ISSN: 2581-5989
PubMed - National Library of Medicine - ID: 101738774

International Journal of Dental Science and Innovative Research (IJDSIR)
IJDSIR : Dental Publication Service
Available Online at: www.ijdsir.com
Volume – 5, Issue – 3, May - 2022, Page No. : 636 - 653

PRF in regenerative dentistry - A systematic review

[1]Dr. Rajhans Nilima, Professor and Head of the department, Department of Periodontology, YCMM & RDF's Dental college, Ahmednagar, Maharashtra, India.

[2]Dr. Pathare Aparna, Post graduate student, Dept of Periodontology, YCMM & RDF's Dental College, Ahmednagar, Maharashtra, India.

[3]Dr. Sushma Bommanavar, Reader, Dept of oral Pathology and microbiology, YCMM & RDF's Dental College, Ahmednagar, Maharashtra India.

[4]Dr. Asawari Lawande, Senior Lecturer, Dept of Periodontology, YCMM & RDF's Dental College, Ahmednagar, Maharashtra, India.

[5]Dr. Tanuja Ugale, Post graduate student, Dept of Periodontology, YCMM & RDF's Dental College, Ahmednagar, Maharashtra, India.

[6]Dr. Chavan Mayur, Post graduate student, Dept of Periodontology, YCMM & RDF's Dental College, Ahmednagar, Maharashtra, India.

Corresponding Author: Dr. Pathare Aparna, Post graduate student, Dept of Periodontology, YCMM & RDF's Dental college, Ahmednagar, Maharashtra, India.

Citation of this Article: Dr. Rajhans Nilima, Dr. Pathare Aparna, Dr. Sushma Bommanavar, Dr. Asawari Lawande, Dr. Tanuja Ugale, Dr. Chavan Mayur, "PRF in regenerative dentistry - A systematic review", IJDSIR- May - 2022, Vol. – 5, Issue - 3, P. No. 636 – 653.

Type of Publication: Review Article

Conflicts of Interest: Nil

Abstract

Background: The aim of this systematic review was to evaluate the effects of platelet-rich fibrin (PRF) membranes on the outcomes of clinical treatments in patients with intrabony defects, root coverage in gingival recession, alveolar socket preservation, endodontic regeneration. Also, the role of injectable PRF in regenerative dentistry is evaluated. This systematic review is aimed to collective articles published till date on PRF in dentistry, which helps better understanding and whether PRF can be used in future dentistry.

Methods: Manuscripts were searched from 2011 to June 2021 systematically and categorized under following topics: intrabony defects, gingival recession, alveolar socket preservation, endodontic regeneration. Randomized control studies conducted on humans were taken in to consideration.

Results: Total 57 articles were taken in to consideration. Role of PRF in intrabony defect had more studies

compared to other procedures. Treatment of alveolar socket preservation with PRF has very little literature evidence. Endodontic regeneration with PRF has sparse studies compared to other procedures which need to be explored more in the future.

Conclusion: Though many research are going on PRF, in regenerative dentistry. Still its role in dentistry need to explored more on humans with huge samples, RCT for future purposes.

Keywords: PRF, Regeneration, Intrabony defect, Socket Preservation, Injectable PRF

Introduction

Healing is a complex process, which repairs the tissue by organizing the cells, sending chemical signals and by secreting extracellular matrix[1]. Oral cavity tissue are intricate in nature due to its diverse cell population from various tissues[2,3]. Tissues in the oral cavity that are damaged due to injury or by disease can be replaced or repaired in regenerative dentistry. There is a drastic advancement in the field of science over the past decades, along with this regenerative dentistry which also has discern its part of development through breakthrough revolution. It is well known that platelets has cardinal role in both hemostasis and in wound healing by activating various biomolecules including growth factors, adhesion molecules, angiogenesis also in activation and proliferation of associated cells[4,5]. In recent decades, these characteristics of platelets has fascinated the researchers to reconnoiter the role of platelets in tissue regeneration both in Medical and dental field. In 1970 regenerative capacity of platelets was first discovered[6] and on further upheaval it leads to categorization of platelet concentrates in to plasma rich protein (PRP) and plasma rich fibrin (PRF)

PRP perform by activating osteoprogenitor cells in the host bone and graft. PRF which was first introduced in early 2000 especially for oral and maxillofacial injuries found to have more precedence compared to PRP[7], due to its easy preparation and no need of any chemical manipulation[8]. PRP is a matrix of autologous fibrin which is formed in final stage of coagulation cascade along with cytokines that are released by platelets, creating PRF as a highly biocompatible material, making them to act as s reservoir of tissues growth factors in areas of damaged tissues[9]. In face of all there still arises a question regarding veritable clinical performance of PRF in regenerative dentistry. Thus the purpose of the present systematic review is to reveal clinical potential of PRF in regenerative dentistry also areas where usage of PRF is needed for betterment of patients those who need repair or regeneration.

Platelets and Fibrin

Platelets that are derived from megakaryocytes is the second most copious corpuscles in the blood, with endurance between 7 to 10 days[10,11]. Platelets play an important role in healing and repair by leukocytes and growth factors, which is the main element in the platelets that helps in differentiation, proliferation, migration and cell metabolism. On activation of growth factors in the platelets, which are trapped in the fibrin matrix, promotes cell mitosis in the place of injury by triggering stem cells and osteogenesis. Fibrin in the platelets contributes a provisional matrix for cells, to proliferate, organize and perform their function in the site of injury and inflammation. Also, this fibrin helps in the migration of fibroblast and endothelial cells and in the angiogenesis process by forming a matrix and paving way for tissue healing. These fibrin networks are formed by soluble fibrinogen thrombin and factor XIII a[12,13].

Plasma Rich Fibrin

PRF is a tetra molecular structure enclosed with cytokines, platelets and stem cells. PRF indulge micro

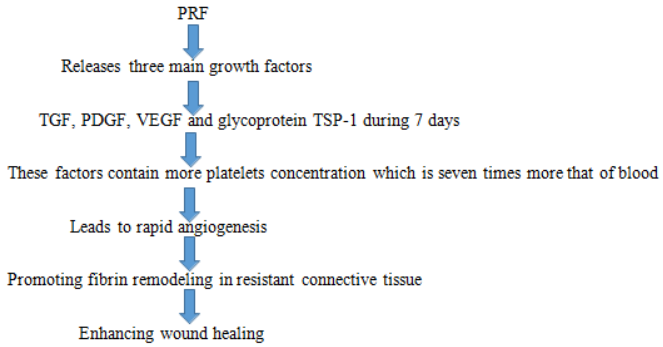
vascularization, acts as a medium in carrying cells that are intricate in tissue regeneration, helps in sustained release of growth factors and thus, makes the environment suitable for wound healing. PRF has greater potential in hard and soft tissue regeneration, promotes hemostasis, bone growth and maturation without inflammatory reactions. Compared to natural blood PRF is more durable, easy to handle and can be placed in an area where it is needed[14].

Protocol for PRF preparation

PRF is prepared without the addition of anticoagulant and bovine thrombin. It is centrifuged at 3000 rpm for 10 minutes. The collected blood should be centrifuged immediately before the commencement of the clotting mechanism. It forms three layers, top layers with cellular plasma, PRF clot in the middle, red corpuscles at the bottom. This PRF clot should be placed in the sterile cup for 10 minutes for proper serum formation present in the PRF. In the case of PRP preparation, bovine thrombin is used with silica particle that causes cytotoxicity, which is doesn't occur in PRF.[15]

PRF over PRP

PRF has many advantages when compared to PRP. They are easy to manipulate, less cost, lower risk due to the absence of bovine thrombin and anticoagulants that are used in PRP. It has better wound healing due to low degree polymerization. The organized fibrin matrix in PRP is more coherent in stem cell migration, bone and wound healing, hemostasis and graft stabilization. When compared to PRP, it has better healing properties and shows promising results.[16]



Methods

In our review we followed the guidelines preferred for systematic review. The following PICO question was framed.

PICO question

P- Patients in need of treatment for hard and soft tissue regeneration/repair

I-Undergoing dental treatment (pulp repair/regeneration, Bone repair/regeneration, gingival recession using PRF

C-Regenerative /reparative procedure carried for treating hard and soft tissue without using PRF

O-soft and or hard tissue reformation periodontium, Alveolar bone and Gingiva

Focused question

Whether PRF has potential role on repai and regeneration in dental procedures?

Does injectable PRF discovered in recent years is more efficient when compared to gel form?

Search strategy

Electronic database searched are MEDLINE, Cochrane Central Register of Controlled Trials, and Embase Web of Science Journal Search. Additionally manual search. Only article published in English were taken in to consideration. The studies were limited to RCT conducted on humans and the articles published from 2011 to 2020 were included in this SR. the search strategy that are included are: role of PRF 1) intrabony defect regeneration 2) management of gingival recession

3) preservation of alveolar socket 4) regenerative endodontics. Manual search were performed on Journal of Periodontology, Journal of Clinical Periodontology, Journal of Periodontal Research, and International Journal of Periodontics & Restorative Dentistry. The studies with case reports, case series and studies without control were excluded.

Study characteristics

Regenerative potential of PRF was determined in clinical dentistry. Studies with intrabony probing pocket depth (PPD) and clinical attachment levels(CAL) were evaluated. For studies dealing with gingival recession root coverage was calculated. Studies evaluated PRF in alveolar socket preservation and endodontics, bone density and healing of pulpal tissue was compared.

Screening method

Articles were screened and the screening was based on question whether Platelet rich fibrin helps in regeneration and repair in various dental procedures? Whether I-PRF plays better role in regenerative dentistry compared to PRF?

Data extraction and analysis

The following data such as author and year of publication, type of defect, number of patients, primary outcome measures and treatment groups were extracted. Metaanalysis were not performed due to size of the study and many treatment procedures were compared using PRF, instead data is reported in separate tables in systematic fashion and discussed accordingly.

Results

Search outcomes: In total, 1881 articles were extracted and separated accordingly in to intrabony defects, gingival recession, extraction socket and pulpal regeneration (Figure 1). In total 57 articles were selected for further evaluation. This article aims to substantiate the role of PRF in treating regenerative dentistry based on published studies. Also outcome of i-PRF in treating various dental procedures.

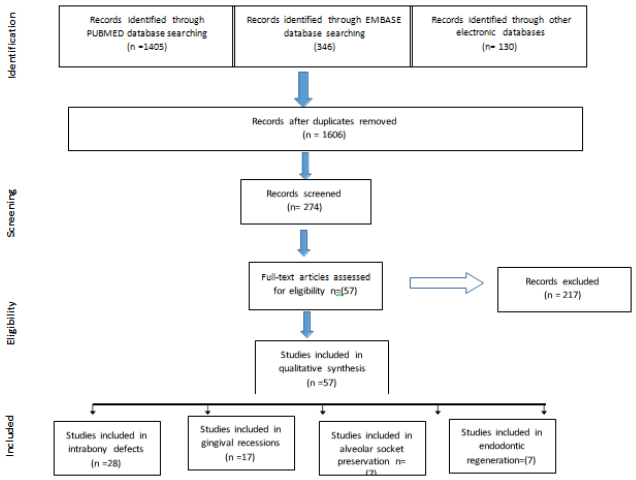


Figure 1: Flow chart showing relevant studies screened for systematic review

Intrabony defect regeneration with PRF[17-44]

PRF has been used mainly for reconstructive surgery in intrabony defects. To date, twenty- eight articles (Table 1) have been published comparing PRF with other techniques in treating intrabony defects. The studies compared PRF with OFD, bone graft, bone grafts versus bone graft+ PRF, PRF with nano-hydroxyapatite. Out of this 14 studies compared the use of PRF as an alternate to OFD. They showed a drastic reduction in PD, improvement in CAL gain and statistically significant when PRF was filled in addition to OFD in intrabony defects. When bone graft versus PRF was evaluated in five studies, there were no Statistical significant results better than PRF. Bone graft versus bone graft + PRF was evaluated in six studies and found PD and CAL gain in two studies compared to BG alone while reaming 4 studies shows Statistical difference. Also, few studies compared PRF versus collagen barrier, PRP versus PRF, EMD versus PRF, EMD versus EMDT+PRF and the outcome were not statically significant and in a few studies, no difference was observed. Also, few studies compared PRF with metformin, bisphosphonates and

static and there was a statistically significant advantage in PD reduction, and CAL gain. Of all above- mentioned studies PRF was found to show the reduction of PD and CAL gain. Till now there is no single study to pervade histological findings to evince actual histological periodontal regeneration in human subjects. Also, it is well established that PRF esteem soft tissue healing when compared to hard tissue. Periodontitis not only occurs because of PDL breakdown but it also occurs due to Cementum, alveolar bone. Hence the regenerative potential of PRF in each of these structures needs to be evaluated histologically to substantiate the role of PRF.

Table 1: Effects of PRF on intrabony defect

Authors	Study design+ follow -up	Number of participants	Groups	Bone defect type	Results
Pradeep and sharma[17] et al(2011)	RCT(parallel) 9 months	42	C: 28, OFD T: 28, OFD + PRF	3 walls	PD reduction greater, CALgain.
Thorat[18] et al. (2011	RCT(parallel) 9months	32	C: 16, OFD T: 16, OFD + PRF	2 and 3 walls	PD reduction, CAL gain followed by more bone defect fill in areas treatedwith PRF.
Rosamma[19]etal. (2012)	CT (split- mouth) 12months	15	C: 15, OFD T: 15, OFD + PRF	2 and 3 walls	Combined use of PRF and OFD better results
Pradeep[20] et al. (2012)	RCT (parallel) 9 months	54	C: 17, OFD T1: 17, OFD + PRP T2: 16, OFD +PRF	3 walls	There was similar PD reduction, CAL gain, and BF at sites treated with PRF or PRP with conventional OFD
Bansal and Bharti[21] (2013)	RCT (split- mouth) 6 months	10	C: 10, OFD + DFDBA T: 10, OFD + DFDBA + PRF	Not reported	PRF showed ,marked reduction in when combined with DFDBA
Gupta[22] et al. (2014)	RCT (parallel) 6 months	30	C: 22, OFD + EMD T: 22, OFD +PRF	3 walls	Both EMD and PRF were effective in the regeneration of IBDs
Ajwani[23] et al. (2015)	RCT (split- mouth) 9 months	20	C: 20, OFD T: 20, OFD + PRF	2 and 3 walls	More areas of bone defect fill when used with PRF and OFD
Mathur [24]et al.	RCT (parallel) 6	25	C: 19, OFD +ABG	2 and 3	Both methods were found

(2015)	months		T: 19, OFD +PRF	walls	to be effective
Shah[25] et al.(2015)	RCT(split- mouth) 6 months	20	C: 20, OFD+ DFDBA T: 20, OFD +PRF	2 and 3 walls	After 6 months PRF showed considerable results and was comparable with DFDBA

Elgendy and Abo [26] (2015)	RCT (split-mouth) 6 months	20	C: 20, OFD +HA T: 20, OFD + HA + PRF	NR	Both group showed significant difference in PD reduction and CAL gain.
Pradeep [27]et al. (2015)	RCT (parallel) 9 months	120	C: 30, OFD T1: 30, OFD + 1% MF T2: 30, OFD + PRF T3: 30, OFD + 1% MF + PRF	3 walls	PRF + 1% MF group showed promising results than other groups.
Panda[28] et al. (2016)	RCT (split-mouth) 9 months	18	C: 18, OFD +BM T: 18, OFD + BM + PRF	3 walls	PRF group showed improved outcome compared to OFD + BM
Aydemir Turkal[29] et al.(2016)	RCT (split-mouth) 6 months	28	C: 24, OFD +EMD T: 25, OFD + EMD + PRF	1, 2, and 3 walls	PRF use doesn't show any improvement
Kanoriya[30] et al. (2016)	RCT (parallel) 9 months	90	C: 30, OFD T1: 30, OFD +PRF T2: 30, OFD + PRF/1% ALN	3 walls	PRF + 1% ALN for IBD Showed promising outcome.
Martande[31] et al. (2016)	RCT (parallel) 9 months	96	C: 30, OFD T1: 30, OFD +PRF T2: 30, OFD + PRF + 1.2% ATV	3 walls	PRF + 1.2% ATV study showed better outcome compared to OFD + PRF

Pradeep[32] et al. (2016)	RCT (parallel) 9 months	90	C: 30, OFD T1: 30, OFD + PRF T2: 30, OFD + PRF + 1.2% RSV	2 and 3 walls	OFD with RSV (1.2%) and PRF was statistically significant compared to other groups.
Chadwick[33]et al.(2016)	RCT (parallel)6 months	36	C: 19, OFD + DFDBA T: 17, OFD +PRF	2 and 3 walls	Both method similarresults.
Galav[34] et al. (2016)	RCT (split-mouth)9months	20	C: 20, OFD + ABG T: 20, OFD+PRF	2 and 3 walls	Both can be used for bony defects
Agarwal [35]et al. (2016)	RCT(split- m outh) 12 months	30	C: 30, OFD + DFDBA T: 30, OFD+DFDBA/PRF	2 and 3 walls	PRF and DFDBA combination is more effective than DFDBA alone
Yajamanya[36] et al.(2017)	RCT (Parallel)	32	C: 28, OFD T1: 28, OFD + BioGT2: 28, OFD +PRF	2 and 3 walls	PRF and BioG showed improved results compared tp OFD alone
Naqvi [37]et al. (2017)	RCT (split-mouth) 9 months	10	C: 10, OFD + BioG T: 10, OFD +BioG + PRF	2 and 3 walls	Both techniques showed better results.
Sezgin[38] et al. (2017)	RCT (split- mouth) 6 months	15	C: 15, OFD + ABBM T: 15, OFD + ABBM + PRF	2 and 3 walls	Both therapies are effective in the treatment of intrabony defects
Bajaj[39] et al. (2017)	RCT (parallel) 9 months	17	C: 27, OFD T: 27, OFD +PRF	2 and 3 walls	Areas treated with PRF showed greater BF compared to conventionalOFD alone.
Patel[40] et al. (2017)	RCT (split-mouth) 12months	13	C: 13, OFD T: 13, OFD + PRF	2 and 3 walls	PRF can be used as an adjunctive.

Pradeep[41] et al. (2017)	RCT (parallel) 9 months	62	C: 18, OFD T1: 19, OFD +PRF T2: 20, OFD + PRF + HA	3 walls	PRF showed better improvement in intrabony defects.
Thorat[42] et al. (2017)	RCT split-mouth) 12 months	15	C: 15, OFD T: 15, OFD + PRF	3 walls	PRF showed better outcome when used along with OFD.
Bodhare[43] et al. (2019)	RCT (split-mouth) 6 months	20	C: 20, OFD + BioGide T: 20, OFD + BioGide + PRF	2 and 3 walls	PRF along with BioGide showed better results.
Boroka[44] et al.(2021)	RCT(full mouth) 6 months	30	C=15 EMD T= 15 A-PRF	2 and 3 walls	No statistically significant differences were found between the two groups

PPD probing periodontal depth, CAL clinical attachment level, OFD open flap debridement, PRF platelet- rich fibrin, DFDBA demineralized freeze-dried bone allograft, MF metformin, HA hydroxyapatite

Treatment of gingival recession with PRF[45-61]

The apical shift of gingival margin in relevance to cemento-enamel junction area and exposure of root surface is termed as gingival recession. Seventeen studies (Table 2) reported to date comparing PRF with single CAF, CAF+CTG, multiple CAF+ CTG. Four studies compared single coronally advanced flap and leukocyte –PRF with single coronally advanced flap and two studies found no statistical difference between both groups. One study showed a statistically significant increase in root coverage in the CAF+PRF group compared to CAF alone. Areas treated with PRF showed increased healing scores in one study and also keratinized tissue width was found to favour CAF+PRF, compared to PRF alone. Five studies compared single CAF+L-PRF with single CAF+CTG and found higher MRC and KTW gain in CTG group. PRF group showed better healing indexes, good comfort and esthetic score compared to CAF+CTG.

Four studies compared CAF+PRF versus multiple CAF+CTG and three studies with multiple CAF+PRF vs. multiple CAF. Their findings showed marginal gingival thickness and recession were more in L-PRF sites compared to multiple CAF alone, but the difference was not statistically significant. Also, CAF+CTG showed increased MRC and KTW gain and increased GT in areas where L-PRF is used.

Table 2: Effect of PRF on treatment of gingival recession

Author	Study type	Patient no.	Duration	Treatment groups
Jankovic[45] 2012	RCT Split-mouth; Miller class I or II	15	6	CAF + PRF CAF + CTG
Padma[46] 2013	RCT Split-mouth; Miller class I or II	15	1, 3,and 6	CAF + PRF CAF
Eren[47] 2014	RCT Split-mouth; Miller class I or II	22	6	CAF + PRF CAF + CTG
Tunaliota[48] 2015	RCT Split-mouth; Miller class I or II	22	12	CAF + PRF CAF + CTG
Thamaraiselvan[49] 2015	RCT Split-mouth; Miller class I or II	20	3 and 6	CAF + PRF
Gupta[50] 2015	RCT Split-mouth; Miller class I or II	26	3 and 6	CAF CAF + PRF
Keceli[51] 2015	Split-mouth; Miller class I or II	40	3 and 6	CAF + PRF CAF + CTG
Dogan[52] 2015	Split-mouth; Miller class I or II	20	6	CAF + CTG + PRF CAF
Rajaram[53] 2015	Split-mouth; Miller class II	20	12 and 24	CAF + PRF DLSBF DLSBF + PRF
Gupta[54] et al. (2015)	RCT (split-mouth) 6 months miller I or II	26	6 months	CAF (C) CAF + PRF (T)
Agarwal[55] 2016	Split-mouth; Miller class I or II	30	3 and 6	CAF CAF + AM CAF + PRF
Kumar[56] et al. (2017)	RCT (parallel) miller I or II	36	6 months	CAF (C) CAF + CTG (T1)CAF + PRF (T2)
Mufti[57] et al. (2017)	RCT (parallel) miller I	32	6 months	CAF + CTG (C) CAF + PRF (T)
Öncü[58] (2017)	RCT (split-mouth) miller I or II	30	6 months	CAF + CTG (C) CAF + PRF (T)
Culhaoglu[59] et al. (2018)	RCT (parallel) miller I	22	6 months	CAF + CTG (C)CAF + PRF (T)
Dixit [60]et al. (2018)	RCT (parallel) miller I or II	12	6 months	CAF (C) CAF + PRF (T)

Kuka[61] et al. (2018)	RCT (parallel) miller I	24	12 months	CAF (C) CAF + PRF (T)

RCT, randomized clinical trial; C, control group; T, test group; CAF, coronally advanced flap; PRF, platelet-rich fibrin; CTG, connective tissue graft.

Role of PRF in socket preservation[62-68]

Alveolar ridge preservation is needed to maintain the hard and soft tissues of the socket after the extraction of teeth. There are several techniques used to preserve extraction sockets such as autografts, allografts, alloplast, xenografts. However placement of graft instigate bone formation still, it has high chances of infection and also it degrades slowly, thereby affecting the healing of hard and soft tissue in the extraction socket. Recent studies have shown PRF promotes better healing and regeneration of hard and soft tissue in alveolar sockets. However, the use of PRF in alveolar ridge preservation remains controversial. Seven studies (Table 3) have been conducted to estimate the role of PRF in alveolar ridge preservation. Two studies evaluated alveolar osteitis in which two patients had alveolar osteitis (1 in control and 1 in the PRF group) two studies recorded soft tissue healing by assessing dimension with a periodontal probe, healing was better in PRF but the difference was not significant. In another study, clinical data showed statically differences between PRF and control groups. Two studies measured mesial and distal bone height changes and found an equal distribution of sockets in both PRF and control groups. Two studies compared bone density and found a statistically significant difference between PRF and the control groups. Though only a few studies are reported in the literature, PRF was found to show better healing of alveolar sockets. Hence it can be used as an ideal material after extraction for improving bone healing/ regeneration to observe the bone density.

Table 3: Effect of PRF on alveolar socket preservation

Authors	Study design and Duration	Number of participants	Intervention
Hauser[62] et al (2013)	RCT Parallel-8weeks	17	PRF (9) Non-PRF (8)
Suttapreyasri and Leepong[63] (2013)	RCT Split-mouth- 8weeks	8	PRF (10) Non-PRF (10)
Marenzi [64]et al(2015)	RCT Split-mouth-7 days	26	PRF (54) Non-PRF (54)
Das [65] et al (2016)	RCT Parallel- 6 months	26	PRF (15) Beta-tricalcium phosphate with collagen (15)
Thakkar[66] et al (2016)	RCT Parallel- 3 and 6 months	36	PRF + DFDBA (18) DFDBA (18)
Temmerman[67] et al(2016)	RCT Split-mouth-3 months	22	PRF (22) Non-PRF (22)
Alzahrani[68] et al (2017)	RCT Parallel-8 weeks	24	PRF (12) Non-PRF (12)

RCT: Randomized controlled trial: PRF plasma rich fibrin

PRF in regenerative endodontics

Regenerative endodontics in the regeneration of pulp tissues, that are damaged by infection, trauma or developmental anomalies. In recent years usage of platelet concentrates as scaffolds found to show promising results clinically and radiographically. Till now five studies have conducted RCT in evaluating the role of PRF in pulpal regeneration.

Shivashankar[69] et al conducted a triple-blind randomized clinical trial on teeth with necrotic pulp to and open apex to predict the effect of PRF, PRF and inducing bleeding. They concluded that PRP was better compared to PRF.

Mittal[70] et al conducted RCT to compare the regaining pulp sensibility in mature necrotic teeth by using periapical bleeding, PRF, collagen and hydroxyapatite. They concluded that the PRF group showed more formation of vital pulp-like tissues compared to other groups.

Rizk [71]et al conducted RCT to evaluate regeneration of necrotic teeth using blood clot and PRF and found PRF teeth with significant growth in radiographic root length, width, increased density compared to the blood clot. Ragab[72] et al conducted RCT, to detect the effect of PRF as blood clot scaffold in the revitalization of necrotic immature teeth and they concluded there was no significant difference between the two groups. Dhiman[73] et al conducted RCT to evaluate the healing potential of PRF in periapical surgeries without PRF and stated both groups showed the same result except PD reduction was more in the PRF group.

Discussion

In this systematic review, randomized clinical studies using PRF in intrabony defect, gingival recession, endodontic regeneration and alveolar socket preservation were discussed. The aim was to evaluate the result of PRF compared to other techniques in regenerative dentistry also, whether i-PRF plays better role compared to PRF used commonly in regenerative dentistry. When the implementation of i-PRF in dentistry was observed, it manifests amended success of periodontal therapy, gingival recession, intrabony and furcation defect. It is prepared easily and delivered conveniently, due to its liquid or polymerized form74. When analyased for articles, to evaluate the role of i-PRF with other techniques, till now very sparse literature evidence have been reported and its role remain unexplored in regenerative dentistry, which need to be evaluated in RCT, with other techniques for its virtue. Thus, there arise a need to focus the role of i-PRF in regenerative dentistry in this article. When injectable PRF was compared with PRF, i-PRF was found to be more effective, in osteoblastic cell migration also, play a notable role in inhibition of oral bacteria compared to other PRF, PRP and whole blood. When the denouement of i-PRF on root coverage of free gingival graft was assessed, remarkable effect was achieved in the closure of the root surface. I-PRF was also found to show more keratinized width and reduced gingival recession. Over the past decade the usage of PRF in dentistry is emerging rapidly, still the usage of I-PRF is minimal which need to be reconnoiter to gauge the role of i-PRF in dentistry.74 For periodontal regeneration shreds of evidence from literature states that the formation of blood clots play an important role when free bacterial pathogens are eliminated. The fibrin scaffold in PRF treatment, is inserted into the periodontal pocket which masquerade as stable clot, with increased platelets, leukocytes and growth factors75. Even though usage of PRF in treating intrabony defect is of late, so far 27 RCT

has been evaluated. When PRF is used with other therapeutic modalities, additional use of PRF favours the outcome of intrabony defects. It has been proven before that PRF favours soft tissue healing compared to hard tissue. However the periodontal disease occurs not only due to the breakdown of PD, it also occurs due to damage of the Cementum, alveolar bone and regenerative potential of this tissue are also need to be evaluated. Till now not even a single study had characterized the role of PRF in intrabony defect regeneration histologically, which needs prospect, to further substantiate the role of PRF in periodontal regeneration. In the management and treatment of gingival recession, PRF evince similar effect to CTG. However, the width of keratinized mucosa was the only parameter in which PRF was not statistically significant with CTG. Though CTG is a gold standard, PRF can be used as surrogate in cases of financial restriction, limited donor tissue, also in individuals with higher postoperative morbidity.76 In pertinence to alveolar socket preservation, PRF is used for soft and hard tissue healing. Till now only a few studies have been reported to assess the role of PRF in alveolar socket preservation. Reduction of horizontal ridge dimension is one of the challenging adverse effects after extraction, which affects implant therapy, as PRF help in rapid healing more studies need to be done to endorse its role. Studies that evaluated the role of PRF in the alveolar socket preservation, have reported that effect of PRF varied from none to significantly positive. Also, in socket healing the histomorphometric analysis showed 50% of bone formation with healing of sockets after 8 weeks, whereas in case of diseased socket 16 weeks later bone formation occurred77. However, due to meagre literature evidence, the role of PRF in alveolar socket preservation is still ambiguous. In regenerative endodontic procedures, when PRF was used as a scaffolding material in an infected necrotic tooth, it shows persuasive results. However, manipulation of PRF inside the canal is arduous78. More inquiry is needed to evaluate the therapeutic benefits of PRF in regenerative dentistry. This systematic review elucidate the various role of PRF in dentistry. i-PRF shows convalescent results in clinical dental procedures be on par with PRF, which needs to be further explored. PRF is easy to use, low cost and ideal biomaterial for a variety of surgical procedures in dentistry. The use of PRF in intrabony defect, root coverage in gingival tissue is propitious, still more corroboration is needed appraise its role in socket preservation and regenerative endodontics. However the role of PRF is still indeterminate as more documentation on PRF in hard and soft tissue healing is needed because of less number of RCT, with chances of more bias.

References

1. Singer AJ, Clark RA. Cutaneous wound healing. N Engl J Med. 1999;341:738–746
2. Dangaria SJ, Ito Y, Walker C, Druzinsky R, Luan X, Diekwisch TG (2009) Extracellular matrix-mediated differentiation of periodontal progenitor cells. Differentiation 78:79–90.
3. Hollander A, Macchiarini P, Gordijn B, Birchall M (2009) The first stem cell-based tissue- engineered organ replacement: implications for regenerative medicine and society. Regen Med 4:147– 148
4. Sánchez-González DJ, Méndez-Bolaina E and Trejo-Bahena NI. Platelet-rich plasma peptides: key for regeneration. Int J Pept 2012; 2012: 1–10.
5. Wright JH. The origin and nature of the blood plates. Boston Med Surg J 1906; 154: 643– 645
6. Tözüm TF and Demiralp B. Platelet-rich plasma: a promising innovation in dentistry. J Can Dent Assoc 2003; 69: 664.

7. Choukroun J, Adda F, Schoeffler C, et al. Une opportunité en paro implantologie: le PRF [An opportunity in implantology: The PRF]. Implantodontie 2001; 42: 55–62.
8. Saluja H, Dehane V and Mahindra U. Platelet-rich fibrin: a second generation platelet concentrate and a new friend of oral and maxillofacial surgeons. Ann Maxillofac Surg 2011; 1: 53.
9. Kang YH, Jeon SH, Park JY, Chung JH, Choung YH, Choung HW, Kim ES, Choung PH (2011) Platelet-rich fibrin is a bioscaffold and reservoir of growth factors for tissue regeneration. Tissue Eng A 17:349–359.
10. Castro HC, Ferreira BLA, Nagashima T, Schueler A, Rueff C, Camisasca D, Moreira G, Scovino G, Borges L, Leal M, Filgueira M, Paschoal P, Bernardo V, Bourguinhon S,
11. Rodrigues CR, Santos DO. Plaquetas: ainda um alvo terapêutico. J Bras Patol Med Lab. 2006;42:321–332.
12. Fernández-Delgado N, Hernández-Ramírez P, Forrellat-Barrios M. Platelet functional spectrum: from hemostasis to regenerative medicine. Rev Cubana Hematol Inmunol Hemoter. 2012;28:200–216
13. Laurens N, Koolwijk P, de Maat MP. Fibrin structure and wound healing. J Thromb Haemost. 2006;4:932–93
14. Silver FH, Wang MC, Pins GD. Preparation and use of fibrin glue in surgery. Biomaterials. 1995;16:891–90
15. Borie E, Oliví DG, Orsi IA, Garlet K, Weber B, Beltrán V, Fuentes R. Platelet-rich fibrin application in dentistry: a literature review. Int J Clin Exp Med. 2015 May 15;8(5):7922- 9. PMID: 26221349; PMCID: PMC4509294
16. Dohan DM, Choukroun J, Diss A, Dohan SL, Dohan AJ, Mouhyi J, Gogly B. Platelet-rich fibrin (PRF): a second-generation platelet concentrate. Part I: technological concepts and evolution. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2006;101:e37–44.
17. Deeb MA. Role of Platelet-Rich Fibrin (PRF) and Platelet-Rich Plasma (PRP) in Oro- Facial Tissue Regeneration: A Narrative Review. Journal of Advanced Oral Research. 2020 May;11(1):5-11.
18. Sharma A, Pradeep AR (2011) Treatment of 3-wall intrabony de- fects in patients with chronic periodontitis with autologous platelet- rich fibrin: a randomized controlled clinical trial. Journal of peri-odontology 82:1705–1712.
19. Thorat M, Pradeep AR, Pallavi B (2011) Clinical effect of autolo- gous platelet-rich fibrin in the treatment of intra-bony defects: a controlled clinical trial. Journal of clinical periodontology 38: 925–932.
20. Rosamma Joseph V, Raghunath A and Sharma N (2012) Clinicaleffectiveness of autologous platelet rich fibrin in the management of infrabony periodontal defects. Singapore Dental Journal 33:5–12
21. Pradeep AR, Rao NS, Agarwal E, Bajaj P, Kumari M, Naik SB (2012) Comparative evaluation of autologous platelet-rich fibrinand platelet-rich plasma in the treatment of 3-wall intrabony defectsin chronic periodontitis: a randomized controlled clinical trial. Journal of periodontology 83:1499–1507.
22. Bansal C, Bharti V (2013) Evaluation of efficacy of autologous platelet-rich fibrin with demineralized-freeze dried bone allograftin the treatment of periodontal intrabony defects. Journal of Indian Society of Periodontology 17:361–366.

23. Gupta SJ, Jhingran R, Gupta V, Bains VK, Madan R, Rizvi I (2014) Efficacy of platelet-rich fibrin vs. enamel matrix derivative in thetreatment of periodontal intrabony defects: a clinical and cone beam computed tomography study. Journal of the International Academy of Periodontology 16:86–96.
24. Ajwani H, Shetty S, Gopalakrishnan D, Kathariya R, Kulloli A, Dolas RS, Pradeep AR (2015) Comparative evaluation of platelet- rich fibrin biomaterial and open flap debridement in the treatment oftwo and three wall intrabony defects. J Int Oral Health 7:32–37
25. Mathur A, Bains VK, Gupta V, Jhingran R, Singh GP (2015) Evaluation of intrabony defects treated with platelet-rich fibrin or autogenous bone graft: a comparative analysis. European journal ofdentistry 9:100–108.
26. Shah M, Patel J, Dave D, Shah S (2015) Comparative evaluation of platelet-rich fibrin with demineralized freeze-dried bone allograft in periodontal infrabony defects: a randomized controlled clinical study. Journal of Indian Society of Periodontology 19:56–60.
27. Elgendy EA, Abo Shady TE (2015) Clinical and radiographic eval- uation of nanocrystalline hydroxyapatite with or without platelet-rich fibrin membrane in the treatment of periodontal intrabony de-fects. Journal of Indian Society of Periodontology 19:61–65.
28. Pradeep AR, Nagpal K, Karvekar S, Patnaik K, Naik SB, Guruprasad CN (2015) Platelet- rich fibrin with 1% metformin forthe treatment of intrabony defects in chronic periodontitis: a ran- domized controlled clinical trial. Journal of periodontology 86: 729–737.
29. Panda S, Sankari M, Satpathy A, Jayakumar D, Mozzati M, Mortellaro C, Gallesio G, Taschieri S and Del Fabbro M (2016) Adjunctive effect of autologous platelet-rich fibrin to barrier mem- brane in the treatment of periodontal intrabony defects. The Journal of craniofacial surgery 27:691-696.
30. Aydemir Turkal H, Demirer S, Dolgun A, Keceli HG (2016) Evaluation of the adjunctive effect of platelet-rich fibrin to enamelmatrix derivative in the treatment of intrabony defects. Six-monthresults of a randomized, split-mouth, controlled clinical study. Journal of clinical periodontology 43:955–964.
31. Kanoriya D, Pradeep AR, Singhal S, Garg V, Guruprasad CN (2016) Synergistic approach using platelet-rich fibrin and 1% alendronate for intrabony defect treatment in chronic periodontitis: a randomized clinical trial. Journal of periodontology 87:1427– 1435.
32. Martande SS, Kumari M, Pradeep AR, Singh SP, Suke DK, Guruprasad CN (2016) Platelet-rich fibrin combined with 1.2% atorvastatin for treatment of intrabony defects in chronic periodon- titis: a randomized controlled clinical trial. Journal of periodontol- ogy 87:1039–1046
33. Pradeep AR, Garg V, Kanoriya D, Singhal S (2016) Platelet-rich fibrin with 1.2% rosuvastatin for treatment of intrabony defects in chronic periodontitis: a randomized controlled clinical trial. Journalof periodontology 87:1468–1473.
34. Chadwick JK, Mills MP, Mealey BL (2016) Clinical and radio- graphic evaluation of demineralized freeze-dried bone allograft ver- sus platelet-rich fibrin for the treatment of periodontal intrabonydefects in humans. Journal of periodontology 87:1253–1260.
35. Galav S, Chandrashekar KT, Mishra R, Tripathi V, Agarwal R, Galav A (2016) Comparative evaluation of platelet-rich fibrin andautogenous bone graft for

the treatment of infrabony defects in chronic periodontitis: clinical, radiological, and surgical reentry. Indian journal of dental research : official publication of Indian Society for Dental Research 27:502–507.

36. Agarwal A, Gupta ND, Jain A (2016) Platelet rich fibrin combined with decalcified freeze- dried bone allograft for the treatment of human intrabony periodontal defects: a randomized split mouth clinical trial. Acta odontologica Scandinavica 74:36–43.
37. Yajamanya SR, Chatterjee A, Hussain A, Coutinho A, Das S, Subbaiah S (2017) Bioactive glass versus autologous platelet-rich fibrin for treating periodontal intrabony defects: a comparative clinical study. Journal of Indian Society of Periodontology 21:32–36.
38. Naqvi A, Gopalakrishnan D, Bhasin MT, Sharma N, Haider K, Martande S (2017) Comparative evaluation of bioactive glass puttyand platelet rich fibrin in the treatment of human periodontal intrabony defects: a randomized control trial. Journal of clinical and diagnostic research : JCDR 11:Zc09–Zc13
39. Sezgin Y, Uraz A, Taner IL, Çulhaoğlu R (2017) Effects of platelet- rich fibrin on healing of intrabony defects treated with anorganicbovine bone mineral. Braz Oral Res 31:e15.
40. Bajaj P, Agarwal E, Rao NS, Naik SB, Pradeep AR, Kalra N, Priyanka N, Kumari M (2017) Autologous platelet-rich fibrin in the treatment of 3-wall intrabony defects in aggressive periodonti-tis: a randomized controlled clinical trial. Journal of periodontology88:1186–1191.
41. Patel GK, Gaekwad SS, Gujjari SK, CV S (2017) Platelet-rich fibrin in regeneration of intrabony defects: a randomized controlledtrial. Journal of periodontology 88:1192–1199.
42. Pradeep AR, Bajaj P, Rao NS, Agarwal E, Naik SB (2017) Platelet-rich fibrin combined with a porous hydroxyapatite graft for the treatment of 3-wall intrabony defects in chronic periodontitis: a randomized controlled clinical trial. Journal of periodontology 88: 1288– 1296.
43. Thorat M, Baghele ON, RP S (2017) Adjunctive effect of autolo- gous platelet-rich fibrin in the treatment of intrabony defects in localized aggressive periodontitis patients: a randomized controlledsplit-mouth clinical trial. The International journal of periodontics& restorative dentistry 37:e302–e309
44. Bodhare GH, Kolte AP, Kolte RA, Shirke PY (2019) Clinical andradiographic evaluation and comparison of bioactive bone alloplast morsels when used alone and in combination with platelet-rich fibrin in the treatment of periodontal intrabony defects—a random- ized controlled trial. Journal of periodontology 90:584–594.
45. Bodhare GH, Kolte AP, Kolte RA, Shirke PY (2019) Clinical andradiographic evaluation and comparison of bioactive bone alloplast morsels when used alone and in combination with platelet-rich fibrin in the treatment of periodontal intrabony defects—a random- ized controlled trial. Journal of periodontology 90:584–594.
46. Jankovic S, Aleksic Z, Milinkovic I, Dimitrijevic B (2010) The coronally advanced flap in combination with platelet-rich fibrin (PRF) and enamel matrix derivative in the treatment of gingival recession: a comparative study. Eur J Esthet Dent 5:260–273
47. Padma R, Shilpa A, Kumar PA, Nagasri M, Kumar C, Sreedhar A (2013) A split mouth randomized

controlled study to evaluate the adjunctive effect of platelet-rich fibrin to coronally advanced flap inMiller's class-I and II recession defects. J Indian Soc Periodontol 17:631–636.

48. Eren G, Atilla G (2014) Platelet-rich fibrin in the treatment of lo-calized gingival recessions: a split-mouth randomized clinical trial. Clin Oral Investig 18:1941–1948.
49. Tunali M, Ozdemir H, Arabaciota T, Gurbuzer B, Pikdoken L, Firatli E (2015) Clinical evaluation of autologous platelet-rich fibrin in the treatment of multiple adjacent gingival recession defects: a12-month study. Int J Periodontics Restorative Dent 35:105–114.
50. Thamaraiselvan M, Elavarasu S, Thangakumaran S, Gadagi JS, Arthie T (2015) Comparative clinical evaluation of coronally ad- vanced flap with or without platelet rich fibrin membrane in the treatment of isolated gingival recession. J Indian Soc Periodontol 19:66–71.
51. Gupta S, Banthia R, Singh P, Banthia P, Raje S, Aggarwal N (2015) Clinical evaluation and comparison of the efficacy of coronally advanced flap alone and in combination with platelet rich fibrin membrane in the treatment of Miller class I and II gingival reces- sions. Contemp Clin Dent 6:153–160.
52. Keceli HG, Kamak G, Erdemir EO, Evginer MS, Dolgun A (2015) The adjunctive effect of platelet-rich fibrin to connective tissue graftin the treatment of buccal recession defects: results of a randomized, parallel-group controlled trial. J Periodontol 86:1221–1230
53. Dohan Ehrenfest DM, Pinto NR, Pereda A, Jimenez P, Corso MD,Kang BS, Nally M, Lanata N, Wang HL, Quirynen M (2018) The impact of the centrifuge characteristics and centrifugation protocolson the cells, growth factors, and fibrin architecture of a leukocyteand platelet-rich fibrin (L-PRF) clot and membrane. Platelets 29:171–184
54. Rajaram V, Thyegarajan R, Balachandran A, Aari G, Kanakamedala A (2015) Platelet rich fibrin in double lateral sliding bridge flap procedure for gingival recession coverage: an original study. J Indian Soc Periodontol 19:665–670.
55. Gupta S, Banthia R, Singh P, Banthia P, Raje S, Aggarwal N (2015) Clinical evaluation and comparison of the efficacy of coronally advanced flap alone and in combination with platelet rich fibrin membrane in the treatment of Miller class I and II gingival reces- sions. Contemp Clin Dent 6:153–160.
56. Agarwal SK, Jhingran R, Bains VK, Srivastava R, Madan R, Rizvi I (2016) Patient-centered evaluation of microsurgical managementof gingival recession using coronally advanced flap with platelet-rich fibrin or amnion membrane: a comparative analysis. Eur J Dent10:121–133.
57. Kumar A, Bains VK, Jhingran R, Srivastava R, Madan R, Rizvi I(2017) Patient-centered microsurgical management of gingival re- cession using coronally advanced flap with either platelet-rich fibrin or connective tissue graft: a comparative analysis. Contemp Clin Dent 8:293–304.
58. Mufti S, Dadawala SM, Patel P, Shah M, Dave DH (2017) Comparative evaluation of platelet-rich fibrin with connective tis-sue grafts in the treatment of Miller's class I gingival recessions.Contemp Clin Dent 8:531–537.
59. Oncu E (2017) The use of platelet-rich fibrin versus subepithelialconnective tissue graft in treatment of multiple gingival recessions: a randomized clinical

trial. Int J Periodontics Restorative Dent 37:265–271.

60. Culhaoglu R, Taner L, Guler B (2018) Evaluation of the effect ofdose-dependent platelet- rich fibrin membrane on treatment of gingival recession RCT J ApplOral Sci 26:e20170278
61. Dixit N, Lamba AK, Faraz F, Tandon S, Aggarwal K, Ahad A (2018) Root coverage by modified coronally advanced flap withand without platelet-rich fibrin: a clinical study. Indian J Dent Res29:600–604.
62. Kuka S, Ipci SD, Cakar G, Yilmaz S (2018) Clinical evaluation ofcoronally advanced flap with or without platelet-rich fibrin for thetreatment of multiple gingival recessions. Clin Oral Investig 22: 1551–1558.
63. Hauser F, Gaydarov N, Badoud I, Vazquez L, Bernard JP, Ammann P. Clinical and histological evaluation of postextraction platelet-rich fibrin socket filling: a prospective randomized controlled study. Implant Dent. 2013;22(3):295-303
64. Suttapreyasri S, Leepong N. Influence of platelet-rich fibrin on alveolar ridge preservation. J Craniofac Surg. 2013;24(4):1088-1094.
65. Marenzi G, Riccitiello F, Tia M, di Lauro A, Sammartino G. Influence of leukocyte- and platelet-rich fibrin (L-PRF) in the healing of simple postextraction sockets: a split-mouth study. Biomed Res Int. 2015; 2015(1):369273
66. Das S, Jhingran R, Bains VK, Madan R, Srivastava R, Rizvi I. Socket preservation by beta-tricalcium phosphate with collagen compared to plateletrich fibrin: a clinico- radiographic study. Eur J Dent. 2016;10(2):264-276.
67. Thakkar DJ, Deshpande NC, Dave DH, Narayankar SD. A comparative evaluation of extraction socket preservation with demineralized freeze-dried bone allograft alone and along with platelet-rich fibrin: a clinical and radiographic study. Contemp Clin Dent. 2016;7(3):371-376
68. Temmerman A, Vandessel J, Castro A, et al. The use of leucocyte and platelet-rich fibrin in socket management and ridge preservation: a split-mouth, randomized, controlled clinical trial. J Clin Periodontol. 2016;43(11): 990-999.
69. Alzahrani AA, Murriky A, Shafik S. Influence of platelet rich fibrin on post-extraction socket healing: a clinical and radiographic study. Saudi Dent J. 2017;29(4): 149-155.
70. Shivashankar VY, Johns DA, Maroli RK, Sekar M, Chandrasekaran R, Karthikeyan S et al. Comparison of the effect of PRP, PRF and induced bleeding in the revascularization of teeth with necrotic pulp and open apex: a triple blind randomized clinical trial. Journal of Clinical and Diagnostic Research: JCDR. 2017; 11(6):ZC34
71. Mittal N, Parashar V. Regenerative Evaluation of Immature Roots using PRF and Artificial Scaffolds in Necrotic Permanent Teeth: A Clinical Study. The journal of contemporary dental practice. 2019; 20(6):720-6
72. Rizk HM, Al-Deen MS, Emam AA. Comparative evaluation of Platelet Rich Plasma (PRP) versus Platelet Rich Fibrin (PRF) scaffolds in regenerative endodontic treatment of immature necrotic permanent maxillary central incisors: A double blinded randomized controlled trial. The Saudi Dental Journal. 2020 Jul 1;32(5):224-31.
73. Ragab RA, Lattif AE, Dokky NA. Comparative study between revitalization of necrotic immature permanent anterior teeth with and without platelet

rich fibrin: a randomized controlled trial. Journal of Clinical Pediatric Dentistry. 2019;43(2):78-85.

74. Dhiman M, Kumar S, Duhan J, Sangwan P, Tewari S. Effect of platelet-rich fibrin on healing of apicomarginal defects: a randomized controlled trial. Journal of endodontics. 2015 Jul 1;41(7):985-91.
75. Agrawal DR, Jaiswal PG. Injectable Platelet Rich Fibrin (i-PRF): A Gem in Dentistry. Int J Cur Res Rev| Vol. 2020 Nov;12(21):25.
76. Miron RJ, Moraschini V, Fujioka-Kobayashi M, Zhang Y, Kawase T, Cosgarea R, Jepsen S, Bishara M, Canullo L, Shirakata Y, Gruber R, Ferenc D, Calasans-Maia MD, Wang HL, Sculean A. Use of platelet-rich fibrin for the treatment of periodontal intrabony defects: a systematic review and meta-analysis. Clin Oral Investig. 2021 May;25(5):2461-2478.
77. Miron RJ, Moraschini V, Del Fabbro M, Piattelli A, Fujioka-Kobayashi M, Zhang Y, Saulacic N, Schaller B, Kawase T, Cosgarea R, Jepsen S. Use of platelet-rich fibrin for the treatment of gingival recessions: a systematic review and meta-analysis. Clinical oral investigations. 2020 Jun 26:1-5.
78. Pan J, Xu Q, Hou J, Wu Y, Liu Y, Li R, Pan Y, Zhang D. Effect of platelet-rich fibrin on alveolar ridge preservation: A systematic review. The Journal of the American Dental Association. 2019 Sep 1;150(9):766-78.
79. Kim SG, Malek M, Sigurdsson A, Lin LM, Kahler B. Regenerative endodontics: a comprehensive review. International endodontic journal. 2018 Dec;51(12):1367-88.