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Effect of Platelet-Rich Plasma (PRP) on the Healing of Intra Bony Defects with Natural Bone Mineral (NBM) and Collagen Membrane

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ABSTRACT

Aim: The study was aimed to evaluate the additional effect of Platelet rich plasma (PRP) on the treatment of deep intra bony defects with natural bone mineral and collagen membrane.

Materials and methods: Total 16 patients with chronic periodontitis aged> 30 years with intra bony defects in either mandibular or maxillary arch. Patients were randomly allocated to one of the treatment groups i.e., Group I treated with PRP, Bovinederived bone graft (Cerabone) and bio-resorbable membrane from bovine derived collagen membrane (Healiguide) and Group II treated using Cerabone and Healiguide. The patients were followed up for a period of 6 months postoperatively. The clinical parameters PI, GI, PD, CAL and Gingival recession were evaluated at base line and 6 months. Radiographic parameters which were measured at base line and postoperatively at 6 months included, Depth of the defect.

Results: Both groups I and II showed statistically significant probing depth reduction, gain in clinical attachment level and reduction in defect depth compared to base line. No statistically significant difference was observed between the groups.

Conclusion: It can be concluded that both the groups were effective in the treatment of Intra bony defects with no statistically significant difference between the two groups.

Keywords: Intrabony defects, natural bone mineral, GTR, PRP.

INTRODUCTION

A plethora of bone substitutes are currently available for use in Periodontics. One very well documented bone substitute is a bovine-derived natural bone mineral(NBM). It is prepared by protein extraction of bovine bone that results in a trabecular structure of hydroxyapatite similar to human cancellous bone, and it has the ability to enhance bone formation. It is clinically well tolerated, and because all organic components are removed it does not elicit any allergic reactions For periodontal regeneration to occur, a number of biologic events, including cell migration, adherence, multiplication and differentiation need to occur in a well orchestrated sequence[1]. GTR involves the placement of barrier membrane between the root and the soft tissue, to guide the selective repopulation of cells on the root surface to help in periodontal regeneration. Collagen is one of the most widely used absorbable barrier membrane as it satisfies most of the above features[2]. Regenerative

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methods based on barrier technique lack predictability, sufficient degree of efficacy and ease of use. To eliminate these problems, the use of polypeptide growth factors, polypeptide differentiation factors and other biomaterials have been suggested.

The use of polypeptide growth factors (PGFs) for periodontal regeneration has recently attracted the attention of periodontal researchers and clinicians[3]. PGFs are biologic mediators that have the ability to regulate cell, proliferation, chemotaxis and differentiation. Among these, platelet derived growth factors(PDGF) and transforming growth factors(TGF-β) have been most extensively studied. PDGF is stored in bone matrix and when released by activation of osteoblasts , results in increased new bone formation, osseous defect fill and gain in clinical attachment[4]. Thus it is generally accepted that PGDF functions as anabolic factor in bone metabolism[5]. TGF-β is also found in high levels in bone and upon activation promotes wound healing under inflammatory conditions.

These two growth factors are known to be abundant in the alfa granules of platelets. A convenient economical approach to obtain autologous PDGF and TGF-β is the use of platelet rich plasma(PRP)[4]. Observations from a case report series have suggested that treatment of deep intrabony defects with PRP combined with a bone allograft and GTR may result in significant clinical improvements compared with base line values[6]. In other words, combining two or more therapies may provide added advantage of each individual material, enhancing synergism between them and ultimately providing more options to treat complex osseous defects. With this background, the aim of the present controlled clinical study was to evaluate the additional effect of PRP on the treatment of deep intra-bony defects comparing the use of NBM+PRP+GTR with NBM+GTR

MATERIALS AND METHODS

The present study was a clinical and radiological study conducted in the Department of periodontics, Mamata Dental College, Khammam. The study sample included 16 patients with chronic periodontitis aged > 30 years with intra bony defects in either mandibular or maxillary arch. Patients were randomly allocated to one of the treatment groups i.e., Group I treated with PRP with Bovine derived bone graft (Cerabone) and bioresorbable membrane from bovine derived collagen GTR membrane (Healiguide) and Group II treated using Cerabone and Healiguide. The patients were followed up for a period of 6 months post operatively.

INCLUSION CRITERIA

- Patients with age 30-50years
- Presence of one intrabony defects in relation to mandibular or maxillary arch with a
- probing depth of at least 6mm and a intra bony component of at least 3mm as detected on radiographs.
- Patients should not have undergone any periodontal therapy and medication prior to sixmonths before initial treatment.

EXCLUSION CRITERIA

- Patients with habits like smoking ,alcoholism and pan chewing
- Patients with known systemic diseases (i.e,diabetes, autoimmune diseases etc)
- Patients with poor oral hygiene maintenance even after phase I therapy
- Patients who are receiving steroid therapy
- Patients with non vital teeth or endo –perio lesions

BONE GRAFT MATERIALS

Cerabone is a highly reliable, dimensionally stable, purified natural bovine bone grafting material. The unique manufacturing process with high-temperature heating removes all organic components and eliminates all potential immunological reactions. Its macroporous structure is ideal in its osteoconductive function and promotes the ingrowth of blood vessels and nerves. It has a grain size of 0.5mm-1mm which permits clot stabilization and revascularization.

BARRIER MATERIAL [HEALIGUIDE]

HealiGuide, a synthetic resorbable membrane made from bovine tendon collagen (advanced biotech products pvt ltd,Chennai). It is a type-1 collagen membrane measuring 15x20mm. Implanted collagenous material is degraded by the action of a series of collagenolytic enzymes present primarily

in inflammatory cells such as granulocytes and macrophages.

Preparation of use:

After opening of the vial in a clean and sterile environment, the sterile HealiGuide membrane is taken out and soaked in saline for approximately 1 min. After soaking, the membrane becomes pliable and may be cut to shape to use for the surgery.

Stent fabrication

The stent is made up of 1mm polyvinyl silicone sheet (3A MEDES Inc. KOREA) in a biostar unit(Jaypee instruments corp. Kerala). Clinical attachment level was measured using a customized acrylic stent, to serve as fixed reference point. The groove was fabricated in the stent in order to duplicate the placement of probe at the end of 6 months, to minimize the error in post-operative measurements.

Radiological procedures

The standard intra oral periapical radiographs(Nikon-8502) were taken using paralleling cone technique(Rinn xcp-dentsplay) with no.2 x –ray films(Kodak). Later the radiographs were imagined with Nikon digital camera and bone defect depth was measured with AUTO CADD-2010. Radiographic intrabony depth of the defect was assessed by the computer analysis and correlated with attachment gain.

Radiographic parameters[7]

Cementoenamel junction(CEJ) - defined as the most apical point of the enamel on the defect side .if the CEJ was masked by the restorative treatment, the margin of the restoration was used as the landmark.

Bony defect(BD) - most coronal point where the PDL space showed a continous width. If no PDL space could be identified, the point where the projection of the AC crossed the root surface was taken as the land mark. If both structures could be identified at one defect, the point defined by the periodontal ligament was used as BD and the crossing of the silhouette of the alveolar crest(AC) crossed the root surface was taken as the land mark. The depth of the infrabony component of the defects (IBD) was calculated as the difference between **CEJ to BD** minus **CEJ to AC.**

Clinical measurements

At baseline, every subject received a full mouth periodontal examination with clinical parameters,

Plaque Index(PI) (**Loe H 1967)**

Gingival Index(GI) **(Loe H 1967)**

Probing Pocket Depth (PPD)

Clinical attachment loss(CAL)

Gingival recession(GR)

All clinical measurements, at base line and 6 month postoperatively, were carried out by a university of North Carolina (UNC) no.15 periodontal probe at six sites per tooth i.e, mesiobuccal, mid buccal, distobuccal, mesiolingual, mid lingual, distolingual. All measurements were rounded to the nearest millimeter. Only one measurement per tooth, the deepest site of the selected defect at baseline was included in the result calculation.

Probing pocket depth (PPD)

It is calculated by subtracting the distance between the reference point to the gingival margin minus reference point to the base of the pocket.

Gingival recession (GR)

Calculated by subtracting the distance between reference point to CEJ and the distance between reference point to the base of the pocket.

Clinical attachment level (CAL)

Calculated by subtracting the distance between reference point to CEJ and the distance between reference point to the base of the pocket.

TREAMENT PROTOCOL

PRP Preperation[8]

For each patient 6 ml of blood sample was collected from the cubital vein and 1ml of anticoagulant, citrate-phosphate-dextrose-adenine(CPDA) solution was added to 5ml of the blood and remaining 1ml of the blood was kept a side for serum. The test tube

containing 5 ml of the blood was kept for centrifugation (REMI Co.) at a spin of 2500 r.p.m for 10 min .This procedure divided the blood into three components: Red blood cells, PRP and platelet-poor plasma. The red blood cell layer formed at the lowest level, the PRP layer in the middle and the

PPP layer at the top. PRP and PPP were collected in a second test tube then, a second spin was performed at 3600 rpm for 15 minute .The platelet pellet concentrated at the bottom of the test tube whereas the PPP concentrated at the top. The PPP was removed so that the PRP remained in the test tube. The other test tube containing 1ml of blood was kept for centrifugation for 5 minute at 3000rpm to obtain serum.

SURGICAL PROCEDURE

The procedure was done with all necessary precautions. The surgical area was anaesthetized by local anaesthetic techniques using 2%xylocaine with adrenaline 1:80,000 dilution. The procedure was done under proper aseptic precautions using continuous aspiration to keep surgical site clean. In Group I i.e, NBM+PRP+GTR intracrevicular incisions were performed extending to the neighboring teeth then full thickness mucoperiosteal flaps were raised vestibularly and orally.All granulation tissue was removed from the defects and the roots were thoroughly scaled and planed by means of hand and ultrasonic instruments. No conditioning of the root surfaces was performed.

At the time of application PRP was achieved by its combination with an equal volume of a sterile saline solution containing 0.2ml of 10%calcium chloride and 0.5ml of serum. The PRP displayed a sticky consistency within a few seconds. Bovine porous bone mineral granules were mixed with the coagulated PRP. Care was taken not to over fill the defects. Following grafting a bioresorbable healiguide was trimmed, adapted and sutured over the entire defect with 4-0 vicryl suture so as to cover 2-3mm of the surrounding alveolar bone and to ensure stability of the wound and the graft material .The reflected flaps were repositioned and sutured externally using interrupted sutures (4-0 black braided silk) for primary soft tissue closure at the site over the regenerated material. The surgical site was then covered with coe-pack

In Group II sites

The same surgical protocol was also used for this group except for the placement of PRP.

Post operative care

Patients were recalled after 14 days for suture removal and pack and the patients were asked to refrain from mechanical plaque control for 2 weeks at the surgical site. They were advised to rinse with 0.2% CHX (Chlorhexidine) mouth wash twice daily for 4 weeks post operatively to aid in plaque suppression.

Post operative appointments were conducted at 7th, 21st and 30th day followed by third month and six months after surgery to evaluate the surgical site and to provide supportive therapy. The parameters(clinical measurements and standardized radiographs) were evaluated at base line and postoperatively after 6 months

RESULTS

The comparison of mean differences in the PI,GI, PPD, CAL,GR and Depth of the defect between the groups i.e clinical and radiological parameters obtained at the baseline and at 6 months post operatively were analyzed statistically using the Student paired t-test and unpaired t-test. After imaging with digital camera, the radiographs were analyzed with the help of AutoCAD. Following radiographic parameters were assessed at base line(Figure1,2) and 6 months(Figure 3,4)for both the groups.

DISCUSSION

“True periodontal regeneration” is the reformation of a functionally oriented periodontal ligament with collagen fibers inserting in both regrown alveolar bone and reformed cementum over a previously diseased root surface. A number of techniques and autogenic, allogenic, xenogenic and alloplastic bone graft materials have been used for regeneration purpose. The results of the histological studies reported that new attachment achieved by bone grafts was usually a result of the formation of long junctional epithelium with slight or no new connective tissue attachment and negligible new cementum formation. Since these techniques have had limited success, more effective regenerative

approaches have been suggested that utilize tissue-engineering techniques i.e. GTR and PRP.[9]

The positive impact of PRP on bone healing is attributed to angiogenic, proliferate and differentiating effect of PDGF and TGF present in high concentration[10]. Accordingly, in this study ,we decided to combine PRP containing PGFs to NBM/GTR, a clinically effective periodontal regenerative therapeutic modality, because PGFs have the potential to directly affect growth and differentiation of cells involved in the regenerative process and therefore augment the known benefits generated by NBM and GTR. Furthermore, another feature of the PRP-enhanced graft is its high content of fibrinogen that enhances wound stability and promotes cellular migration. Thus the aim of the present study was to evaluate the additional effect of PRP on the treatment of deep intrabony defects comparing the use of NBM+PRP+GTR with NBM+GTR. The results of the present study indicated that both the regenerative approaches could lead to significant clinical improvement in terms of PD reduction and CAL gain, although no statistical significant differences were found between the two treatment modalities.

In group I the mean PD was 6.57±1.7mm at base line and 3.61±0.693mm at six months. For group II the mean PD was 6.12±0.399mm at base line and 3.3±0.63mm at six months. This difference at base line and six months within the groups was statistically significant($p<0.05$) and between the groups was not significant ($p>0.05$). The reason for the reduction in pocket depth can be attributed to the reduction in gingival inflammation and shrinkage of the pocket wall.

At base line, the mean CAL was 6.5±1.04mm in group I and 6.9±0.845mm in Group II. At six months the CAL for group I was 5.0±1.01mm & for group II was 5.1±0.91mm. These changes obtained were statistically significant within the groups ($p<0.05$) and were not significant between the groups($p>0.05$). The reason for the CAL gain can be attributed to the regenerative materials used and surgical techniques which included a, careful preservation of supracrestal soft tissues.

Camargo etal[11] carried out a reentry study comparing treatment with PRP+NBM+GTR and NBM+GTR and showed no statistical significant difference between the groups. **Lekovic etal**[12] reported significant probing depth reduction in the BPBM+PRP+GTR and BPBM+PRP groups ,with no significant difference between the groups. **Dori etal**[6] compared the treatment of deep intrabony defects with NBM+PRP+GTR and NBM+GTR. They concluded that no statistically significant difference was found between the groups. **Iigenli etal**[7] compared DFDBA/PRP combination with PRP alone and showed greater PD reduction, CAL gain ,bone fill in the DFDBA/PRP group than PRP alone. **Prerna etal** [13]compared three groups ie., PRP with OFD & PRP+DFDBA+OFD & only OFD and attributed that the amount of defect depth reduction and defect resolution treated with PRP alone group were significantly < PRP + DFDBA. The results pertaining to these parameters were significantly better than the control group. **Gouri etal** [14]conducted a study to evaluate the use of porous hydroxyapatite bone graft with and without platelet-rich plasma (PRP) in the treatment of intrabony defects. It was concluded that PRP addition to a bone graft in the treatment of periodontal intrabony osseous defects shows improved defect fill as compared to the use of bone graft alone. **Jalaludin etal**[15] conducted a study and showed no statistically significant difference in the treatment outcome between open flap debridement and PRP alone.

The present results obtained in the NBM+GTR group compared well to those obtained in previous controlled clinical studies of Camargo **2000** which have shown higher PD reduction and CAL gain in the NBM+GTR group compared to OFD.

It has been documented that differences in the level and proportion of various growth factors may be found between currently available commercial systems that in turn may affect outcomes[18]**.** There is possibility that PRP beneficial effect may be masked when used in combination with NBM due to the fact that treatment with NBM alone resulted in significant improvements. In this study no blood parameters or growth factor concentration were evaluated[18]. Of course, this entails the risk of production of PRP volumes with low platelet/growth factors concentration that can result in disappointing results. The rather limited result obtained in PRP group may be explained by use of natural bone mineral which does not contain

any vital bone cells and thus, may be either not or only to a minor extent be influenced by PRP[6] When PRP is considered for use in the clinical practice of periodontics, several factors have to be taken into account ,including the clinician efficiency in drawing the necessary blood, the cost of the centrifugation machine, disposable materials, extra time and steps to prepare the coagulated PRP for its actual use. To avoid technical and financial restrictions ,some clinicians have to elect blood laboratories to perform the centrifugation of platelets prior to the surgical procedure[19].

To entirely evaluate the regenerative therapies used in this study, radiographic comparisons would have given us information on the effects of the PRP on crestal heights and/or bone densities related to the intrabony defects. It must be kept in mind that the radioopaque nature ofthe grafting material used in this study would not have been a valid comparison .An alternative assessment of osseous behavior would have been through direct measurements of the defects at reentry procedures. At present data from histologic studies are not available for evaluating healing following treatment with NBM+PRP+GTR and thus, it is still unclear to what extent the use of PRP may enhance or impair the regeneration process compared with other, less complicated treatment modalities such as NBM+GTR. Long term evaluation is preferable as it could indicate the clinical stability of the results obtained.

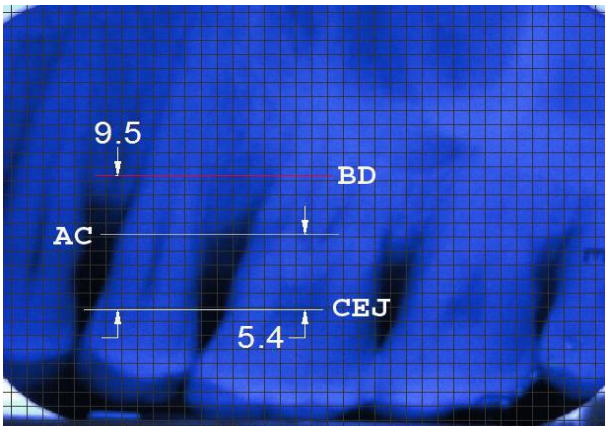

Fig 1: Group 1 Baseline radiograph.

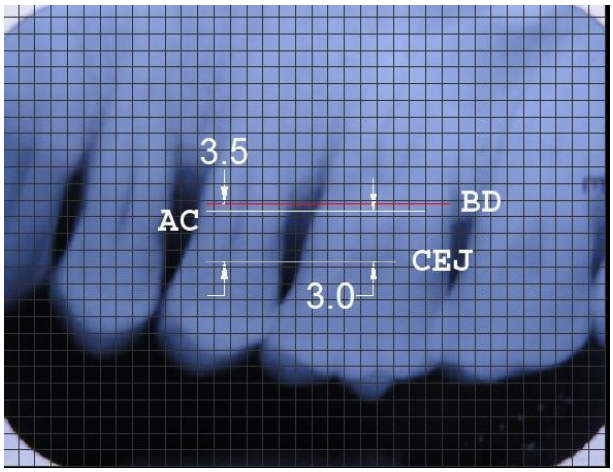

Fig 2: Group 1 6 month radiograph.

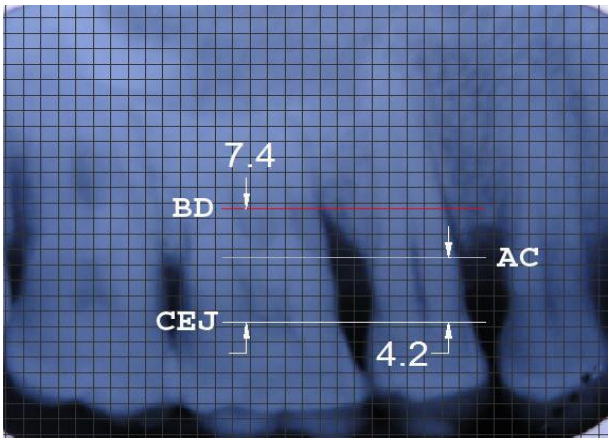

Fig 3: Group 2 Baseline radiograph.

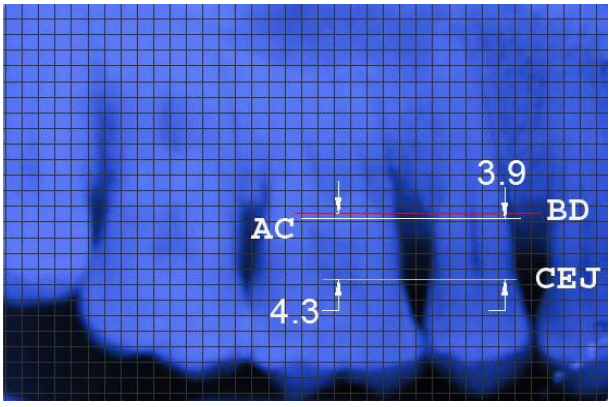

Fig 4: Group 2 6 month radiograph.

Table I: Comparison of Plaque Index between Group I and Group II at base line and after 6 months.

Groups	Baseline			6 months			t value	P value
	N	Mean	SD	N	Mean	SD		
Group I	8	0.9	0.139	8	0.07	0.116	16.909	0.00[S]
Group II	8	0.8	0.282	8	0.08	0.210	5.738	0.001[S]
t- value	0.450			-0.147				
P- value	0.659[NS]			0.885[NS]				

Table II: Comparison of Gingival Index between group I and group II at base line and at 6 months

Groups	Baseline			6 months			t value	P value
	N	Mean	SD	N	Mean	SD		
Group I	8	1.150	.407	8	.3100	.45507	5.569	.003[S]
Group II	8	1.287	.524	8	.325	.4367	5.020	.002[S]
t- value	-0.585			-0.057				
p-value	0.568[NS]			0.955[NS]				

Table III: Comparison of Probing Pocket depth between Group I and Group II at base line and at 6 months

Groups	Baseline			6 months			t value	P value
	N	Mean	SD	N	Mean	SD		
Group I	8	6.575	1.715	8	3.6125	.693	5.152	.001[S]
Group II	8	6.125	.399	8	3.3625	.639	8.930	.000[S]
t- value	0.723			0.750				
P- value	0.482[NS]			0.466[NS]				

Table IV: Comparison of Gingival Recession between Group I and Group II at base line and at 6 months

Groups	Baseline			6 months			t value	P value
	N	Mean	SD	N	Mean	SD		
Group I	8	1.000	.509	8	1.7500	.845	-1.976	.000[S]
Group II	8	1.012	.659	8	2.0125	.467	-8.478	.000[S]
t- value	0.398			-0.722				
P- value	0.696[NS]			0.482[NS]				

Table V: Comparison of Clinical Attachment Level between Group I and Group II at base line and at 6 months.

Groups	Baseline			6 months			t value	P value
	N	Mean	SD	N	Mean	SD		
Group I	8	6.562	1.041	8	5.137	1.014	4.115	.004[S]
Group II	8	6.950	.8451	8	5.075	.9130	13.66	.000[S]
t- value	-0.817			0.130				
P- value	0.428[NS]			0.899[NS]				

Table VI: Comparison of intrabony defect depth(IBD) between Group I and Group II at base line and at 6 months.

Groups	Baseline			6 months			t value	P value
	N	Mean	SD	N	Mean	SD		
Group I	8	3.98	0.51	8	0.85	0.37	27.3	0.00[S]

Group II	8	3.72	0.59	8	0.56	0.34	23.9	0.00[S]
t- value	0.93			1.59				
P- value	0.36[NS]			.133[NS]				

CONFLICTS OF INTEREST

The authors declare they have no potential conflict of interests regarding this article.

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