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Mandibular Degree II Furcation Defect Treatment With 1%Alendronate Gel Alone or In Combination with Platelet-Rich Fibrin

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Abstract

Aims of the study: To evaluate the clinical efficacy of PRF with 1%alendronate gel combination in mandibular degree II furcation defect treatment in comparison with 1%ALN and access therapy alone.

Materials and Methods: Twenty-four mandibular molar furcation defects were treated with either access therapy alone (group 1), access therapy with1% ALN gel (group 2), or access therapy with PRF and 1% ALN (group 3). Plaque index, modified sulcus bleeding index, probing pocket depth (PPD), relative vertical attachment level (RVAL) and relative horizontal attachment level (RHAL), and intrabony defect depth were recorded at baseline and 6 months postoperatively. Radiographically, defect fill , was evaluated at baseline before surgery, and 6months post-therapy.

Results: : Group3 demonstrated significant reduction in PPD , RVAL and RHAL gain in compare to ALN and control groups postopratively .Furthermore, group3 showed greater significant reduction in intrabony defect(1.25±0.49) when compared to group2(0.45±0.17) and group 1(0.16 ±0.5).

Conclusions: The local delivery of 1% ALN gel combined with autologous PRF in Furcation defect treatment showed better clinical parameters outcomes with greater bone defect depth reduction in comparison to 1%ALN and access therapy alone.

Keywords: Alendronate; chronic periodontitis; furcation defects; growth factors; osteoclasts; regeneration.

INTRODUCTION

Periodontal disease of the oral cavity is multifactorial and microorganisms playing a fundamental role in its initiation and pathogenesis, in addition the host immune system activates the inflammatory reaction to the microbial insult which in turn defends and destroys the periodontal tissues[(1)] .In molar teeth, the degree of furcation involvement investigate the severity of attachment loss. The anatomy of furcation area is complex because the presence of many ridges, peaks and depression forming a collection of convexities and concavities, also limited furcation entrance dimension .Thus, represent a clinical challenge for the daily oral hygiene practice and render a thorough cleaning performed with routine instruments very difficult. In addition, the distal position of the molars interfere with adequate self-performed hygiene and implicate a relatively difficult access to professional debridement [(2)] .Many reports in the past has been found the successful treatment of furcation defect with regenerative material such as autogenous grafts, bovine-derived xenografts, demineralized freeze-dried bone allografts (DFDBA) alone or with a barrier membrane [(3-5)].

Various biomimetic agents support an endogenous regenerative therapy such as bone morphogenetic proteins (BMPs), platelet-derived growth factor (PDGF), enamel matrix derivatives (EMDs),platelet concentrates such as platelet rich fibrin (PRF) [(6-8)].Recently applications of platelet-rich products; platelet rich in growth factor (PRGF) and the platelet rich fibrin (PRF), have been proposed as an aid to enhance regeneration of osseous and epithelial tissues in oral surgery. Platelet rich fibrin was developed originally in France by ***Choukroun et al. in 2000,*** it is considered as a second-generation of platelet concentrate and characterized by its fibrin mesh that is enriched with platelets and growth factors, so accelerates physiologic wound healing and new bone formation [(9)].The PRF preparation is a simple protocol made by centrifugation of natural blood without any additives[(10)]. In addition to the biologic mediators, different techniques implicated to enhance the quantity and quality of the bone being regenerated ,one of these agents are bisphosphonates viz. Alendronate (ALN) , chemical analogues of pyrophosphates, which have an affinity to bind to hydroxyapatite crystals and prevent their dissolution. Thus, prevent osteoclastic bone resorption with osteostimulative properties and matrix formation[(11, 12)].

Recently, it has been found that topical use of ALN in experimental periodontitis minimize localized inflammation, helps with tissue regeneration , and increases bone formation in furcation defect . However, its systemic administration for treatment of periodontitis is related with risk of onset of osteonecrosis of the jaw[(13, 14)]. The assessment of reconstruction by clinical parameters is not enough. Besides, since surgical re-entry is invasive ,intraoral periapical radiograph has been recommended for pre and postoperative assessment of intra bony defect of furcation defect [(15)].So that ,taking into account the aforementioned facts that application of PRF combined with 1%ALN may be give up synergistic effect in periodontal regeneration .

MATERIALS AND METHODS:

Patient Selection

A total of 24 systemically healthy patients (21 males and 3 females, aged rang 30 to 55 years; were enrolled from the outpatient section of the Department of Periodontology, in the teaching hospital of College of Dentistery- University of Baghdad , Al-Sadr Specialized Dental Center and Al

kadamia Specialized Dental Center for the purpose of periodontal treatment . The study was carried out from October 2017 to October 2018.

Inclusion Criteria

After etiotorpic phase evaluation (phase I therapy)i.e. scaling and root planning (SRP),patient with degree II furcation defect buccally in vital, asymptomatic mandibular first and second molar with a radiolucent furcation area on an intraoral periapical radiograph and with vertical probing pocket depth ≥5mm and horizontal probing depth ≥3mm were included in this study with no history of periodontal or antibiotic therapy in the last 6 months .

Exclusion criteria

Any patient how were with a history of known systemic disease , under medication known to effect periodontal therapy outcomes, patient with immunodeficiency, smokers ,tobacco chewers ,pregnant and lactating mothers. In addition , patients with non vital teeth and degree II mobile [16] teeth, teeth with extensive gingival recession, poor oral hygiene (plaque index [17] [PI]>1) after phase I therapy were excluded from the study .

Presurgical Therapy

Each patient was subjected to pre-surgical hygiene treatment and measures consisting of a session of oral hygiene instructions, full mouth SRP by using ultrasonic and hand instrumentation was don using local anesthetic solution .after etiotropic phase (3 weeks) Periodontal examination was performed to verify of desired sites for the study. These patients were randomly divided into three groups . Group 1 consisted of 7 sites treated with access therapy, i.e.,open-flap debridement; group 2 consisted of 8 sites treated with access therapy+ 1%ALN gel ; and group 3 included 9 sites treated with access therapy and autologous PRF + 1% ALN gel.

Clinical and Radiographic Measurements

Before surgical procedures performed the patients were evaluated for clinical data which include plaque index [16] (site specific), modified sulcus bleeding index[17] (mSBI), probing pocket depth and relative vertical and horizontal attachment level (RVAL and RHAL). modified acrylic stents with grooves were used to standardize the recorded probe angulation and position prior to the surgery.using Goldman fox periodontal probe for vertical measurement and a Naber's probe (Nordent,Color-Coded Nabors Furcation Probe)for horizontal measurement. All furcation defects were assessed at baseline and at 6 months postoperatively. Furcation fornix to the base of the defect distance was considered for measurement of the furcation defect. The paralleling technique with bite block was used For obtaining standardized radiographs. IBD depth on radiographs was measured using a computer-assisted software program(Sidexis xg plugin).

Preparation of PRF

The method was described for the first time by Dohan et al.[18]PRF preparation method was followed as per the protocol proposed by Choukroun et al. [19] After patient preparation and and before sulcular incision **,** blood collected to prepare the PRF, Rubbing the puncture site with a gauze sprayed by medical alcohol after identifying the appropriate vein for venipuncture (mostly the median cubital vein in the antecubital fossa, 10 mL of autogenous venous blood was collected using 10 mL disposable syringe with needle gauge 21.The obtained blood was immediately transferred to a plain 10 mL blood collecting tube and centrifuged by using 80-1 electric centrifuge machine at 3000 rpm for 10 minutes. At the end of this process, the yellow shiny gelatinous part in the middle of the tube was PRF just between the red corpuscles at the bottom and platelet- poor plasma(PPP) at the top.PRF can easily separate by using using tweezers gently the PRF were pulled out and placed in a sterile wet gauze mesh, scraping the bulk of RBC layer carefully by surgical scalpel leaving the buffy coat intact.

1% ALN Gel Preparation

ALN gel was prepared as described by Reddy et al. [20] to achieve 1% ALN concentration sodium ALN powder dissolved in distal water of required amounts .To this ,a weighed quantity of polyacrylic acid (PAA) 940P (2 wt/wt %)which used as gelling agent was added. Gradually, the mixture was stirred, and PAA was allowed to soak for about 2 hours.PAA was neutralized and formed into a gel by adding (1%)of triethanolamine which adjusted pH to 6.8 and finally Methylparaben(0.1%) and propylparaben(0.05%) were dissolved in ethanol of required amounts and added to the mixture.

Surgical Procedure

Patient's preparation began with wearing surgical head cup then disinfect the perioral skin with a sterile gauze dipped in Povidone iodine 10%, the patients were instructed to rinse the mouth with 0.12% chlorhexidine before the surgical procedure. The surgery was performed under local anesthesia. Intracrevicular incisions were performed on both sides (buccal and lingual)with preserving interdental papilla as possible .Then , a mucoperiosteal flap was reflected to gain adequate access to the furcation defect . after that ultrasonic instruments(woodpecker ® UDS-k(LED)) and area-specific curette (Henry Schein, Gracey) were used to perform defect debridement and root planing thoroughly, no osseous recontouring was attempted. In group 1 (access therapy), only conventional surgery was Performed , without placement of any regenerative material in to furcation defect. In group 2(access therapy + 1%ALN) 1%alendronate gel was injected into the furcation defects using a syringe with a blunt cannula after thorough debridement. In group 3(access therapy + PRF+1%ALN) PRF was mixed with 1% ALN gel in equal amount (1:1) then placed into the furcation defect following debridement. After that remaining PRF compressed ,PRF membrane were trimed and placed over furcation defects to protect(PRF +1% ALN gel)in the furcation defect space.Full thickness flaps were reposioned and fixed by 3/0 silk sutures,Periodontal dressing (COE-PAK) was placed to cover and protect the surgical area.

Postoperative Care and instructions

All patients had received a standard administration of systemic antibiotic postoperatively (500-mg amoxicillin capsules three times daily for 7 days; 500-mg metronidazole tablets three times daily for 7 days) and analgesics (800-mg ibuprofen tablets three times daily) also, applying ice bag extraorally for first 8 hours (applied for 15 min and removed 15 min) after sugery.The postsurgical instructions were: Chlorhexidine mouthwash rinse (0.12%) was prescribed two times daily for 2 weeks , and patients were reinstructed and motivated to brush with a toothbrush having soft bristles and to refrain from chewing hard or sticky foods, brushing treated sites, or using any interdental aids for 1 week and

Measurement after 6 months

All the clinical paremeters were revaluated by the same occlusal stents after 6 months.for hard tissue ,another radiograph for the same oprated site were taken

Statistical Analyses

Analysis of data by using SPSS version 16.0 .The p-value < 0.05 was considered as statistically significant. PLI ,mSBI ,PPD ,RVAL and RHAL presented as mean and standard deviation. The Kruskal Wallis was used for comparison among three independent groups, and the Wilcoxon test was used for comparison between pre and post for each group (paired group) , while Mann-Whitney test was used for the two independent groups .

RESULTS:

Out of 95 evaluated for eligibility, only 34 patients met the inclusion criteria, and 24 patients accomplished the study as 10 among them were not able to follow up. Therefore, only 24 sites (one site per participant) were statistically assessed for clinical and radiographical parameters at baseline and 6-months time intervals. All the three groups showed improvement in PLI and mSBI at 6 months postoperatively ,however, the difference statistically non significant among the groups(Table 1).This indicate that all the participant in the three groups maintained an equivalent oral hygiene during the course of the study .Table 2 depicts mean and SD values for PPD,RVAL,RHAL and IBD parameters at different time interval . P value (<0.05) gives statistical significance among the groups at baseline and 6 months for evaluated parameters.Mean changes in the parameters (baseline to 6 months) are demonstrated in Table 3. Group 3 and group2 treated sites demonstrated a significantly greater PD reduction than control (group 1) at 6 months postoperatively ($p<0.05$). PD reduction was greater in group 3 (2.14±0.95mm) when compared to group 2 (1.31±0.46mm) and group 1 (0.33±0.39mm).Also, group 3 treated sites demonstrated more RVAL and RHAL gain in comparison to the rest groups , the difference being statistically remarkable. RVAL and RHAL gain was dominant in group3 with mean change (1.94±1.23mm, 1.72±0.90mm) when compared to Group 2 (0.92±0.83mm, 0.21±0.39mm) and group 1(0.50±0.44mm, 0.50±1.20 mm).Greater intra bony depth reduction was found in group 3 than group 1 and group 2 at 6 months ($P <0.05$). i.e, statistically significant.

Table (1): Mean±SD of PLI, mSBI at baseline and after 6 months.

Parameters	Visit	Group 1	Group2	Group3	P Value
PLI	B/L	1.16±0.15	1.17±0.19	1.17±0.19	0.99
	6M	1.20±0.35	1.35±0.39	1.18±0.32	0.62
mSBI	B/L	2.10±1.35	2.20±0.80	2.80±1.58	0.72
	6M	1.41±0.73	1.34±0.74	0.73±0.52	0.28

B/L=baseline,M=Months

Table(2): Mean±SD of PPD,RVAL,RHAL and IBD at different time interval .

Parameters	Interval	Group 1	Group2	Group3	*P value*
PPDmm	B/L	4.65±0.69	4.24±0.86	5.04±1.04	0.26
	6M	4.31±0.78	2.92±0.57	2.90±0.40	0.003*
RVALmm	B/L	7.00±0.63	7.00±1.63	7.33±1.22	0.92
	6M	6.66±0.60	5.50±0.1.50	4.88±0.78	0.01*
RHALmm	B/L	7.00±0.40	7.00±0.47	7.33±0.88	0.83
	6M	5.16±0.40	5.42±0.60	5.50±0.93	0.005*
IBDmm	B/L	3.20±1.03	2.50±0.93	3.37±1.10	0.33
	6M	3.21±0.97	2.04±0.87	2.12±1.03	0.10

B/L=baseline,M=Months* Kruskal Wallis test, significant at P <0.05

Table(3): Comparison of mean changes in the PPD, RVAL, RHAL, and IBD Over 6-Month Period Among the study Groups.

parameters	Group1	Group2	Group3	*P Value*	
Mean PPD change (mm)	0.33±0.39	1.31±0.46	2.14±0.95	G1vs G2 G1vs G3 G2 vs G3	0.006* 0.001* 0.03*
Mean RVAL change (mm)	0.50±0.44	0.92±0.83	1.94±1.23	G1vs G2 G1vs G3 G2 vs G3	0.38 0.004* 0.07
Mean RHAL change (mm)	0.50±1.20	0.21±0.39	1.72±0.90	G1vs G2 G1vs G3 G2 vs G3	0.79 0.02* 0.03*
Mean IBD change(mm)	0.16 ±0.5	0.45±0.17	1.25±0.49	G1vs G2 G1vs G3 G2 vs G3	0.002* 0.001* *0.002**

* mann-whitney test. Significant at P <0.05

DISCUSSION

The present in vivo study evaluate the clinical effectiveness of PRF combined with 1% ALN for mandibular degree II furcation defect treatment. The main principles of our study focused on correct soft tissue handling, wound stability, and infection control. PD, RVAL and RHAL, osseous and histologic periodontal regeneration can be used to measure therapeutic outcomes. Although the histological assessment serves as the best method for evaluation , surgical closure of the furcation defect and improvements in PD, RVAL, and RHAL act as suitable and practical result outcomes ***(21)***. Furcation defect treatment represent the greatest challenge to the success of periodontal therapy, as its reduced the efficacy of periodontal therapy and increase the risk of the tooth loss regardless the treatment modality employed .Regenerative therapy might be regarded the ideal treatment for furcation involvement. Current outcomes inward in this study revealed that that furcation defect sites treated with PRF + 1% ALN (group 3) and ALN (group 2) resulted in marked reduction of PD (2.14±0.95mm, 1.31±0.46 mm respectively)and significant reduction in IBD depth (1.25±0.49mm, 0.45±0.17 mm respectively) . The difference was statistically significant when compared with sites that treated with conventional periodontal flap surgery alone **.** Besides that , group 3 showed significant gain in RVAL and RHAL (1.94±1.23 and 1.72±0.90 mm, respectively) when compared with other groups. The remarkable reduction in pocket depth and gain in clinical attachment seen in PRF+1% ALN group suggested the intensified combined efficacy of growth promoting factors delivered by platelet rich fibrin and bone synthetic activity of alendronate . The present study also revealed that ALN+PRF treated site showed significant reduction in the defect depth than other groups exemplifying the beneficial effects of growth promoting factors in regeneration. This remarkable improvement in PRF+ALN group can be supported by discussing favorable effect of PRF and ALN gel for periodontal tissue regeneration.The dense fibrin matrix of PRF clot ,polymerized in to tretramolcuar structure (3 D structure). During the slow polymerization of PRF fibrin matrix its concentrate platelets, leukocytes, cytokines, glycan chains and circulating stem cells. This result implies that PRF, unlike the other platelet concentrates, would be able to progressively release cytokines during fibrin matrix remodeling. Such a mechanism might explain the clinically observed healing properties of PRF[22, 23]**.** In addition ***Dohan et al ;2006*** demonstrated that PRF could stimulate leukocyte degranulation and cytokine from proinflammatory mediators, such as (IL)-1b, IL-6, and TNF-a, to anti-inflammatory cytokines, such as IL-4. It was also found that PRF fibrin matrix when slows down the blood activation process its enmeshed with a high number of leukocytes which concentrated on the end part of the clot, with a specific slow release of growth factors (e.g., TGF-1b, PDGF-AB, andVEGF) and glycoproteins (e.g., thrombospondin-1) for more than a week[24, 25]**.**Alendronate is a high influential inhibitor of bone resorption mediated osteoclasts and once taken up by bone, it acts as an antiosteolytic agent[26]. ALN target the surfaces where the resorption occur and its released locally during the acidification related with activity of osteoclast . Furetheremore ,this release leads to an increase in the local concentration of ALN, resulting in an alteration in the ruffled border membrane characteristic of osteoclasts without destroying the cell of bone. Therefore, ALN seems to have a potential to be used as an inhibitor of alveolar bone resorption in the treatment of periodontitis[27, 28]**.** So that , even though, the application of both ALN gel alone as well as PRF+ALN onto the furcation defects lead to significant improvements in clinical parameters, a better regenerative potential with PRF+ ALN could be confirmed radiographically.

CONCLUSIONS

The result of present study show that combined approach therapy using PRF and potent bone stimulator pharmacological medium ALN is effective in the treatment of classII furcation defect. within limitation of this trail ,PRF+1%ALN group show substantial improvement in clinical and radiographic parameters depicted by significant reduction in PPD, RVAL and RHAL gain, and significant bone defect fill in comparison to ALN and control groups. Thus, the combination proved to be beneficial in achieving better periodontal

regeneration. The evaluation of regeneration obtained by digital radiograph and clinical measurements has definitely increased our ability to determine the treatment outcome without a re-entry procedure.

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