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PLASMA RICH FIBRIN IN TREATMENT OF GRADE 2 FURCATION MANAGEMENT – A SYSTEMATIC REVIEW

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Abstract:Furcation involvement is defined as bone resorption and attachment loss in the bifurcation and trifurcation of multirooted teeth that results from plaque associated periodontal disease. Prevention of periodontal disease progression along with lost periodontal tissues regeneration forms the main goal of periodontal treatment. Platelet-rich fibrin (PRF), is a second-generation platelet concentrate incorporates platelets and growth factors within fibrin membranes. In recent times platelet rich fibrin plays a important role periodontal regeneration. The aim of this review is to systematically evaluate the clinical efficacy of platelet rich fibrin as an adjunct in the treatment of grade 2 furcation. A systematic search was carried out in electronic database PubMed and google scholar using the key words furcation, bone defect, plasma rich fibrin. Relevant outcomes and data were extracted from the included studies. Following the removal of the duplicate results, the primary search resulted in 33 articles and 21 articles were excluded based on title and abstract. Hence, 12 articles were read completely for eligibility. After exclusion of 4 irrelevant studies, eight articles were included. All were RCT's, two human and six animal studies.

Keywords:PLATELET RICH FIBRIN; FURCATION DEFECTS; PERIODONTAL REGENERATION; BONE DEFECTS.

1. INTRODUCTION:

Furcation involvement is defined as bone resorption and attachment loss in the bifurcation and trifurcation of multirooted teeth that results from plaque associated periodontal disease. The destructive pattern in a furcation involvement varies in different cases and with degree of involvement. A proper knowledge of the anatomy of the furcation area and the tooth morphology is very essential for initiating furcation therapy. The main objective of furcation

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treatment is to eliminate microbial plaque and to establish a proper tooth contour to facilitate self-performed plaque control.Various treatment modalities, have been proposed to improve the prognosis of furcation involvement.

Several classifications have been proposed over the years, based either on the severity of horizontal probing depth into the furcation defect or on the vertical amount of alveolar bone loss within the defect. The most popular classification was developed by Glickman, which divides furcation defects into four grades. Nonsurgical strategies such as scaling and root planning, furcation-plasty, etc. are employed to treat the furcation with Grade I initial involvement which restores the gingival health. Conversely, surgical procedures including regenerative and resective approaches, are performed for the treatment of more advanced lesions, to allow access to the internal complex areas of furcation. The traditional resective approach may negatively affect the prognosis of the treated teeth, however, it is considered as the treatment of choice for grade III and grade IV furcation lesions. Regenerative approaches are aimed at furcation closure by the formation of new bone, PDL and cementum in the involved inter-radicular space. Thorough debridement with adequate instrumentation following surgical exposure of furcation involved area, is one of the earliest and most well-documented treatment protocols to achieve regeneration in grade II furcation lesions.

Choukroun's Platelet-rich fibrin (PRF), a second generation platelet concentrate, is a close congregation of platelets, cytokines, structural glycoproteins, glycanic chains entangled in complex fibrin meshwork that can be used as fibrin membrane enriched with platelets and growth factors (platelet-derived growth factor (PDGF) and TGF- β). The significant slow persistant release of key growth factors for at least one week and up to 28 days, have well known additive effects on healing process. Numerous beneficial effects are reported such as osteoconductive filling material in sinus-lift procedures, in facial plastic surgery, and multiple gingival recession treatment, bone tissue engineering, treatment of mandibular degree II furcation defects.

2. PRIMARY OBJECTIVE QUESTION:

To review current literature, analyse the adjunctive effect of platelet rich fibrin in grade 2 furcation management both qualitatively and quantitatively.

2.1. CRITERIA FOR SELECTION OF STUDIES:

The **inclusion criteria** for this study were:

1) articles published from 2015-2019,
2) original studies published in English language,
3) animal and human studies,
4) cell culture studies.
5) interventional studies

The **exclusion criteria** for the study were

1) historic reviews,
2) letter to the editor,
3) case series and reports,
4) non clinical trials.

2.2. SEARCH METHODOLOGY:

An electronic database was carried out using the keywords 'furcation' and 'platelet rich fibrin' via the PubMed/Medline and Cochrane databases for relevant articles published from 2009 to 2019.

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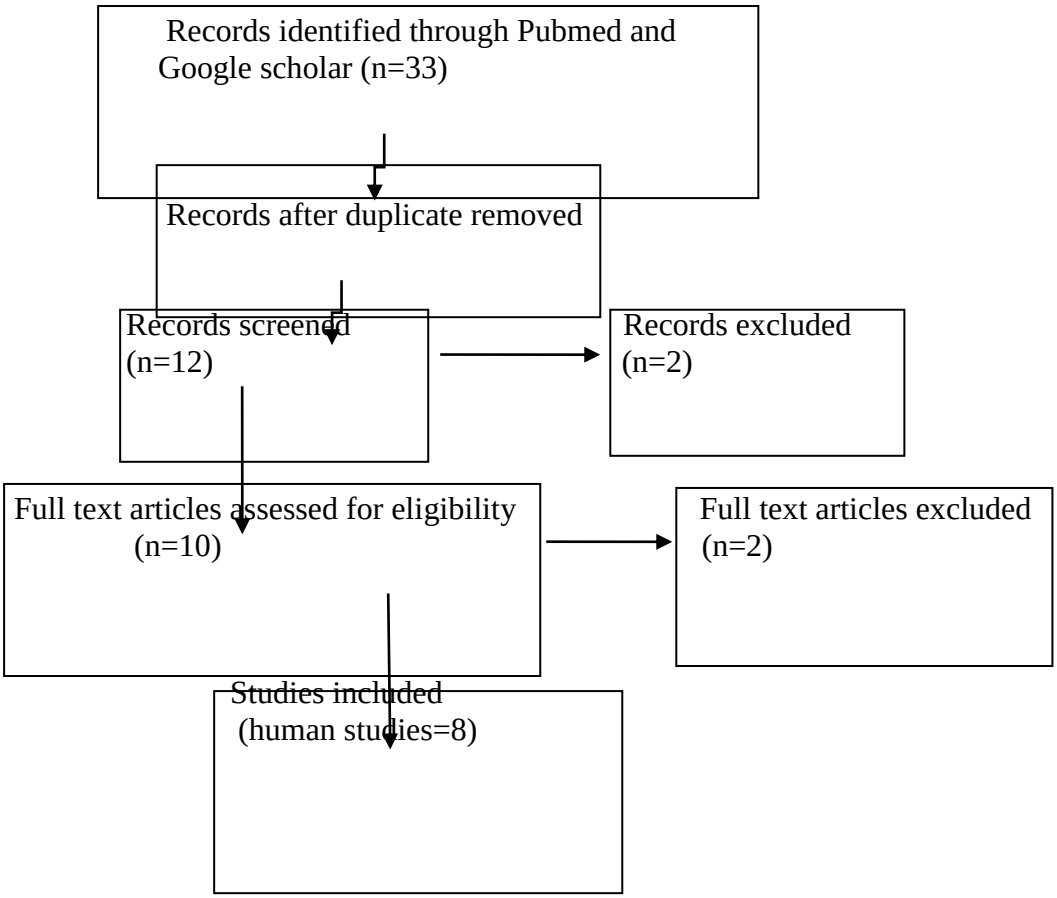

Table 1. General characteristic features of human studies

STUDY AUTHOR AND YEAR	STUDY DESIGN	NUMBER OF PATIENTS	GENDER	AGE/ MEAN/ RANGE	STUDY ANALYSIS	CONCLUSION AND OUTCOME
A R Pradeep et al, 2015	A Randomized control study	136	68-male 68-female	Mean age - 41 years	Group 1-34 sites treated with open flap debridement Group 2-34 sites treated with open flap debridement with autologous PRF Group 3-34	There was a greater improvement in clinical parameters elucidated by greater PD reduction & RAL gain and greater radiographic defect depth reduction in

					sites treated with open flap debridement with 1% metformin gel Group 4-34 sites treated with open flap debridement with autologous PRF and 1% metformin gel	PRF+ 1% MF group as compared to MF alone, PRF alone and OFD groups thus suggesting combined potential effect of PRF and MF in periodontal regeneration.
A R Pradeep et al, 2015	A randomized control study	110	60-male 50-female	25-55years	Group 1-OFD + Placebo gel. Group 2-PRF+HA with OFD. Group 3-RSV 1.2mg gel+ PRF+ HA with OFD.	Treatment of furcation defects with RSV 1.2mg in situ gel combined with autologous PRF and porus-HA bone graft, results in significant improvements of clinical and radiographic parameters
AlaaMoustafaAttia, 2015	Clinical and radiographic study	18	6-females 12-males	41.7 years	Group 1: Naanocrystalline hydroxyapatite Group 2: NcHA with PRF	PRF combined with NcHA bone graft resulted in clinically, radiographically and statistically significant compared with NcHA bone graft alone.

DharmendraKanoriya, 2016	A randomized control study	72	36-male 36-female	Mean age - 38 years	Group 1- Seventy two mandibular molar furcation defects were treated with either access therapy alone. Group 2- Access therapy with PRF. Group 3- Access therapy with PRF+1% ALN.	Furcation defects treatment with autologous PRF combined with 1% ALN gel results in significant therapeutic outcomes when compared with PRF and access thrapy alone.
Hima S Loh et al, 2017	Clinical and radiographic study	16	4-females 12-males	25-65 years	Group 1: BCCG Group 2: BCCG + PRF	The present study favors the adjunctive use of PRF with BCCG over BCCG alone in the management of mandibular Class II furcation defects. Currently, there is sparse evidence to support the use of PRF with bone graft in the management of periodontal osseous defects in general and

						furcation defects in particular
Neetu Rani et al, 2018		20	Irrespective of sex	25-50 years	Group 1: A total of 20 mandibular Grade II furcation defects sites were assigned in the study and treated with either β‑ TCP alone Group 2: β‑ TCP with PRF membrane.	PRF has enormous potential for surgical wound healing. PRF + bone graft has been shown to be an effective regenerative material in the management of Grade II furcation, displaying a greater reduction in vertical and HDD and gain in clinical attachments.
AravindaBasireddy et al, 2018	Clinical and radiographic study	14	-	30-50 years	Group 1: Demineralised freeze dried bone allograft alone. Group 2: DFDBA and PRF	The addition of PRF to DFDBA seems to favor soft‑ tissue healing but did not affect the bone fill
DhruvBipinchandra Mehta, 2018	A randomized control study	15	-	-	Group 1: DFDBA and PRF Group 2: DFDBA and collagen	Both the PRF as a membrane and collagen membrane in combination with DFDBA has shown promising

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						results in themanagement of furcation.

OFD- OPEN FLAP DEBRIDEMENT; PRF- PLATELET RICH FIBRIN; HA- HYDROXYAPATITE; RSV- ROSUVASTATIN; β‾ TCP- β TRICALCIUM PHOSPHATE; NcHA- NAANOCRYSTALLINE HYDROXYAPATITE; DFDBA- DEMINERALISED FREEZE DRIED BONE ALLOGRAFT; BCCG- BIOACTIVE CERAMIC COMPOSITE GRANULES

Table 2: Mean changes and clinical parameters reported by selected studies.

STUDY AUTHOR	FOLLOW UP	GROUP	PI	mSBI	PD (mm)	RAL (mm)	RVAL (mm)	RHAL (mm)	IBD (mm)	GML (mm)
A R Pradeep et al, 2015	BASELINE	GROUP 1	9	11	8.766 ±1.040	7.76± 0.935	N/A	N/A	5.26± 0.348	1.63± 0.132
		GROUP 2	11	10			N/A	N/A		
		GROUP 3	10	11	8.60± 1.354	7.63± 1.325	N/A	N/A	5.25± 0.323	1.64± 0.150
		GROUP 4	10	9	8.50± 1.252	7.50± 1.252	N/A	N/A	5.25± 0.309	1.64± 0.122
					8.60± 1.220	7.60± 1.22			5.260 ±0.304	1.64± 0.127
	9 MONTHS	GROUP 1	17	16	5.76± 1.040	4.80± 0.961	N/A	N/A	4.76± 0.106	1.70± 0.147
		GROUP 2	9	8	4.60± 1.354	3.60± 1.354	N/A	N/A	2.71± 0.067	1.36± 0.118
		GROUP 3	9	8	4.56± 1.356	3.56± 1.356	N/A	N/A	2.68± 0.058	1.37± 0.134
		GROUP 4	4	3	3.70± 1.368	2.70± 1.368			2.482 ±0.060	1.31± 0.079
A R	BASELINE	GROUP 1	22.9	28.6	7.34± 0.76	N/A	7.54± 0.56	7.45± 0.50	5.96± 0.15	N/A
			42.9			N/A				N/A
		GR	25.7	42.9	7.65± 1.05	N/A	7.57± 0.50	7.48± 0.61	5.94± 0.13	N/A

Pradeep et al, 2015		OUP 2 GROUP 3		28.6	7.65± 1.05		7.51± 0.50	7.42± 0.60	5.93± 0.15	
	9 MONTHS	GROUP 1 GROUP 2 GROUP 3	25.7 42.9 17.1	28.6 28.6 14.3	5.22± 0.91 3.97± 0.16 3.02± 0.16	N/A N/A N/A	5.71± 0.45 4.25± 0.44 3.34± 0.48	5.82± 0.38 4.51± 0.50 3.37± 0.49	5.36± 0.28 2.69± 0.10 2.25± 0.15	N/A N/A N/A
AlaaMoustafa Attia,2015	BASELINE	GROUP 1 GROUP 2	0.55± 0.057 0.60± 0.033	N/A N/A	5.66± 0.437 5.53± 0.464	N/A N/A	7.16± 0.491 7.01± 0.584	9.58± 0.454 9.53± 0.460	N/A N/A	N/A N/A
	6 MONTHS	GROUP 1 GROUP 2	0.49± 0.035 0.52± 0.028	N/A N/A	4.66± 0.437 4.19± 0.136	N/A N/A	4.72± 0.325 4.58± 0.392	6.91± 0.827 6.57± 0.639	N/A N/A	N/A N/A
	12 MONTHS	GROUP 1 GROUP 2	0.56± 0.059 0.55± 0.044	N/A N/A	3.66± 0.405 3.54± 0.287	N/A N/A	3.78 ± 0.51 3.58± 0.516	7.24± 0.284 6.93± 0.432	N/A N/A	N/A N/A
DharmendraKanoriya, 2016	BASELINE	GROUP 1 GROUP 2 GR	11 10 12	10 11 14	7.66± 1.27 7.73± 1.35 7.52± 1.22	N/A N/A N/A	7.41± 0.92 7.56± 0.94 7.52± 0.91	7.08± 0.82 7.13± 0.75 7.16± 1.02	5.09± 0.31 5.23± 0.33 5.22± 0.33	N/A N/A N/A

		OUP 3								
	9 MONTHS	GROUP 1 GROUP 2 GROUP 3	14 12 12	13 10 12	5.25± 1.15 4.04± 0.87 3.12± 0.88	N/A N/A N/A	5.08± 0.88 4.17± 0.83 3.4±0 .57	5.04± 0.80 4.26± 0.81 3.52± 0.65	4.56± 0.29 2.64± 0.14 2.29± 0.17	N/A N/A N/A
Hima S Loh et al, 2017	BASELINE	GROUP 1 GROUP 2	0.59± 0.090 0.61± 0.105	N/A N/A	5.63± 1.41 4.90± 0.57	7.00± 0.93 5.90± 0.88	N/A N/A	N/A N/A	N/A N/A	N/A N/A
	6 MONTHS	GROUP 1 GROUP 2	0.50± 0.064 0.51± 0.072	N/A N/A	2.25± 0.46 2.50± 0.53	4.00± 0.54 4.00± 0.82	N/A N/A	N/A N/A	N/A N/A	N/A N/A
Neetu Rani et al,2018	BASELINE	GROUP 1 GROUP 2	N/A N/A	N/A N/A	5.60± 2.59 6.10± 2.92	6.40± 2.80 7.00± 2.98	N/A N/A	N/A N/A	N/A N/A	0.30± 0.67 0.00± 0.00
	6 MONTHS	GROUP 1 GROUP 2	N/A N/A	N/A N/A	2.10± 0.57 3.30± 1.42	3.60± 2.07 4.00± 2.40	N/A N/A	N/A N/A	N/A N/A	1.00± 0.94 0.40± 0.52
AravindaBasireddy et al, 2018	BASELINE	GROUP 1	N/A N/A	N/A	5.14± 0.363	N/A N/A	10.36 ±1.15	9.907 ±1.43	N/A N/A	5.14± 0.864

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		GROUP 2		N/A	5.21± 0.426		10.29 ±0.82	9.86± 1.791		5.07± 0.829
	6 MONTHS	GROUP 1 GROUP 2	N/A N/A	N/A N/A	2.79± 0.426 2.71± 0.469	N/A N/A	8.57± 1.158 7.93± 0.829	7.57± 1.342 5.29± 0.825	N/A N/A	5.93± 1.072 5.29± 0.825
DhruvBipinchandra Mehta, 2019	BASELINE	GROUP 1 GROUP 2	0.98± 0.2 1.02± 0.3	N/A N/A	5.51± 0.7 5.24± 0.7	11.02 ±0.7 10.75 ±1.1	N/A N/A	N/A N/A	N/A N/A	0.53± 0.63 0.53± 0.74
	3 MONTHS	GROUP 1 GROUP 2	0.58± 0.1 0.56± 0.1	N/A N/A	3.35± 0.5 3.17± 0.5	8.62± 0.5 8.60± 0.6	N/A N/A	N/A N/A	N/A N/A	N/A N/A
	6 MONTHS	GROUP 1 GROUP 2	0.52± 0.1 0.53± 0.1	N/A N/A	3.06± 0.3 2.40± 0.4	8.22± 0.5 7.75± 0.7	N/A N/A	N/A N/A	N/A N/A	N/A N/A

PI- PLAQUE INDEX; mSBI- MEAN SULCUS BLEEDING INDEX; PD-PROBING DEPTH; RAL-RELATIVE ATTACHMENT LOSS; RVAL-RELATIVE VERTICAL ATTACHMENT LOSS; RHAL-- RELATIVE VERTICAL ATTACHMENT LOSS; IBD- INTRABONY DEFECT; GML- GINGIVAL MARGINAL LEVEL

3. RESULTS:

3.1. SEARCH RESULTS:

Following the removal of the duplicate search results, the primary search resulted in 12 articles in total. Two articles wereexcluded based on title and abstract. Hence, remaining ten articleswere read completely for eligibility. After exclusion of another twoirrelevant studies, eight studies(A R Pradeep et al, 2015, A R Pradeep et al, 2015, AlaaMoustafa Attia,2015,DharmendraKanoriya, 2016,Hima S Loh et al, 2017,Neetu Rani et

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al,2018,AravindaBasireddy et al, 2018, DhruvBipinchandra Mehta, 2019) were includedin this review.

3.2. HUMAN STUDIES:

All human studies were randomized control trials (RCTs)trials Number of patients included the studies ranged from 14to 136 in which the number of female subjects ranged from 4 to 68, the number of male subjects ranged from 12 to 68. The age of the patients ranged from 25 to 65 years. In all studies, PRF was used in combination with other treatment modalities. In 2015, Dr.A R Pradeep doneoral flap debridement with PRF in Group 1 and oral flap debridement with 1% MF in Group 2and oral flap debridement + PRF gel + 1%MF in Group 3 and the control group received oral flap debridement only.In the study[2]Test Group 1 received PRF+ HA with OFD, Group 2 received Rosuvastatin 1.2 mg gel+PRF+ HA with OFD and the control group received OFD+ placebo gel.In the study[3] test Group received PRF+Nanocrystalline hydroxyapatite, and the control group received Nanocrystalline hydroxyapatite.In the study[4] Test Group 1 received access therapy with PRF, Group 2 received access therapy + PRF + 1% Alendronate gel and the control group received access therapy alone.In the study[5] the test group was treated with a PRF and bone graft, while in the control group Bioactive Ceramic Composite Granules alone.In the study[6] grade 2 furcation defect treated with β-trcalciumphosphate with PRF or β-trcalcium phosphate alone. In the study[7]the test group was treated with a combination of DFDBA and PRF, while in the control group DFDBA was used alone.In the study[8] the test group was treated with a combination of DFDBA and PRF, while in the control group DFDBA and collagen.

3.3. ASSESSMENT OF PARAMETERS

Clinical parameters like site specific plaque index (PI), modified sulcus bleeding index (mSBI), probing depth (PD), relative attachment level (RAL) and gingival marginal level (GML) were recorded at baseline, before surgery and 9 months postoperatively. Percentage radiographic intra-bony defect depth reduction was evaluated using computer-aided software at baseline and 9 months[1].Clinical and radiological parameters; probing depth (PD), and relative vertical (RVAL) and horizontal (RHAL) attachment levels, intrabony defect depth and percentage defect fill were recorded at baseline and at 9 months postoperatively[2].Clinical parameters include: plaque index (PI), gingival index (GI) vertical probing depth (VPD), relative vertical clinical attachment level (RVCAL) and relative horizontal clinical attachment level (RHCAL) at baseline, 6 months and 12 months after periodontal surgery. The radiographic evaluation of bone defects by measuring the bone density through using of image analysis software[3].Plaque index (PI), modified sulcus bleeding index (mSBI), probing depth (PD), relative vertical attachment level (RVAL) and relative horizontal attachment level (RHAL), intrabony defect depth (IBD) at baseline and 9 months post-operatively were recorded. Radiographically defect fill assessed in percentage was evaluated at baseline before surgery and 9months post therapy[4]. Soft tissue parameters (probing pocket depth and clinical attachment loss), hard tissue parameters (vertical and horizontal depth of furcation defects) and radiographic parameter (radiographic alveolar bone density) were measured at baseline and 6months post-surgery[5].The clinical parameters analyzed were probing pocket depth (PPD), clinical attachment level (CAL), gingival recession (GR), horizontal defect depth (HDD), and vertical defect depth (VDD), recorded baseline and at 6-month re-entry[6]. Clinical parameters such as probing depth, relative vertical clinical attachment level, relative horizontal clinical attachment level (RHCAL), gingival margin level (GML), plaque index, and sulcus bleeding index were measured at baseline and 6 months. Radiographic parameters, such as vertical defect depth, horizontal defect depth and defect fill, were measured using

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cone beam computed tomography, taken at baseline and 6 months[7]. Plaque index, probing depth (PD), relative vertical clinical attachment level (RVCAL),gingival marginal level, and radiographic bone levels were recorded at baseline, 3 months, and 6 months postoperatively[8].

3.4. OUTCOME OF STUDIES:

In study[1]PRF, 1%MF and PRF+1% MF groups showed significant PD reduction and RAL gain than OFD group. Mean PD reduction and mean RAL gain was found to be greater in PRF+1% MF group as compared to PRF alone or MF alone at 9 months. Also PRF+1% MF group sites showed a significantly greater percentage radiographic defect depth reduction as compared to MF alone, PRF alone and OFD at 9 months.In the study[2] Mean PD reduction was greater in PRF+ HA with OFDandRSV 1.2mg gel+ PRF+ HA with OFD than OFD + Placebo gel while mean RVAL and RHAL gain was also found to be greater in PRF+ HA with OFD and RSV 1.2mg gel+ PRF+ HA with OFD compared to OFD + Placebo gel. and RSV 1.2mg gel+ PRF+ HA with OFDcompared to OFD + Placebo gel.In the study[3]At 6months, VPD and RHCAL were significantly increased in NcHAand PRF versus NcHA, while at 12 month; VPD, RVCAL and RHCAL were significantly increased in NcHA and PRF compared to NcHA. In the study[4]Access therapy with PRF+1% ALN. showed greater PD reduction and RVAL and RHAL gain as compared to access therapy alone and access therapy with PRF post-operatively. Moreover, Access therapy with PRF+1% ALN. sites showed a significantly greater percentage radiographic defect fill as compared to access therapy with PRFand access therapy alone at 9 months.In the study[5]Statistically significant improvement was observed in the test group compared to the control group with respect to all the measured parameters.In the study[6]The results of the present study showed that treatment of furcation defects with both PRF+β- TCP and β- TCP alone leads to significant PPD, CAL, GR, HDD, and VDD improvement as compared to baseline values. In the study[7]The intergroup comparison of mean change in the parameters showed, statistically significant difference in RHCAL and GML, and no significant difference in other parameters.In the study[8]Both the groups showed statistically significant outcomes in intragroup comparison from baseline to 3 and 6 months. However, there was no statistical difference between PRF membrane and collagen membrane groups on intergroup comparison.

4. DISCUSSION:

All the studies were reviewed. In 2015, Dr.A R Pradeep,categorized 120 patients with single defects into four treatment group, OFD alone, OFD with PRF, OFD with 1% MF and OFD + PRF+1% MF.Results revealed that there was a significant PD reduction, RAL gain and greater radiographic defect depth reduction, in PRF+ 1% MF group, MF group and PRF group as compared to OFD group[1].

In this study[2]105 mandibular furcation defects were treated either with OFD + Placebo gel (Group 1) or PRF+HA with OFD (Group 2) or RSV 1.2mg gel+PRF+HA with OFD (Group 3). Results revealed that treatment of furcation defects with RSV 1.2mg in situ gel combined with autologous PRF and porus-HA bone graft, results in significant improvements of clinical and radiographic parameters when compared with OFD alone.

In this study[3]Eighteen systemically healthy individuals were presenting at least one class II furcation defect, the defects were treated by NcHA (Group 1) and by NcHA/PRF (Group 2). Results revealed thatthe PRF in combination with NcHA bone graft established clinical advantages further than that done by the NcHA alone.

In this study[4] 72 mandibular molar furcation defects were treated with either access therapy alone (Group 1), access therapy with PRF (Group 2), and access therapy with PRF+1% ALN (Group 3). Results revealed thatthere was greater reduction in PD, and more RVAL and RHAL gain with significant bone defect fill with PRF+1% ALN in degree II furcation defects

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treatment. However, histological assessment to evaluate newly constructed tissues is required to support the findings of this trial in future in this aspect.

In this study[5]Twenty Mandibular Class II furcation defects were treated with PRF and bone graft, or BCCG alone.Results revealed that,adjunctive use of PRF with bone graft may be a more effective treatment modality in the management of mandibular Class II furcation defects when compared to bone graft alone.

In this study[6]A total of 20 mandibular Grade II furcation defects sites were treated with either β‑ TCP alone (Group I) or β‑ TCP with PRF membrane (Group II).Results revealed thatthere is significant improvement in both groups, but the combination of PRF with β‑ TCP allograft led to more favorable improvement in the management of Grade II furcation defect except PPD. Further, studies are necessary to assess the histology of the regenerated tissue and mechanisms to maximize the growth factor delivery while using PRF.

In this study[7] Twenty‑ eight defects in 14 patients with bilateral Degree II mandibular furcation defects whichwas treated by combination of DFDBA and PRF or DFDBA alone.Results revealed that,within the limitations of the present study, PRF seems to favor soft‑ tissue healing but has no additional benefit in bone regeneration when used in combination with DFDBA.

In this study[8] A split‑ mouth study was planned with 18 patients having 2 sites of Grade II furcation defects which was treated by DFDBA + PRF (test group) or DFDBA + collagen (control group)Results revealed that there was a significant reduction of PD, improvement in RVCAL, and defect fill with autogenous PRF as membrane. This indicates its role as a regenerative material in treating furcation defects, which can be used as alternative to other expensive membranes.

2. CONCLUSION:

In conclusion, PRF has shown to be an effective treatment modality in regenerative treatment of grade 2 furcation defects. Platelet rich fibrin may be used as an adjunct to open flap debridement in the management of grade 2 furcation. Further studies are necessary to evaluate the histology of the regenerated tissue using PRF.

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