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Triple Combination Therapy – A 12 Month Case Series

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Abstract: ***The ultimate goal of periodontal therapy is complete regeneration of the periodontal attachment apparatus. The combination of various regenerative biologic agents has recently attracted the interest of researchers in the field of reconstructive periodontal surgery. The role of polypeptide growth factors in periodontal regeneration has been documented through animal and human studies. In the last decade, platelet rich plasma (PRP) has been used for its potential in delivering growth factors in intrabony defects. Platelet-rich-fibrin (PRF) is second generation platelet that has several advantages over the traditionally prepared PRP. 10 patients with chronic Periodontitis presenting grade III furcation involvement were included in the study. The following clinical parameters were evaluated prior to treatment and after 6 and 12 months: vertical probing depth, horizontal probing depth and clinical attachment level at the furcation site. The post operative healing was uneventful in all cases, and no complications were observed throughout the entire study period. At 6 & 12 months, out of the 10 cases in our case series 8 cases only showed complete closure of furcation involvement had occurred and improvement in vertical & horizontal probing depths and gain in clinical attachment level, were as 2 cases showed partial closure and minimal gain in clinical attachment level. The purpose of this case series was to evaluate the effect of combining bonegraft, guided tissue regeneration (GTR) and Platelet rich fibrin (PRF) in the surgical treatment of grade III mandibular furcation involvement. This paper reports the use of triple combination therapy which has been shown to be effective in promoting clinical signs of periodontal regeneration.***

Keywords: regeneration, platelet rich fibrin, guided tissue regeneration, furcation

1. Introduction

Periodontal diseases are among the most prevalent diseases world wide. They are the major causes of tooth loss in adults [1]. The ultimate objective of periodontal therapy is to regenerate tissues lost as a consequence of periodontal disease. Periodontal regeneration can be achieved by surgical debridement with adjunctive root surface or wound conditioning, implantation of bone, bone derivatives and substitutes and placement of barrier membranes for Guided tissue regeneration (GTR) [2] .

One of the greatest challenges in the field of Periodontics continues to be the treatment of multirooted teeth demonstrating interradicular loss of Periodontium. The furcation is an area of complex anatomic morphology that may be difficult or impossible to be debrided by routine periodontal instrumentation. Teeth with furcation involvement undergo more extensive and rapid clinical attachment loss and are lost with greater frequency than are single rooted teeth [3]. Since several therapeutic approaches like conservative, resective or regenerative, are proposed a proper diagnosis of these lesions is demanding [4].

The treatment of mandibular grade III furcation involvements constitutes a challenge for the clinician. Usually treatment of these defects consists of tunnel preparation or root resection. However, both of these treatments involve a risk of complications on a long term basis [5]. The complete closure of the furcation depends on the size of the entrance of the furcation and the height of the defect [6]. The goals of therapy in furcation areas are the same as the goals in all periodontal therapy; arresting the disease process, and ultimately, maintaining the teeth in health and function with appropriate esthetics. Resorbable barriers and bone replacement grafts and more recently, the application of polypeptide growth factors to the surgical wound are some of commonly employed techniques used to promote periodontal regeneration [7]. The use of growth factors (platelet derived growth factors (PDGFs) has recently attracted the attention of periodontal researchers. In the first human study of growth factors, furcation lesions responded more favorably to the application of both platelet-derived growth factor and insulin-like growth factor [8]. Autologous platelet rich plasma is a novel method for obtaining autologous PGFs. Using this platelet preparation in combination with bone graft, Marx et al have shown a bone maturation increase in large human mandibular continuity defects[9].

Platelet rich plasma has become a valuable adjunct in wound healing in dentistry [10]. Post surgically, blood clots initiate the healing and regeneration of hard and soft tissues. PRP (platelet-rich plasma) is a platelet concentrate that has been used widely to accelerate soft tissue and hard tissue healing. Platelet rich fibrin (PRF) belongs to a new generation of platelet concentrates geared to simplified preparation without biochemical blood sampling [11]. This second generation platelet concentrate (PRF) eliminates the risk associated with the use of bovine thrombin. Clinicians and scientists are investigating the use of PRF in dentistry as a way to enhance the body's natural wound healing mechanism.

In this case series the addition of PRF (Platelet-rich-fibrin) to bone graft and GTR has been shown to significantly enhance gain in clinical attachment, decrease in probing depth level in the vertical & horizontal direction and radiographic evidence

of bone fill in furcation defects.

2. Method and Materials

10 patients between 25 – 45 years of age, with a total of 10 mandibular molars with grade III furcation involvement, were selected for the present clinical trail from among patients referred to the Department of Periodontics, Meenakshi Ammal Dental College from the Department of Oral Medicine and Radiology.

Patients were selected on the basis that they had at least one grade III furcation involved mandibular molar associated with gingival inflammation, recession and pocket formation. The degree of furcation involvements of the defects was assessed by using a calibrated probe measuring the clinical vertical probing depth, horizontal probing depth and clinical attachment level. In addition patient selection criteria included: good health, no systemic disease and no systemic use of antibiotics for atleaset 6 months prior to the start of the study.

Following initial examination, treatment planning, and case presentation, each patient was given instructions in proper plaque control measures. In addition they receive basic periodontal therapy, i.e scaling and root planning. Three months after the completion of the basic periodontal therapy, the following clinical assessments were made on the selected mandibular molars with grade III molar furcation defects. Customized light cure occlusal stents were fabricated on the study casts and trimmed to the height of contour to serve as a fixed reference point for VPD, HPD and CAL measurements. One vertical groove was performed in the stent for each furcation that was being measured. This groove corresponds to the measurement site for VPD, HPD and CAL.

3. Case Presentation

In the present case series, on examination, inflammation of the attached gingiva and pain on percussion was present. Grade II mobility was also noted. The tooth had attrition and presented with plaque, calculus and recession which was treated with GIC (Glass Ionomer cement) filling (Fig.1).

Figure 1: Pre-operative view in relation to 36.

Periodontal probing revealed a pocket depth of 8mm and clinical attachment loss of 10mm in relation to 36. Radiographic examination revealed a radiolucency extending till the middle third and also on the furcal aspect of the tooth 36 (Fig 2).

Figure 2: Pre- operative radiograph

Initial phase of treatment included complete scaling and root planning. After one week, the patient was recalled and surgical treatment was planned for the treatment of furcation defect with bone graft, platelet gel (PRF) and GTR membrane.

3.1 PRF Preparation

The advantages of PRF over PRP are its simplified preparation and lack of biochemical handling of the blood. The required quantity of blood is drawn in 10 ml test tubes without an anticoagulant and centrifuged immediately. Blood is centrifuged using a tabletop centrifuge (REMY Laboratories,Chennai,Tamilnadu) at 12 min for 2,700 RPM. The resultant product consists of the following 3 layers (Fig.3):

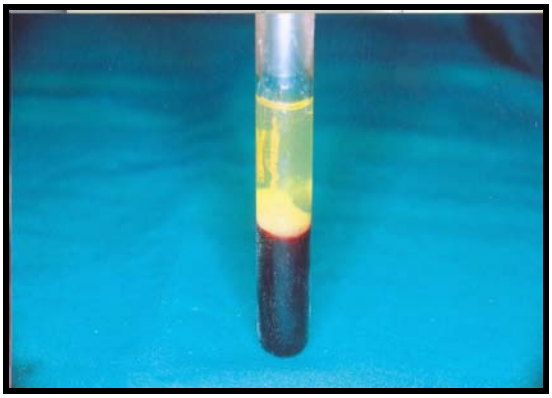


Figure 3: PRF gel

1) Top most layer consisting of acellular PPP(platelet-poor-plasma)
2) PRF clot in the middle
3) RBCs at the bottom (Red blood cell)

PRF can be obtained in the form of a membrane by squeezing out the fluid‘s in the fibrin clot [12].

3.2 Surgical Procedure

The same surgical protocol was involved in this study. After proper isolation of the surgical field, the operative sites were

anaesthetized using 2% xylocaine hydrochloride with adrenaline (1:200000). Crevicular incisions were made using Bard–Parker No.15 blade (Kehar surgical Pvt ltd, Kanpur, India) on the facial and lingual surfaces of each tooth, segment or area involved. A full thickness muco-periosteal flap was reflected using periosteal elevator taking care to preserve the maximum amount of gingival connective tissue in the flap. After exposure, the furcation defect was thoroughly debrided (Fig.4).

Figure 4: Flap reflected & Root planing done in relation to 36

The root surface was then planed and the flap trimmed to remove granulation tissue tags and minimize bleeding. After debridement and pre-suturing bonegraft (periobone-g, top-notch, health care products pvt.ltd, kerala; india) was prepared by mixing with coagulated platelet gel (PRF) preparation in a sterile dappen dish (Fig.5)

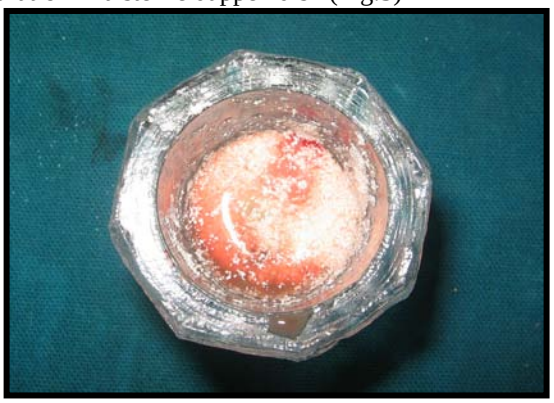


Figure 5: PRF mixed with bone graft (Periobone G).

and placed into the defects to the level of the surrounding bony walls taking care not to over fill (Fig.6).

Figure 6: Bone graft (Periobone-G) placed in relation to 36

It has been suggested that under filling or over filling may be counterproductive because it may preclude proper flap closure, there by retarding healing and possibly resulting in loss of the graft material [13]. Periobone-G is synthetic hydroxyapatite (a calcium phosphate similar in composition to bone and dental mineral) biocompatible and osteoconductive bone repair material [14]. This was followed by placement of guided tissue regeneration membrane[15] (Fig 8).

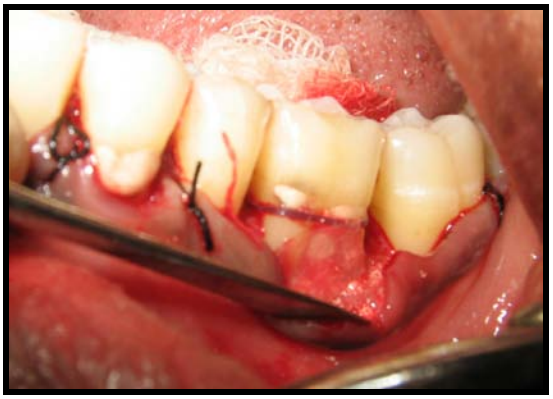


Figure 7: Guided tissue regeneration membrane (Healiguide) in relation to 36.

Healiguide (HEALIGUIDE, ADVANCED BIOTECH PRODUCTS PVT LTD, CHENNAI) is a thin sheet of high purity type I collagen based membrane that is indicated for guided tissue regeneration procedure to enhance regeneration of the bone loss. Resorbable ethicon suture (Resorbable-Braided coated Polyglactin 910, Johnson & Johnson;4-0) was used to stabilize the membrane which was followed by placement of non resorbable ethicon suture (Black braided silk, Johnson & Johnson;4-0), for the closure of the flap.

Figure 8: Sutures placed

The mucoperiosteal flap was replaced and primary wound closure was achieved by means of black silk, 4-0 sutures (Fig.8).

3.3 Post Operative Care

Following surgery the patients were instructed to rinse with a solution of 0.2% Chlorhexidine digluconate three times per day for 6 weeks postoperative. For the same period they were also advised not to brush the operated period area. In addition, all patients received Antibiotics (Amoxycillin 500

mg 3 times a day for 5 days) and Analgesic (Ibuprofen 400mg 3 times a day for 3 days) for 1 week postoperative. The sutures were removed after 2 weeks of healing.

Figure 9: 3 weeks Post operative

Recall appointments were scheduled once in 10 days for the 1st month (fig.9). At every recall appointment oral hygiene was checked and reinforced. Patients were reexamined and radiographs were taken at 6 months

Figure 10: 6 months post operative

and 12months(fig.10 & fig.11). During the follow up periods, the VPD, HPD, and CAL at the treated teeth were recorded.

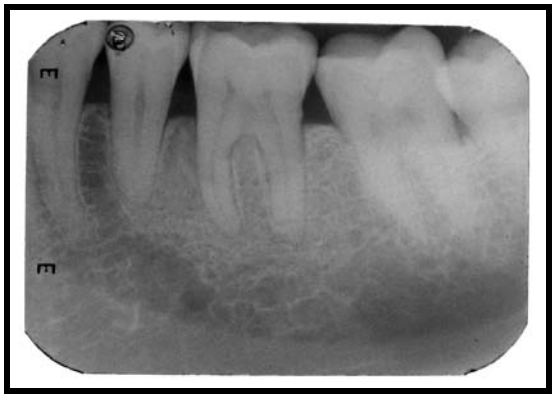


Figure 11:12 months post operative

3.4 Statistical Analysis

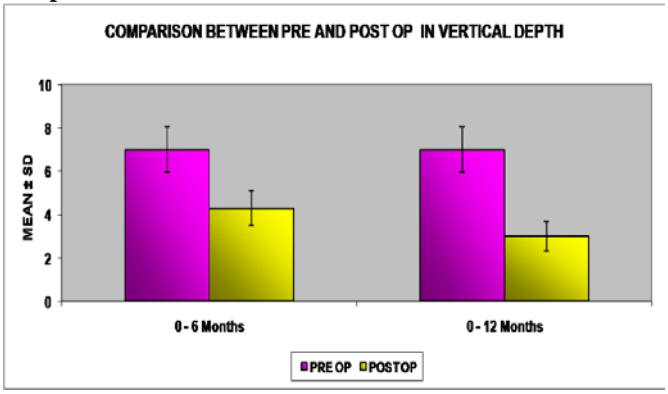
Mean and standard deviation were estimated from the sample for each experimental site. Mean changes were compared against the null hypothesis. Student's paired t-test was employed to test the significance of mean differences between 0-day, 6months and 12months.

3.5 Results

Table 1: Comparison of mean & standard deviation values between pre and post op in VPD

	Group	N	Mean	Std.Deviation	Sig
Vertical Depth - Pre op		10	7.00	1.054	0.03
Vertical Depth - Post op	0-6 Months	10	4.30	.675	0.001
	0-12Months	10	3.00	.816	0.001

Graph:1

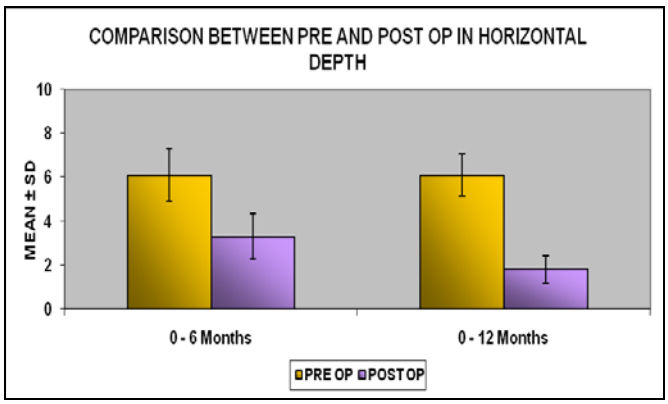


In the present case series for all the defects the mean vertical probing depth (VPD) on 0 day was 7.0±1.0mm which was reduced to 4.3 ±1.0mm and 3.0±0.6mm on 6thmonth and 12thmonth respectively which was statistically significant.

Table 2: Comparison of mean & standard deviation values between Pre and Post Op in HPD

	Group	N	Mean	Std. Deviation	Sig
Horizontal Depth-Pre op		10	6.10	1.197	0.04
Horizontal Depth-Post op	0-6 Months	10	3.3	1.059	.001
	0-12 Months	10	1.80	0.632	.002

Graph: 2

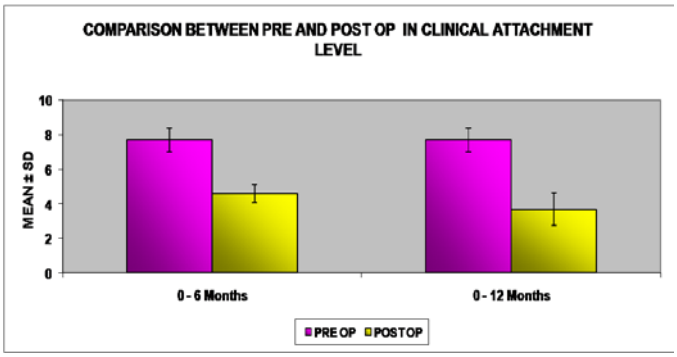


In the present case series for all the defects the mean horizontal probing depth (HPD) on 0 day was 6.1±0.6mm which was reduced to 3.3 ±0.5mm and 1.8±0.9mm on 6th month and 12thmonth respectively which was statistically significant.

Table 3: Comparison of mean & standard deviation values between Pre and Post Op in CAL

	GROUP	N	Mean	Std. Deviation	Sig
Clinical Attachment Level - Pre op		10	7.70	.675	0.21
Clinical Attachment Level - Post op	0 - 6 Months 0 - 12 Months	10 10	4.60 3.70	.516 .949	0.017 0.020

Graph:3



In the present case series for all the defects the mean clinical attachment level (CAL) on 0 day was 7.7±1.1mm. The mean gain in CAL was 4.3±0.8mm and 3.0±0.6mm on 6th month and 12thmonth respectively which was statistically significant.

3.6 Discussion

Periodontal regeneration is a multi factorial process and requires an orchestrated sequence of biological events including cell adhesion, migration, multiplication and differentiation. The classic approach to periodontal regeneration in the last 30 years has been the use of bonegrafts or substitutes to repair periodontal defects. Current understanding of periodontal healing is based on a hypothesis by Melcher, who proposed that the cell type which repopulates the exposed root surface at the periodontal repair site will define the nature of attachment or repair that takes place [11]. The combination of various regenerative biologic agents and techniques has recently attracted the interest of researchers in the field of reconstructive periodontal surgery.

A series of clinical techniques have emerged that permit tissue engineering to be performed for more efficient regeneration and repair of periodontal defects and improved implant site development [12]. The use of bone grafts and bone substitutes, guided tissue regeneration and more recently, the application of polypeptide growth factors to the surgical wound are some of the most commonly employed techniques used to promote periodontal regeneration.

Platelets contain important growth factors that, when secreted, are responsible for increasing collagen production, recruiting other cells to the site of injury, initiating vascular in growth, and inducing cell differentiation[13]. These are all crucial steps in early wound healing. The combination of PRP, bone graft (Periobone-G) and Guided tissue regeneration (Healiguide) has been shown to be effective in promoting clinical signs of periodontal regeneration in intrabony defects in humans. This triple combination therapy for intrabony defects was first described by Obarrio et al [14].

Results obtained from studies have revealed the positive effects of bonegrafts for the treatment of furcation defects especially vertical defect fill. According to Tsao et al additional membrane placement does not seem to enhance the treatment outcome achieved by bonegraft alone [15]. However in this case series due to the magnitude of the lesion a resorbable GTR membrane was placed to support the graft in place and for ideal healing outcome. A critical factor for successful regeneration of grade II and grade III furcation defects following application of the GTR treatment principle is the soft tissue management and complete coverage of the membrane during the healing period.

The regenerative procedures used in these cases include bone grafts and guided tissue regeneration. The bonegraft used in this report was a hydroxyapatite material. It has been shown that porous hydroxyapatite(HA) bone grafting material have excellent bone-conductive properties that permit outrowth of osteogenic cells from existing bone surfaces in to the adjacent bone graft material. Because there were no organic components contained in HA, it does not induce any allergic reaction and is clinically well tolerated [10]. By filling the defect, it also prevents collapse of the soft tissues into the bone defect and, if appropriately porous, facilitates stabilization of the blood clot and ingrowth of new blood vessels [16]

In addition to this PRF which is an autologous source of platelets was used to enhance the results of the regenerative procedure. The use of autologous PRF is said to enhance the wound healing process due to the high concentration of platelets present in it. Because of the absence of an anticoagulant, blood begins to coagulate as soon as it comes in contact with the glass surface. Therefore, for successful preparation of PRF, speedy blood collection and immediate centrifugation, before the clotting cascade is initiated, is absolutely essential. Strayhorn et al [17] suggested that PDGF might act mostly on osteoblastic cell proliferation, exerting most of its effects during the early phases of wound healing. Therefore, there are several ways in which PDGFs may affect all cells involved in periodontal wound healing process.

Results of this clinical trial demonstrate that the functioning of GTR in association with grafting material includes an improved space making effect of the barrier which is conductive to cell events leading to periodontal regeneration and facilitation of mineralized tissue formation due to osteoconductive properties possibly inherent in the graft material [18]. The use of PRF in the form of platelet gel in conjunction with bone grafts, which offers several advantages including promoting healing, bone graft and maturation, graft

stabilization, wound sealing and hemostasis, and improving the handling properties of graft materials. Other treatment modalities that have been used successfully are root resection and hemisection procedures. In an attempt to eliminate the defect and to create access within the interradicular area root resection has been proposed in the literature [19]. Anderegg et al [20] have shown that the vertical component of the defect can predict the extent of osseous repair following regenerative surgery. Although the vertical component in these case series were extensive the lack of mobility and the presence of good bone support on the buccal side were factors that prompted us to make use of regenerative procedures instead of root resection.

Thus we have seen that furcally-involved teeth present unique challenges to the success of periodontal therapy. Anatomical and morphological complicating factors dictate modifications in treatment approaches used for managing these areas. Clearly only closure of the furcation defect should be regarded an end point of therapy. Therefore a thorough surgical assessment of factors increasing the chances to obtain this result seems to be necessary.

In conclusion, the results of this report suggest that use of this triple combination therapy is effective in treating furcation defects. The field of transfusion medicine, as it applies to wound healing and the formation of an autologous platelet gel still is a young scientific field in which many discoveries are yet to be made. Ideal ratios of the components of PRF preparation still are being investigated and more clinical research with long-term results are needed.

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