

## Treatment of Degree II Furcation Defects Using Autogenous Grafts with and without Alendronate - A Split Mouth Clinical Study

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### ABSTRACT

**Aim:** This study was conducted to evaluate the efficacy of the combination therapy i.e. inverted periosteal graft (IPG) with autogenous bone used alone and in conjunction with an osteoclast inhibitor - 1% alendronate (ALN) sodium gel, in the treatment of mandibular buccal degree II furcation defects.

**Materials and Method:** A total of 28 buccal degree II furcation defects in 14 patients were selected and randomly divided into Group A and Group B. Experimental sites in Group A were treated using inverted periosteal graft and autogenous bone mixed with 1% alendronate gel and experimental sites in Group B were treated with inverted periosteal graft and autogenous bone only.

**Results:** Both the experimental groups showed significant reduction in probing pocket depth, gain in clinical attachment level and mean percentage of horizontal defect fill (41.82% vs 49.09%) at 6 months. Experimental sites in group B showed a significant loss in mean vertical defect height compared to experimental group A (1.52% Vs -1.59%).

**Conclusion:** It can be suggested that bisphosphonates such as alendronate sodium have the potential to inhibit the surgery induced bone loss.

**Keywords:** Alendronate sodium, Furcation defect, Grafting, Periosteum.

### INTRODUCTION

Management of furcation involved teeth is one of the challenging aspects of periodontal treatment because of their unique anatomical characteristics and variable response to treatment<sup>1</sup>. Degree II furcations have presented, however, a clinical problem where various regenerative procedures have been tried with the aim of complete closure of the furcations. An evidence-based consensus report concluded that



guided tissue regeneration in combination with or without bone replacement grafts is the treatment of choice for class II furcation defects<sup>2</sup>. Systematic reviews (Murphy & Gunsolley, 2003) provide strong evidence that Class II furcations respond most favorably and predictably to a combination approach using GTR and a bone grafting material together<sup>3</sup>.

Periosteum, a highly vascular connective tissue contains progenitor cells that have the ability to differentiate into fibroblasts, osteoblasts, chondrocytes, adipocytes and skeletal myocytes.

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Periosteum can be described as an osteo progenitor cell containing bone envelope, capable of being activated to proliferate and has been viewed as having regenerative potential (Ishida et al, Ueno et al). Periosteum when used as a guided tissue regeneration membrane can provide a rigid enough barrier to maintain space of the periodontal defect and also provides cells to migrate in and regenerate lost periodontal tissues<sup>4</sup>. Amongst the various bone grafts that have been evaluated for periodontal regeneration, autogenous bone grafts are still considered a gold standard for grafting procedures<sup>5</sup>. Autogenous grafts are considered to promote bone healing mainly through osteogenesis and/or osteoconduction.

All the periodontal surgical regenerative procedures require access to the alveolar bone. When the periosteum is separated from the alveolar bone, osteoclastic activity is stimulated, which ends in a resorptive phase that leads to bone ridge loss (Staffileno et al 1962; Ramfjord and Costish 1968; Yaffe et al 1994)<sup>6</sup>. This loss, resulting from the surgical exposure of bone, is an undesired outcome of the repair process, and many studies have been conducted in an attempt to find a way to avoid or minimize it (Yaffe et al 1995<sup>7</sup>; Kaynak et al 2003<sup>8</sup>). It has been proved that bisphosphonates such as alendronate (ALN) are effective in reducing alveolar bone loss following periodontal surgery. Topical application of alendronate solution at a concentration of 200µg at the time of surgery demonstrated marked reduction of bone resorption while maintaining the alveolar crest height (Binderman et al 2000)<sup>9</sup>.

The present study was designed to evaluate the relative efficacy of the combination therapy, inverted periosteal graft with autogenous bone graft used alone and in conjunction with an osteoclast inhibitor, 1% alendronate sodium gel in the treatment of mandibular buccal degree II furcation defects.

## **MATERIALS & METHOD**

### **Study population**

Fourteen patients (10 males and 4 females) who were 24 to 49 years of age at the time of baseline examination (mean age  $38.9 \pm 4.6$ ) with at least two bilateral buccal degree II furcation defects

in the mandibular molars were selected from the outpatient Department of Periodontics and Oral Implantology, GITAM Dental College and Hospital, Visakhapatnam. Patient selection criteria for this study included the following: 1) systemically healthy patients; 2) Age  $\leq 50$  years old; 3) Patients who were willing to give informed consent and to attend the study; 4) Patients who had two buccal degree II furcation defects (Hamp et al 1975) on contra lateral mandibular molars, with horizontal probing depths of 3 – 6 mm; 5) Gingival margin at the roof or coronal to the furcation defect; 6) No history of antibiotic use 3 months prior to enrollment; 7) Width of keratinized tissue  $\geq 1$  mm; 8) Patients who had not received any type of periodontal therapy for the past 6 months. Patients with any of the following conditions were excluded from the study: 1) Patients unable to perform routine oral hygiene procedures; 2) Patients who were current smokers; 3) Patients with thin gingival biotype; 4) Pregnant females; 5) Patients with clinical signs or symptoms of trauma from occlusion.

### **Study design**

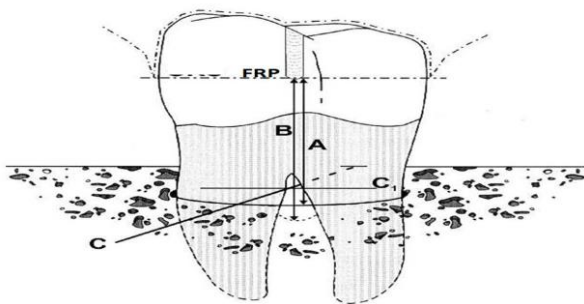
This was a randomized, controlled, prospective and double blinded clinical trial. Patients were given a detailed description of the study proposal and signed an informed consent. All the furcation defects were identified by careful probing with a 3 mm incrementally marked Nabers' probe. Prior to surgical care, all patients completed non-surgical periodontal treatment including plaque control instructions, scaling and root planing.

The selected sites were divided into experimental site A and experimental site B according to the type of treatment given, by using split mouth design. The type of treatment to be performed was decided just before the surgical procedure by the toss of a coin.

All the sites in experimental group A were treated with inverted periosteal pedicle graft and autogenous bone mixed with 1% alendronate gel whereas all the sites in experimental group B were treated with inverted periosteal pedicle graft and autogenous bone alone. Clinical outcomes were measured at baseline and 6 months postoperatively.

## Clinical measurements

Clinical parameters recorded were: Plaque index (PI, Silness and Løe) and gingival index (GI, Løe) were assessed at 6 sites per tooth at baseline (1<sup>st</sup> visit of the patient), 3 months and 6 months post-operatively. The probing depth (PD), clinical attachment level (CAL), gingival recession (GR) were assessed at baseline and 6 months. Additional clinical measurements, such as horizontal open furcation depth (HOFD) and vertical open furcation depth (VOFD) were recorded at the time of initial surgery and at 6-month reentry surgery. Direct defect measurement was performed using a prefabricated acrylic stent and University of North Carolina (UNC) probes. The stent was grooved to record the orientation of the probe. When the stent was placed on the occlusal surface of the tooth and adjacent teeth, the lower/apical limit of the groove was used as the fixed reference point (FRP) for measurements. If the fixed reference point was between two markings of the probe, then the reading was rounded off to the next whole number in millimeter. Probing depth was measured with the acrylic stent over the selected teeth, at the mid furcation area of the buccal surface using UNC-15 periodontal probe from the crest of the gingiva margin to the base of the pocket. Gingival recession was measured from a fixed reference point to the crest of the gingival margin using a UNC-15 probe. Clinical attachment level was determined by adding probing depth and relative recession for each site. Following debridement defect measurements of each molar's furcation area were recorded using the FRP. Two measurements to the nearest millimeter were taken for VOFD (Figure 1): i) Vertical distance (VD) from the FRP to the most coronal aspect of the alveolar crest at mid furcation, ii) Vertical distance from the stent to base of intrabony defect (ID) in the furcation.



**Fig 1:** Measurements taken for vertical open furcation depth.

HOFD was measured horizontally from a line tangential, using a second probe placed tangential to the root convexities as a reference point.

## Measurement of furcation defect<sup>10</sup>

Clinical measurements

A = Vertical distance from the fixed reference point (FRP)

B = Vertical distance from the fixed reference point (FRP) to base of intrabony defect

C = Horizontal probing depth measured horizontally from a tangential.

C1 = A second probe placed tangential to the root convexities as a reference point

## Preparation of 1% alendronate gel

The gel containing alendronate sodium for local delivery was prepared using pharma grade materials as described by Veena et al (2010)<sup>11</sup>. The formulations were transferred to 5 ml airtight glass bottles under sterile conditions and dispensed for the clinical study.

## Surgical procedure

Sulcular incisions were given on the facial and lingual side and were extended to two teeth mesial to the defect and one tooth distal to the defect. A full thickness mucoperiosteal flap was reflected using the periosteal elevator, just apical to the base of the furcation defect. Care was taken to retain the interdental papillary tissue as much as possible.

After reflection of the flap and exposure of the osseous defect, thorough surgical debridement of both soft and hard tissues (Figure 2) was done using curettes and scissors. The surgical site was thoroughly irrigated with 0.9% normal saline. No root conditioning was done. After debridement, the hard tissue parameters were registered with two UNC-15 probes and acrylic stent. The inverted periosteal pedicle graft (IPG) was reflected (Figures 3-6) as a graft, similar to the technique described by Ajay Mahajan et al (2009) such that it covered at least 2 mm beyond the coronal aspect of the furcation defect<sup>10-13</sup>.

Autogenous cortical bone graft was collected from the exposed alveolar bone adjacent to the defect using a back action chisel in the form of

ribbon like shavings and was transferred to the dappen dish. The derived matrix of ribbon like shavings and blood had a mortar like consistency and was adapted to the defect (Figure 7) with a cumine scaler.

In case of experimental Group A 0.1 ml of 1% alendronate gel was added to the graft and then packed into the defect. The inverted periosteal graft was stabilized in position with help of a sling suture and the flaps were sutured securely with interrupted sutures (Figure 8) using 4-0 polyglactin 910.

### Postoperative Care

Post-operative antibiotic regimen of Amoxicillin 500 mg thrice a day for 5 days and Ibuprofen 400 mg twice daily for 3 days was prescribed. The patients were advised to rinse with 10 ml aqueous 0.2% solution of chlorhexidine gluconate for 1 minute twice a day for two weeks. After 1 week, the dressing was removed and the surgical site was gently irrigated with saline.

The sutures were removed 2 weeks after surgery. Patients were recalled 24 hours after surgery and one week after surgery to evaluate signs of post-operative complications like swelling, hematoma, hemorrhage and symptoms like pain, discomfort and sensitivity. During the initial 2 weeks, patients were instructed to brush only the uninvolved teeth. Recall visits were carried out at 1 month, 3 months, and 6 months following surgery and at these visits, oral hygiene instructions were reinforced and the areas were gently debrided.

At 6 months the initial presurgical measurements were repeated and a buccal full thickness reentry flap was used to repeat the measurements of the osseous defects.

Soft tissue found covering bone on reentry flap surgery was not disturbed, in order to preserve the quality of fibrous tissue obtained during healing. Changes in osseous defect measurements were taken using the same stent (Figures 9- 14) to ensure a reproducible position of the probe. Flaps were approximated using interrupted sutures.

### Inverted periosteal pedicle graft (surgical procedure)



Fig 2: The debrided defect.

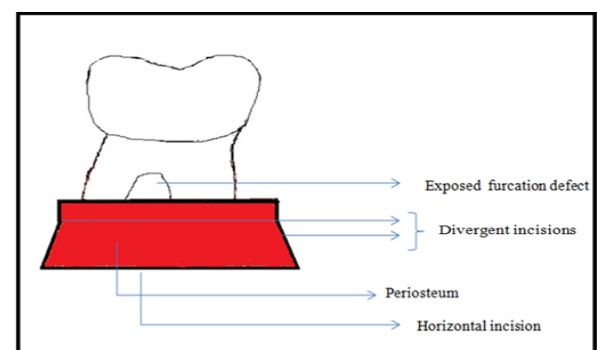


Fig 3: Incisions for inverted periosteal pedicle graft

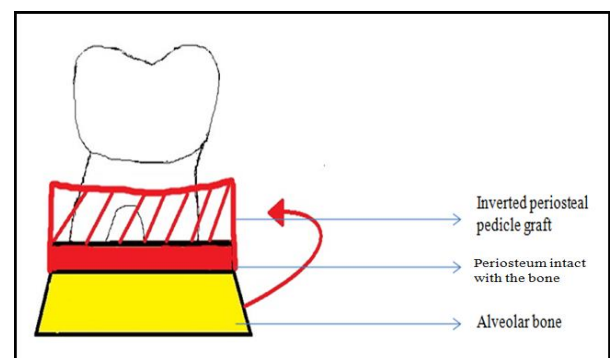


Fig 4: Rotation of the graft

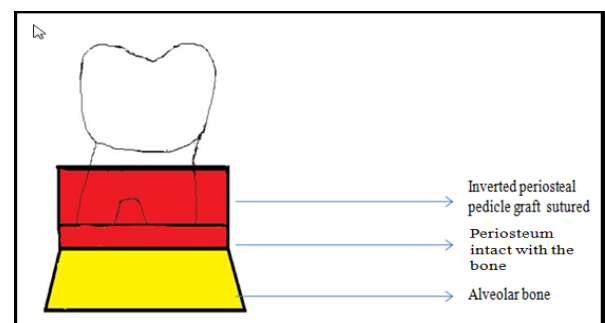
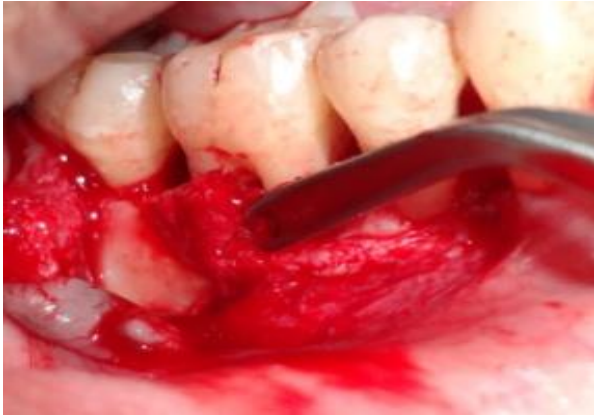


Fig 5: Suturing of the graft



**Fig 6:** Inverted periosteal pedicle graft.



**Fig 7:** Graft placement done.



**Fig 8:** Inverted periosteal pedicle graft sutured.

### Data analysis

All the clinical parameters recorded were subjected to the statistical analysis: 1) For intragroup variations, paired t-test/ Wilcoxon matched paired test was performed. 2) For comparison between the two groups / inter-group variations, unpaired t test/ Mann Whitney U Test were performed.

### RESULTS

During the course of this study, all patients showed good compliance, with no observed infections, delayed healing, adverse tissue reactions or clinically detectable localized allergic responses. Plaque Index (PI) and Gingival Index (GI) scores were significantly reduced from baseline to 6 months and remained low during the entire study period.

A mean reduction (Graph 1) in Probing Depth (PD) of  $1.93 \pm 0.92$  mm (50%) in group A and  $2.07 \pm 0.47$  mm (52%) in group B was observed which was statistically significant from that of baseline values. A mean gain (Graph 2) in Clinical Attachment Level (CAL) of  $2.21 \pm 0.89$ mm (50.822%) in group A and  $2.21 \pm 0.70$  mm (50%) in group B was observed which was statistically highly significant from that of baseline values.

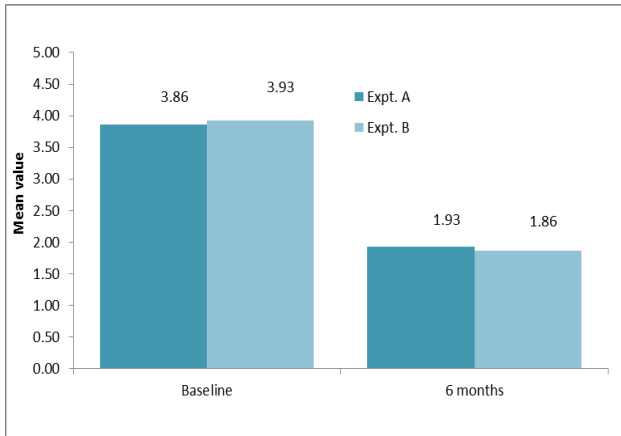
Gingival Recession (GR) increased slightly in both the groups, with no significant difference from the baseline values (Table 1). Intergroup comparison of the probing depth, clinical attachment gain and gingival recession revealed no statistically significant difference between the two groups.

Hard tissue measurements recorded, following the surgical reentry showed a significant improvement in defect fill in both the groups. A mean change (Graph 3) in the Horizontal Defect Depth (HDD) of  $1.64 \pm 0.50$  mm (41.82%) in group A and  $1.93 \pm 0.47$  mm (49.09%) in group B was observed which was statistically highly significant ( $p < 0.05$ ).

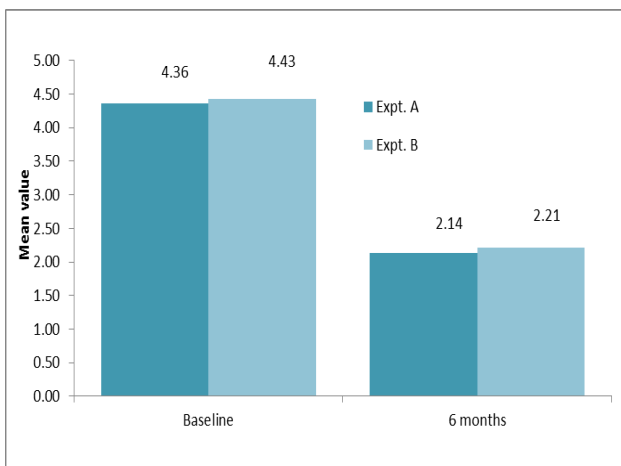
A slight improvement (Graph 4) in Vertical Defect Depth (VDD) reduction of  $0.14 \pm 0.36$  mm, significant from baseline to 6 months was observed in group A (1.52%). There was a slight increase in vertical defect depth in the experimental group B that was significant from baseline to 6 months (1.59%) was observed.

There was a significant defect fill in the Intrabony Defect Depths (ID) in both the groups from baseline to 6 months. The mean bone fill in experimental group A was 0.36 mm and in experimental group B was 0.29 mm. (Table 2)

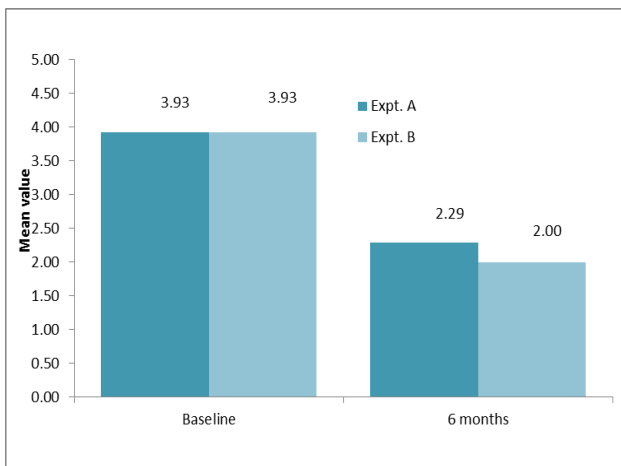
**Graph 1:** Comparison of experimental group A and B probing pocket depth scores (in mm) at baseline and 6 months.



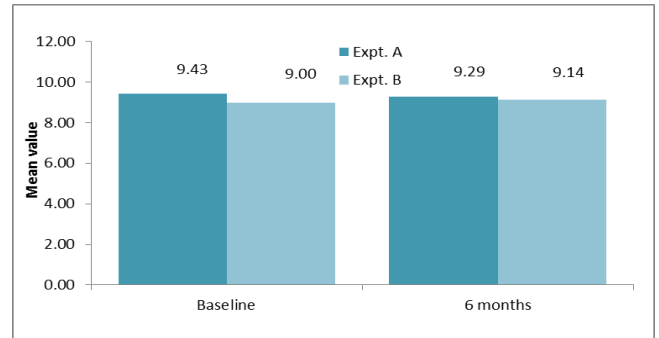
**Graph 2:** Comparison of experimental group A and B clinical attachment level – mid facial (in mm) scores at baseline and 6 months.



**Graph 3:** Comparison of experimental group A and B mean change in bone fill (horizontal) scores at baseline and 6 months.



**Graph 4:** Comparison of experimental group A and B mean change in vertical bone fill scores at baseline and 6 months.



**Direct defect measurements:**

**Experimental site A:**

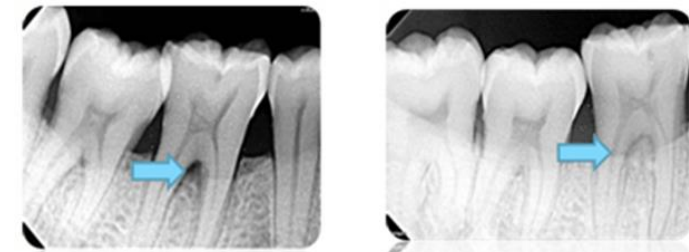


**Fig 9:** Horizontal open furcation depth at baseline & 6 months post- operative.



**Fig 10:** Vertical open furcation depth at baseline & 6 months post- operative.

**Radiographic evaluation:**



**Fig 11:** Radio Visio Graphs of pre & post-operative Experimental site A.

**Experimental site B:**

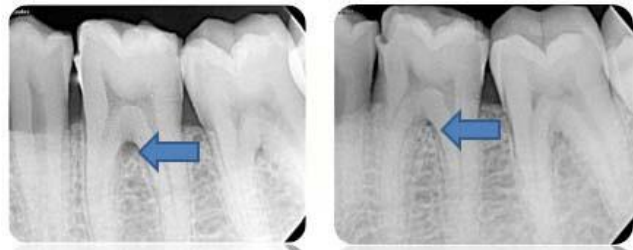


**Fig 12:** Horizontal open furcation depth at baseline & 6 months postoperative.



**Fig 13:** Vertical open furcation depth at baseline & 6 months post-operative.

**Radiographic evaluation**



**Fig 14:** Radio Visio Graphs of pre & postoperative Experimental site B.

**DISCUSSION**

Various regenerative procedures have been attempted for treatment of degree II furcations, such as open flap debridement, bone replacement grafts, coronally repositioned flaps, guided tissue regeneration barriers and combinations of these techniques. Combining osseous grafting with guided tissue regeneration may enhance the response to membrane only therapy via the inductive effects of the graft and supporting the membrane to a more optimal position. Similarly, the combination may enhance grafting-only therapy in selective areas via better containment of the graft and epithelial exclusion. Autogenous cortical bone, applied as small chips (Rosenberg et al. 1979)<sup>14</sup>, or mixed with blood prior to the placement in the defects (Robinson 1969)<sup>15</sup>, was reported to be effective in producing regeneration in periodontal osseous defects.

The degree of periodontal destruction and characteristics of the remaining periodontal osseous components like depth, width and number of osseous walls are one of the critical factors that may cause wide variations in the outcome of the guided tissue regeneration. These factors can limit the number of progenitor cells and the amount of biologic mediators required to repopulate periodontal defects. Autogenous periosteum provides a rich source of progenitor cells along with sufficient strength and hence can be used as a guided tissue regeneration membrane<sup>13</sup>.

**Table 1:** Soft tissue parameters at Baseline and 6 Months (mean ± SD [mm]).

	PD			CAL			GR		
	Baseline	6 months	Difference	Baseline	6 months	Difference	Baseline	6 months	Difference
Exp A	3.85±0.9 5	1.93±0.4 7	1.93±0.92 p - 0.0009*	4.36±1.15 15	2.14±0.5 3	2.21±0.89 p - 0.0009*	0.50±0.65 65	0.29±0.47 3	0.21±0.70 p - 0.3105
Exp B	3.93±0.6 2	1.86±0.5 3	2.07±0.47 p - 0.0009*	4.43±0.65 65	2.21±0.5 8	2.21±0.70 p - 0.0009*	0.43±0.65 65	0.21±0.4 3	0.21±0.58 p - 0.2249
A to B			p - 0.4484			p - 0.9268			0.9451

\*p<0.05

**Table 2:** Hard tissue parameters at Baseline and 6 Months (mean ± SD [mm]).

	HDD			VDD			ID		
	Baseline	6 months	Difference	Baseline	6 months	Difference	Baseline	6 months	Difference
Exp A	3.93±0.8 3	2.29±0.8 3	1.64±0.50 p - 0.0009*	9.43±1. 60	9.29±1.6 4	0.14±0.36 p - 0.0009*	9.79±1. 48	9.43±1.5 5	0.36±0.63 p - 0.0009*
Exp B	3.93±0.9 2	2.00±0.9 6	1.93±0.47 p - 0.0009*	9.00±1. 71	9.14±1.6 1	0.14±0.53 p - 0.0009*	9.36±1. 95	9.07±1.6 4	0.29±0.61 p - 0.0009*
A to B			p - 0.2413			p - 0.2507			0.7652

\*p<0.05

Periosteum contains fibroblasts on the outer layer and osteoblasts on the inner layer and their progenitor cells that respond to surgical release by a thickening of the periosteum and an increase in cellular activity. In the inverted periosteal graft, osteoblasts and their progenitor cells cover the layer of fibroblasts and are immediately available for osteogenesis. During healing, the cells with the potential to regenerate cementum and periodontal ligament are the first cells presented to the root surface. Osteoblasts and their progenitor cells are immediately behind the fibroblasts and populate the osseous defect. The inverted periosteal graft places the proper cells in the proper location for regeneration of the diseased periosteum. Owing to the above reasons, the periosteum offers a rich cell source for bone tissue engineering and hence, the regenerative potential of the periosteum is immense<sup>4</sup>.

In the present study inverted periosteal graft and autogenous bone graft with or without 1% alendronate gel were evaluated in the treatment of degree II furcation defects. The mean probing depth reduction in both the experimental groups was almost the same which indicated that the addition of 1% alendronate gel in the experimental group A had no significant effect on the reduction of probing depth. (Brunsvold et al 1992<sup>16</sup> and Reddy et al 1995<sup>17</sup>)

Since soft tissue measurements alone are sometimes misleading, a systematic conservative reentry flap exposure of all defects, allowing a precise assessment of the hard tissue status following treatment was undertaken. There was a significant horizontal bone gain in both the groups (Paolantonio et al 2009)<sup>18</sup>. Lekovic et al 1998<sup>19</sup> used

free periosteal grafts for the treatment of class II furcation defects and obtained a significant gain in horizontal defect fill of 1.6 mm (34%) after 6 months as assessed by surgical reentry. The percentage of horizontal defect fill obtained in the present study is slightly higher in both the experimental groups when compared to Lekovic's study. It suggested that additional use of graft material has an added advantage over guided tissue regeneration alone in the treatment of degree II furcation defects (Murphy and Gunsolly 2003)<sup>3</sup>.

No significant horizontal fill was observed in the alendronate treated group compared to the control group in the present study (Azza M. Ezz El-Arab et al 2002 & Ahmet Arslan et al 2012)<sup>20, 21</sup>. Contrary to these studies, Veena et al 2005 and Pradeep et al 2013<sup>22</sup> found a significant gain in defect fill using 1% alendronate gel as a local drug delivery agent.

There was a slight increase in vertical defect depth in the experimental group B that was significant from baseline to 6 months (-1.59%), similar to studies done by Vijay et al 2002<sup>23</sup> and Christopher et al 2002<sup>10</sup>. This could be due to crestal bone resorption that occurred because of the resorptive phase due to regional accelerated phenomenon following mucoperiosteal flap surgeries. Tsao et al 2006<sup>24</sup> observed a crestal bone resorption of 0.7 mm following treatment with mineralized bone cancellous allograft and a collagen membrane. In contrast to this finding, a slight decrease in vertical depth reduction, significant from baseline to 6 months was observed in group A (1.52%). This could be explained by the addition of an osteoclastic inhibitor- alendronate - to the graft. Alendronate can effectively inhibit the osteoclastic



activity initiated at the surgical wound due to regional accelerated phenomenon, thereby preventing bone loss. Yaffe et al 2003<sup>25</sup> conducted a study, to know the effect of alendronate on bone formation and resorption on a rat ectopic model. They concluded that alendronate is effective in inhibiting bone loss, but ineffective during the bone formation phase. So they suggested that alendronate should be administered in procedures where bone resorption is expected. Binderman et al 2000<sup>8</sup> conducted a histologic study on rats to evaluate the effect of topical administration of alendronate on bone resorption. They concluded that alendronate effectively reduces bone loss in periodontal procedures involving mucoperiosteal flap surgery.

There was a significant defect fill in the intrabony defects in both the groups from baseline to 6 months. The mean bone fill in experimental group A was 0.36 mm and in experimental group B was 0.29 mm. This is in contrast to the study done by Christopher et al 2002<sup>10</sup> who did not find a significant fill in the intrabony defects.

Complete furcation fill was not observed in only 5 sites of the cases treated in both the groups. This finding is contrary to the studies done by Camelo et al 2000<sup>26</sup>, where they obtained complete furcation fill in 89% of the sites and McClain et al 1993<sup>27</sup>, where they obtained complete furcation fill in 74% of the sites. But these studies were non controlled studies and the authors did not mention about the pre-operative defect measurements.

## CONCLUSION

Based on the findings, it was concluded that the combined regenerative therapy i.e. inverted periosteal pedicle graft and the autogenous cortical bone grafting with or without alendronate was effective in the treatment of degree II furcation defects with respect to probing depth reduction, gain in clinical attachment level and horizontal furcation fill. Addition of 1% alendronate gel to the autogenous cortical bone graft has no added advantage with respect to horizontal furcation fill, but a slight decrease in vertical furcation defect depth was observed.

From the current study, it appears that both the treatment modalities gave similar

outcomes and were successful in showing promising results in the treatment of degree II furcation defects. Addition of 1% alendronate gel has an added advantage of slight gain in vertical furcation defect depth. 1% alendronate gel used in the study was well tolerated by oral tissues with no adverse tissue responses. Harvesting and manipulation of the periosteal pedicle graft was easy and there was no need of a second surgery for graft harvesting and membrane removal.

## CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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