



## Effect of Bone Graft and Platelet Rich Fibrin with and Without Alendronate in the Management of Intrabony Periodontal Defect – A Randomized Clinical Study

Dr. Selvalakshmi Saravanan<sup>1</sup>, Dr.Gautham kumar N <sup>2</sup>, Dr.Tamilselvan kumar<sup>3</sup>, Dr. Ramakrishna Saradha<sup>4</sup>, Dr.Rohan Vasanth Raj<sup>5</sup>, Dr.Jesintha Mary<sup>6</sup>

<sup>1</sup>Assistant professor,Department of Periodontology,Vinayaka Mission's Sankarachariyar Dental College,Vinayaka Mission's Research Foundation (Deemed to be University under section 3 of the UGC Act 1956),Sankari Main Rd,Salem,Tamilnadu 636308

<sup>2</sup>Professor and Head of the Department,Department of Periodontology,Madha Dental College and Hospital,Madha Nagar,Kundrathur,Chennai,Tamilnadu 600069

<sup>3</sup>Associate professor,Department of Periodontology,Vinayaka Mission's Sankarachariyar Dental College,Vinayaka Mission's Research Foundation (Deemed to be University under section 3 of the UGC Act 1956),Sankari Main Rd,Salem,Tamilnadu 636308

<sup>4</sup>Assistant professor,Department of Periodontology,Vinayaka Mission's Sankarachariyar Dental College,Vinayaka Mission's Research Foundation (Deemed to be University under section 3 of the UGC Act 1956),Sankari Main Rd,Salem,Tamilnadu 636308

<sup>5</sup>Assistant professor,Department of Periodontology,Vinayaka Mission's Sankarachariyar Dental College,Vinayaka Mission's Research Foundation (Deemed to be University under section 3 of the UGC Act 1956),Sankari Main Rd,Salem,Tamilnadu 636308

<sup>6</sup>Private practitioner,Sp.Koil,Chengalpattu,Tamilnadu 603001

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### KEYWORDS

Periodontal regeneration, PRF, Open flap debridement, Bioactive glass, Alendronate

### ABSTRACT:

**Background:** Periodontal disease is characterized by the presence of gingival inflammation, periodontal pocket formation, and loss of connective tissue attachment and alveolar bone around the affected teeth. The ultimate goal of periodontal therapy is to regenerate the lost periodontal tissues, including cementum, periodontal ligament and alveolar bone. The aim of the present study is to evaluate the effect of bone graft and platelet rich fibrin with and without alendronate in the management of intrabony periodontal defect.

**Materials and method:** Study sample included 20 patients who were randomly divided and treated with one of the following: Site-A open flap debridement followed by placement of platelet rich fibrin (PRF) and bone graft (Perioglas®). Site-B open flap debridement followed by placement of platelet rich fibrin (PRF), alendronate (ALN) and bone graft (Perioglas®). Clinical parameters and radiographic parameters were recorded at baseline and 6 months. Statistical analysis was done using SPSS software.

**Results:** The results of present study demonstrate that in all the sites there was a significant improvement in clinical and radiographic parameters, thereby improving periodontal status.

### Conclusion:

Perioglas®, PRF and ALN were all shown to be safe to use and combination therapy with



bioactive glass + PRF is also found to be effective. The present study found that adding a single titrated dose of host modulating agent like ALN marginally improved the predictability of bone formation.

## INTRODUCTION

Periodontitis is a multifactorial disease of the oral cavity with the microorganisms playing a key role in its initiation and pathogenesis<sup>1</sup>. The host immune system triggers an inflammatory response to the microbial insult that defends and destroys the periodontium<sup>2</sup>. The primary clinical features of periodontitis include gingival inflammation, periodontal pocketing, clinical attachment loss (CAL) and alveolar bone loss (BL)<sup>3</sup>. Among these, the intra osseous vertical defects are at a higher risk of disease progression when left untreated<sup>4</sup>. One of the most important, and at present, unsolved problems in clinical periodontology is resolving progressive bone loss. Treatment of intra-bony defects encompass several treatment modalities that intends to reconstruct the attachment apparatus which includes bone grafts, guided tissue regeneration, biomolecular techniques, or combination of these techniques<sup>5</sup>

A class of recently developed drugs, bisphosphonates<sup>6</sup> has been shown to be a potent inhibitor of bone resorption<sup>7</sup>. Alendronate (ALN), an aminobisphosphonate is a potent inhibitor of osteoclast-mediated bone resorption with no adverse effect on the mineralization of bone<sup>8</sup>.

In recent years, researchers have focused on biological mediators which have the ability to enhance wound healing and improve clinical benefits of bone replacement grafts. PRF has been demonstrated to release polypeptide growth factors such as transforming growth factor  $\beta$ 1, platelet-derived growth factor, vascular endothelial growth factor and matrix glycoproteins (such as thrombospondin-1) gradually over at least 1 week<sup>9</sup>. PRF has been used in different surgical procedures. It also stimulates osteoblastic activity leading to regeneration of intrabony and mandibular grade II furcation defects<sup>10-13</sup>.

From this viewpoint, the present study was designed to evaluate the relative efficacy of the alloplast used in conjunction with an osteoclast inhibitor and growth factors in the treatment of human periodontal infrabony defects.

## AIMS AND OBJECTIVES

To evaluate whether an additional benefit exists when alendronate is combined with bone graft (Perioglas) and PRF in the management of intrabony periodontal defects.

## MATERIALS AND METHODS

The present randomized single blinded clinical study was conducted in the Department of Periodontology, Madha Dental College and Hospital, Chennai. The study protocol was approved by the Institutional Ethical Committee and Review Board of Madha Medical College and Hospital, Chennai.

## PATIENT SELECTION

The patients who participated in the present study were selected from the out patients who visited the Department of Periodontology, Madha dental college, Chennai. A total of 20 patients including both males and females aged between 25- 50 years were selected. Written and verbal consent was obtained from the selected patients in English/Tamil language. The inclusion criteria of the study was patient in the age group of 25- 50 years, having periodontal pocket with probing depth of  $\geq 5$ mm with radiographic evidence of vertical osseous defects

who are co-operative and able to attend the hospital for regular follow up. The exclusion criteria for the study were patients who are allergic to materials and drugs used or prescribed in this study, patients who are medically compromised or under any therapeutic regimen that may decrease the probability of soft tissue and bone healing, pregnant and lactating women, who



had undergone any periodontal therapy one year prior to the initiation of the study, study tooth exhibiting mobility greater than grade II, patients using any form of tobacco. Sites were selected randomly by coin toss method and assigned to either experimental site A (bone graft+ PRF) and experimental site B (200µg ALN + bone graft + PRF).

### CLINICAL PARAMETERS

Individually fabricated occlusal stents were made for standardization of the measurements. Probing depth was measured at baseline and at 6 months using a Williams' calibrated periodontal probe. The distance from the base of the pocket to the apical border of the stent was measured to get the relative attachment level (RAL). Radiovisiography (RVG) of each defect was taken. Defect depth were measured from periapical radiographs by a computer-aided technique, using an image analysis software (Digimizer software, MedCalc Software Ltd, Ostend, Belgium). The distances from cemento enamel junction (CEJ) to base of the defect (BD) were recorded at baseline and 6 months. The following radiographic parameters were recorded.[Fig 1]

- i. Linear bone growth (LBG) was calculated as the difference between the CEJ to BD distance at baseline(a) and CEJ to BD distance at 6 months(b).
- ii. Bone fill percentage (%BF) was obtained by dividing LBG by the radiographic defect depth at baseline and multiplying by 100.  $[\frac{(a-b)}{a} \times 100]$

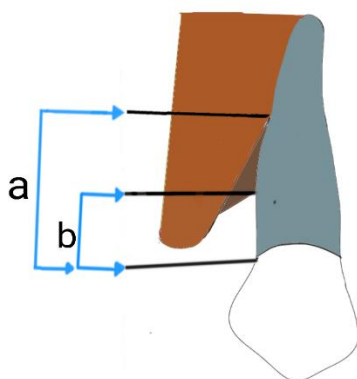


Fig 1: Schematic diagram illustrating the base of the defect (BD) at baseline and 6 months

CEJ to BD distance at baseline(a)

CEJ to BD distance at 6 months(b)

### PREPARATION OF PRF

Platelet rich fibrin was prepared according to the protocol developed by Choukroun et al in the year 2001<sup>14</sup>.

### PREPARATION OF ALENDRONATE

ALN solution was prepared as described by Gupta et al<sup>13</sup> by crushing 2 tablets of 35mg ALN (Osteofos, Cipla Ltd., Haridwar, India) and dissolved in 3.5 ml of normal saline. 10µl of this solution was measured with a fixed value pipette (Microlit, Lucknow, India) which contains 200µg of ALN<sup>15</sup>. ALN was freshly prepared for each patient

### PRE-SURGICAL THERAPY

Full mouth scaling and root planing were carried out and OHIs were given as part of phase I therapy. Six to eight weeks following phase I, the patients were re-evaluated to confirm the suitability of the sites for flap surgery.

### SURGICAL PROTOCOL

Intraoral and extraoral antisepsis was maintained using povidone iodine. Under LA(2% lignocaine local anesthetic agent containing adrenaline in the ratio of 1:80,000), modified flap operation (Kirkland flap) was performed in the selected sites. For this intrasulcular and interdental incisions were given using 15 size BP blade. Full thickness mucoperiosteal flap was elevated and meticulous root planing, curettage and defect debridement was done using appropriate curettes and other surgical instruments(Fig 2). Copious saline irrigation was used in the surgical area. For the test group patients, 10 µl solution containing 200µg of ALN, was added to the graft material using a micro pipette (Microlit, Lucknow, India). The ALN soaked Perioglas® was allowed to sit for 10 minutes to permit binding of the drug into the Perioglas® graft particles(Fig 4). If the graft was not completely wet, then the necessary amount of saline was carefully added to completely wet the graft so as to get a moldable implantable material. The graft was gently packed into the intrabony defect and overfilling was avoided. The



graft was then covered subsequently by the prepared PRF membrane. Pre-suturing was done prior to grafting using non resorbable 3-0 black braided silk. For the control group patients, Perioglas® was soaked only in

saline and used for implantation. Control site also received the identical treatment except the alendronate. Periodontal pack was used to protect the surgical sites.

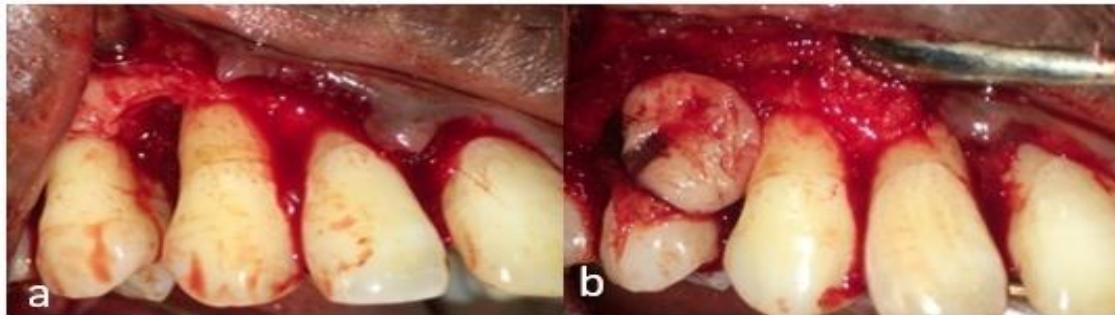


Fig 2 – Experimental site A a) Flap reflection & debridement b) Placement of Perioglas® and PRF into defect site

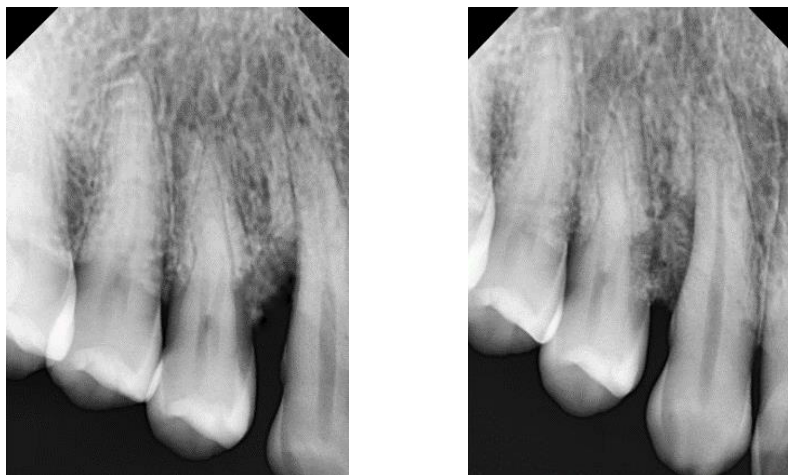


Fig 3 – Experimental site A – Pre-operative radiograph  
Experimental site A Post-operative radiograph

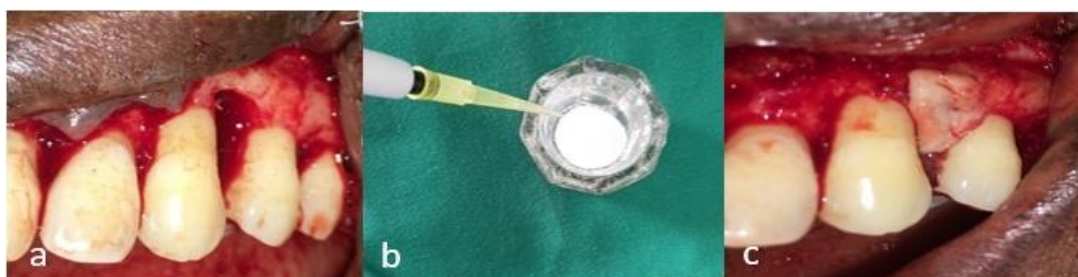


Fig 4 – Experimental site B a) Flap reflection & debridement b) Mixing alendronate solution with the bone graft c) Placement of Perioglas®, alendronate and PRF into defect site

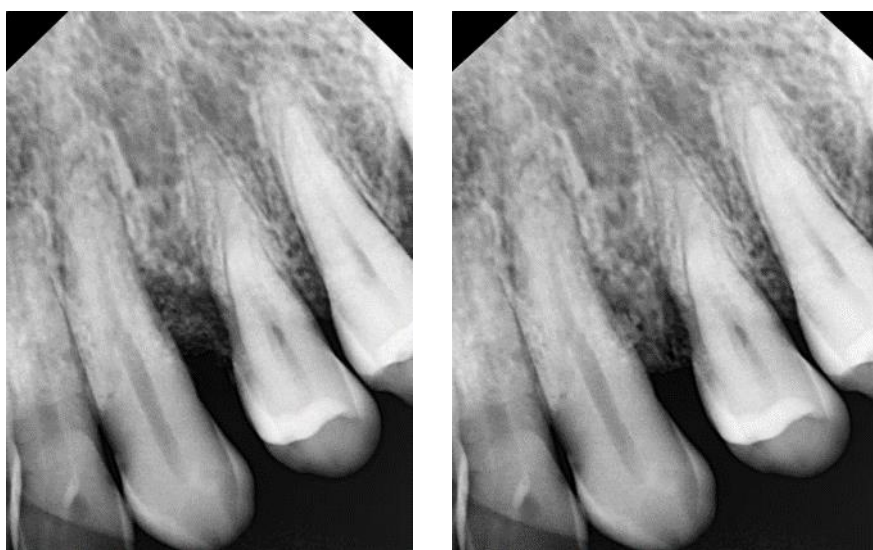


Fig 5 – Experimental site B – Pre-operative radiograph

Experimental site B Post-operative radiograph

### POST OPERATIVE CARE

Suture and periodontal dressing were removed one week after surgery. The operated area was rinsed carefully with normal saline. Gentle brushing with a soft brush was recommended. Oral hygiene maintenance was reinforced in all the patients. The patients were recalled every one week for one month and 6 months post operatively. All the clinical measurements and radiographs were repeated at the end of the 6 months.

**Statistical software** - Descriptive and Inferential statistics were analyzed by IBM SPSS version 20.0 (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp). Mean and SD were used to summarize quantitative data between main treatment groups. Independent samples t test was used to analyze the inter-group difference in clinical parameters between both experimental groups. Repeated Measures ANOVA was used to assess the intragroup changes in each of the clinical index in each of the two groups. Microsoft word and Excel were used to generate graphs and tables. Throughout the study a P

value of  $< 0.05$  with 95% Confidence Intervals were considered as statistically significant difference.

### Results

The basic demographic characteristics of the patients are shown in table 1. There was no significant differences between the groups in terms of age and gender.

**Table 1 - Demographic characteristics of the patients**

PARAMETER	GROUP A	GROUP B
N	10	10
Mean age	41.1	42.1
Male/Female	4/6	5/5

There was no statistically significant difference between the PI and GI values obtained among the two groups, thus reiterating the fact that plaque control was adequately maintained by the patients and had no negative influence on test results. Comparison of baseline and 3<sup>rd</sup>, 6<sup>th</sup> month plaque index and gingival index value between both the groups are shown in table 2 and table 3

**Table 2 - Comparison of baseline and 3<sup>rd</sup>, 6<sup>th</sup> month plaque index value between both the groups**

Variable	Group	Mean	Std. Deviation	SEM	P value
Plaque Index baseline	Grp A	0.7800	0.15492	0.04899	0.50
	Grp B	0.7300	0.17029	0.05385	
Plaque Index 3 months	Grp A	0.8300	0.11595	0.03667	0.73
	Grp B	0.8100	0.14491	0.04583	
Plaque Index 6 months	Grp A	0.9000	0.08165	0.02582	0.25
	Grp B	0.8400	0.13499	0.04269	

**Table 3 - Comparison of baseline and 3<sup>rd</sup>, 6<sup>th</sup> month gingival index value between both the group**

Variable	Group	Mean	Std. Deviation	SEM	P value
Gingival Index baseline	Grp A	0.8300	0.12517	0.03958	0.09
	Grp B	0.6800	0.23944	0.07572	
Gingival Index 3 months	Grp A	0.8400	0.10750	0.03399	0.21
	Grp B	0.7600	0.16465	0.05207	
Gingival Index 6 months	Grp A	0.8900	0.08756	0.02769	0.69
	Grp B	0.8700	0.13375	0.04230	

Comparison between the two experimental sites revealed that the PPD reduction at 6 months post-operatively was slightly higher in sites treated with platelet rich fibrin, bone graft and ALN than those treated with platelet rich fibrin and bone graft alone;

however this was not statistically significant. Comparison of baseline and 6<sup>th</sup> month probing depth value between both the groups are shown in table 4.

**Table 4 - Comparison of baseline and 6<sup>th</sup> month probing depth value between both the groups**

Variable	Timeline	Mean	Std. Deviation	P value	Variable
Probing Depth baseline	Grp A	7.6000	0.96609	0.30551	0.210



	Grp B	8.1000	0.73786	0.23333	
Probing Depth 6 months	Grp A	3.7000	0.94868	0.30000	0.46
	Grp B	3.4000	0.84327	0.26667	

Comparison between the two experimental sites revealed that the relative attachment level at 6 months post-operatively was marginally higher in sites treated with platelet rich fibrin, bone graft and ALN than those treated with platelet rich fibrin and bone graft alone; however this was not statistically significant. The

gain in the relative attachment level was thought to represent resolution of tissue inflammation, reformation of collagen fibers, new attachment and the bone fill. Comparison of baseline and 6<sup>th</sup> month relative attachment level between both the groups are shown in table 5

**Table 5 - Comparison of baseline and 6<sup>th</sup> month relative attachment level between both the groups**

Variable	Timeline	Mean	Std. Deviation	P value	Variable
Relative attachment level baseline	Grp A	11.9000	1.10050	.34801	0.83
	Grp B	12.0000	1.05409	.33333	
Relative attachment level 6 months	Grp A	7.9000	.73786	.23333	0.24
	Grp B	8.4000	1.07497	.33993	

The comparison between the two experimental sites revealed that the percentage of bone fill at 6 months post-operatively was marginally higher in sites treated with platelet rich fibrin, bone graft and ALN

than those treated with platelet rich fibrin and bone graft alone. Comparison of bone fill between both groups at 6<sup>th</sup> month are shown in table 6.

**Table 6 - Comparison of bone fill between both groups at 6<sup>th</sup> month**

Variable	Group	Mean	Std. Deviation	SEM	P value
Bone Fill %	Grp A	30.6464	2.79265	.88311	0.051
	Grp B	34.1230	4.23830	1.34027	



## DISCUSSION

Effective regeneration of periodontal structure lost due to inflammatory periodontal disease remains an elusive goal. One important regeneration strategy is to use biomaterials to restore the defects produced by disease process. The combination of one or more techniques currently available for periodontal regeneration has the potential to enhance clinical results as compared to any of the techniques used alone. Various biological approaches like use of growth, differentiation factors and use of mediators for bone remodelling has been advocated for better results<sup>16</sup>.

In the present study only those patients were considered for periodontal surgery who showed good oral hygiene maintenance following the Phase-I therapy. Oral hygiene status was assessed by taking the plaque index and gingival index. After SRP was carried out, baseline evaluations were done after 2-6 weeks of waiting period. After the flap surgery, the PI and GI were recorded at 3<sup>rd</sup> and 6<sup>th</sup> month and the Pocket Depth (PD), Relative Attachment Level (RAL) were recorded at 6<sup>th</sup> month.

There were no significant inter-group differences in any of the measured clinical and radiographical variables at baseline, assuring the same starting point for both procedures and the prevention of selection bias. Comparison between the two experimental sites revealed that the PPD reduction at 6 months post-operatively was slightly higher in sites treated with platelet rich fibrin, bone graft and ALN than those treated with platelet rich fibrin and bone graft alone; however this was not statistically significant.

Comparison between the two experimental sites revealed that the relative attachment level at 6 months post-operatively was marginally higher in sites treated with platelet rich fibrin, bone graft and ALN than those treated with platelet rich fibrin and bone graft alone; however this was not statistically significant. The gain in the relative attachment level was thought to represent resolution of tissue inflammation, reformation of collagen fibers, new attachment and the bone fill.

Our results are in agreement with the previous studies of Pradeep et al<sup>17</sup> who treated intra bony defects with autologous platelet concentrates and found mean PD reduction and CAL gain in the PRF group.

Results of the present study are in accordance with the study conducted by Mengel et al<sup>18</sup> and Froum et al<sup>19</sup> who treated intra-bony defects with bioactive glass and reported greater reduction in probing pocket depth, gain in relative attachment level in bioactive glass group.

Also, a study by Sharma et al<sup>20</sup> who treated intrabony defects either with 1% ALN gel or placebo gel reported mean significant PD reduction, significant gain in CAL and greater mean percentage of bone fill in the ALN group at 6 months

The comparison between the two experimental sites revealed that the percentage of bone fill at 6 months post-operatively was marginally higher in sites treated with platelet rich fibrin, bone graft and ALN than those treated with platelet rich fibrin and bone graft alone.

Our results are in accordance with the previous studies of Singh et al<sup>21</sup> who reported significant reduction in probing pocket depth and gain in relative attachment level, defect fill at the end of 6 months using PRF with bioactive glass in intra bony defects.

Lovelace et al<sup>22</sup> used bioactive glass and DFDBA in intra bony defect and reported that bioactive glass was capable of producing similar results to that of DFDBA at the end of 6 months. Kanoriya et al<sup>23</sup> who treated intrabony defect with combination of PRF and alendronate and reported significant reduction in PD gain in relative attachment level, and significant radiographic defect fill, when compared to PRF alone.

Thus this study reiterated the findings in previous studies<sup>17,18,19,22,23</sup>, that bioactive glass combined with PRF produce favourable results in the management of intrabony defects and that the addition of an antiresorptive agent like ALN produces a synergistic effect albeit marginally within the limits of the study. These findings throw up many options for the periodontist, who wishes to tap the synergistic and pleiotrophic effects of ALN as an adjunct to bone graft and PRF in the management of intrabony defects.

## CONCLUSION

Perioglas®, PRF and ALN were all shown to be safe to use, without causing any immunologic or antigenic reactions in any of the treated patients. Perioglas® appears to be a suitable vehicle to administer biologic substances like PRF and growth factors to induce new bone regeneration. A combination



therapy with bioactive glass + PRF is also found to be effective. The present study found that adding a host modulating agent like ALN to bone graft materials improved the predictability of bone formation. Further studies with better imaging techniques, large sample size and longer follow up period must be undertaken, to determine the beneficial effects of the adjunctive use of PRF, ALN and bioactive glass before arriving into a definitive conclusion.

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