of Dental Sciences, September 2011, under open access policy with Creative Commons Attribution-NonCommercial-NoDerivs (CC BY-NC-ND) license. (**https://www.elsevier.com/journals/journal-of-dental-sciences/1991-7902/open-access-journal**) (64)

PRF also used in treating furcation defect in chronic periodontitis (47–49), in generalized aggressive periodontitis(50),for correction of intrabony defect(51–55), to prevent osteoclastic effect and thus help in periodontal bone regeneration(56–62)Clinical application of platelet-rich fibrin as the sole grafting material in periodontal intrabony defects by Yu-Chao Chang et al. (24)has showed a succesfull outcome. Figure: 5,6,7

B: PRF IN ORAL AND MAXILLOFACIAL SURGERY:

PRF membrane can be used for management of dry socket (65), Sam Paul et al have found platelet-rich fibrin better than zinc oxide eugenol in cases of established dry socket for controlling pain, reducing inflammation, and improving wound healing.(66) PRF also used for better healing and bone regeneration after extraction (67,68), to enhances soft tissue support and regeneration after surgery (69),for improving bone growth around dental implant (70) and to increase the width of keratinized mucosa around implants (71), accelarte early implant placement after PRF placement in extracted socket(72) and also healing of periodontal tissue and bone regeneration after infected radicular cyst enucleation (73,74). Also used in medication related to Osteonecrosis of the jaw. (75)

C: PRF IN ENDODONTICS:

PRF membrane can be used for pulpal regeneration and tooth revitalization (76),for apexogenesis in young permanent tooth (77),management of perforation in furcation regeneration followed by endodontic treatment (78)

D: PRF IN PERIO-ENDO LESIONS:

Periodontal lesions spread apically with an already existing periapical lesion, or an endodontic lesion combines with an existing periodontal lesion to form perio-endo lesions. A true combined perio-endo lesion's prognosis is frequently poor or even hopeless, especially if it is chronic. Increased bony support through bone grafting and guided tissue regeneration, as well as the introduction of polypeptide growth factors to the surgical area, can enhance the prognosis of such afflicted teeth.(79) El-Sharkawy et al. (80) proposed using PRF in conjunction with tissue regeneration techniques to treat intrabony defects in such a case.

E: PRF IN PEDIATRIC DENTISTRY:

One article by Priya Nagar and Deppak Viswanath has mention in their review article regarding uses of PRF in Pediatric dentistry specially in Pulp capping, Pulpotomy and Apexogenesis and also in extracted socket. (81)

F: PRF AND PERIODONTALLY ACCELERATED OSTEOGENIC ORTHODONTICS

Periodontally Accelerated Osteogenic Orthodontics (PAOO) is a procedure that combines orthodontic forces with cortcotomies and alveolar bone plate grafting to enhance tooth movement. A case report of a patient with a high buccal canine and bimaxillary protrusion where PRF was used alongside other treatment modalities has also been presented in the literature. This was thought to improve healing after a segmental osteotomy and a single tooth cortcotomy around the canine, both of which were performed under local anaesthesia. According to the authors, this resulted in a decrease in canine retracton time.(82)

DRAWBACKS OF PRF MEMBRANE:

Over time, one of the reported disadvantages included its use of anticoagulants or known inhibitors of clot formation. Thus decreasing the long-term release of growth factors and ultimately diminishing its regenerative potential. It resorbs in around 7 days,(83) which is far faster than the 4–6 weeks (84) necessary for conventional periodontal regeneration procedures. Another big downside of PRF is its preservation after it has been prepared.PRF membrane should also be used as soon as possible after preparation because they can shrink, causing dehydration and undermining the structural integrity of PRF. (20,85)

DISCUSSION :

PRF is now well eastablished regenrative materials in dentistry specially in Periodontology to manage severe bone destruction and attachment loss. PRF is easier to make and less expensive. PRF has also been found to have an antimicrobial function due to the presence of leukocytes.(86) As a result, when PRF was compared to other growth factors, considerably improved clinical radiographic outcomes were reported. Before regenerative surgery with PRF, systemic diseases should exclude to get better prognosis. Different types systemic diseases, aggravate periodontal diseases are more significant in Bangladesh.

Some meta-analysis report that, Bangladesh has a relatively high prevalence of pre-diabetes (10.1%) and diabetes (7.8%), with a notable variation between rural and urban areas. (87)

Diabetic patients are more likely to develop various oral diseases (88,89). The most common of these oral health problems is periodontal disease, which has been labeled "the sixth complication of diabetes" (90). Several studies have found that diabetics have a higher prevalence and severity of periodontal disease than non-diabetic persons (91,92). A recent single-center hospital-based study in Bangladesh revealed that individuals with diabetes had a greater prevalence of periodontal disease (55.8%) (93)

Periodontal regenerative surgery in uncontrolled diabetes should be controlled or adjunctive systemic antimicrobial therapy may improve the prognosis.(94)

Other systemic diseases such as osteoporosis, thyroid and parathyroid problems should be considered before undergoing this type of surgery, and smoking (95) may also have a role in the prognosis of periodontal regenerative surgery.

In Bangladesh, there are just a few case studies on regenerative surgery with PRF membrane in dentistry. No original study has been found on this subject. Because there are so many patients available, an interventional research should be conducted to determine the prognosis and identify other factors that contribute to healing and future advance applications of PRF in different arena of dentistry in

Bangladesh.

CONCLUSSION

PRF has been shown in studies to have a safe and beneficial effect on hard and soft tissue healing in periodontal surgery. Under proper manipulation, current evidence-based dentistry reveals that PRF can be utilized routinely in periodontal regenerative surgery with good biological effects and appropriate clinical results. PRF's beneficial effects allow it to be used in diverse dental fields in Bangladesh with additional study.

CONFLICT OF INTEREST: None

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