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Research Article

EVALUATION OF EFFICACY OF CONCENTRATED GROWTH FACTOR (CGF) BIOMATERIAL IN THE TREATMENT OF INTRABONY DEFECTS –A RANDOMIZED CLINICAL TRIAL

Beanish Bashir., Suhail Majid Jan., Roobel Behal., Reyaz Ahmed Mir and Syed Saima

Department of Periodontics, Government Dental College and Hospital, Srinagar, Jammu and Kashmir, India

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A B S T R A C T

Aim: To document the beneficial role of CGF as an adjunct to open flap debridement (OFD) in treatment of intrabony defects in chronic periodontitis patients.
Materials and Methods: 20 intrabony defects in 20 patients were randomly divided into 2 groups and were treated with OFD (group A) or CGF +OFD (group B). Clinical parameters such as plaque index (PI), probing depth (PD), relative attachment level (RAL) and the hard tissue parameter Alveolar crest to the base of the defect (AC-BOD) were assessed at baseline and 9 months postoperatively.
Results: Statistically significant intra group improvements were seen with all the hard tissue and soft tissue parameters in both test and control groups. Statistically significant improvements were seen with the mean defect fill (AC-BOD) when intergroup comparisons were made.
Conclusions: The study demonstrated that CGF improves clinical and radiological parameters compared to OFD alone in intrabony defects.

INTRODUCTION

The aim of periodontal therapy is to eliminate inflammatory process, prevent the progression of periodontal disease and regenerate the lost periodontal tissues.[1]Various techniques and biomaterials have been attempted to regenerate the lost bone structures in addition to autogenous and allogenic bone grafts, but complete and predictable reconstruction of periodontal tissues is still difficult to obtain. Concentrated growth factor introduced by Sacco in 2006, in its solid form, is obtained by centrifuging of blood samples collected in vacuum tubes, using a special centrifuge device, similar to Choukroun's platelet rich fibrin (PRF).[2-7] CGF technology has an interesting characteristic: i.e. the easy and speedy one-step preparation of a larger, denser and richer in growth factors fibrin matrix than the other solid PRPs. Rodella and colleagues[8] showed the presence of a fibrin network constituted by thin and thick fibrillar elements with multiple platelets trapped among the fibrin network. The growth factors, are a class of natural biological mediators that regulate key cellular events in tissue repair, including cell proliferation, differentiation and extracellular matrix synthesis. Platelet activation and degranulation causes the release of a large number of biological factors, including Platelet Derived Growth Factor (PDGF), Vascular Endothelial Growth Factor (VEGF), Insulin-like Growth Factor (IGF), Transforming Growth Factor (TGF), Tumor Necrosis Factor (TNF), Brain Derived Growth Factor (BDNF) and Bone Morphogenetic Proteins (BMP).[9-12] Previous studies have demonstrated that local application of growth factors alone or mixed with bone allograft increased bone growth, by accelerating healing of soft tissues and facilitating periodontal ligament repair in both animal and human studies.[13] The presence of autologous cells such as platelets and leukocytes, including the CD34 positive cells, have also been described.[8] Increasing evidences points to the role of circulating CD34 positive cells[14,15] in vascular maintenance, neovascularization and angiogenesis.[16,17] The presence of these cells in PRP preparations, promotes tissue regrowth.[18] Application of CGF may prove to be an effective method of improving the healing of bone defects and can also serve as a resorbable interpositional membrane. CGF layer avoids early invagination of gingival epithelium, thereby serving as a barrier to epithelial migration.[19]

The present study was carried out to document the beneficial role of CGF as an adjunct to open flap debridement(OFD) in treatment of intrabony defects in chronic periodontitis patients.

MATERIALS AND METHODS

A 9 month randomized, parallel group interventional study was conducted compromising of 20 patients with chronic periodontitis. The participants enrolled for the study were informed verbally, and written consent was obtained before the start of the trial. Inclusion criteria included systemically healthy patients diagnosed with chronic periodontitis having ≥20 teeth and ≥30% of sites with >4 mm clinical attachment loss (CAL), probing depth (PD) ≥5 mm, and presence of intrabony defect (IBD) ≥3 mm (measured from alveolar crest

Corresponding author:* **Beanish Bashir
Department of Periodontics, Government Dental College and Hospital, Srinagar,Jammu and Kashmir, India

to the base of the defect on intraoral periapical radiograph). Subjects with known systemic disease or on any medications known to interfere with the outcomes of periodontal therapy, or subjects using tobacco in any form, or subjects who have undergone any periodontal therapy in the preceding 6 months, pregnant or lactating mothers, were excluded from the study. Patients who had unacceptable oral hygiene after the reevaluation of Phase 1 therapy were also excluded from the study.

Nonsurgical Periodontal Therapy (Phase 1 therapy): At the baseline all the patients received oral hygiene instructions and non surgical periodontal therapy.

Randomization: Allotment of participants within the groups was performed randomly by creating a computer generated randomization list. The treatment allocation of the patients was prepared and sealed in the numbered opaque envelopes and were opened during surgery immediately after completing the defect debridement. All the surgical procedures in two groups were performed by a trained periodontist. The pre and postoperative assessments were performed by another examiner (RS) without knowledge of the nature of intervention.

Clinical Parameters: Plaque scores were assessed using Silness and Loe.[20] Probing depth (PD) was measured as the distance from gingival margin to the base of the pocket. An occlusal stent was prepared with cold cure acrylic resin and a groove was made on the stent in relation to each selected tooth to guide the probe position.[21] Relative attachment level (RAL) was measured from apical border of the stent to the base of the pocket. All measurements were recorded to the nearest millimetre using University of North Carolina no. 15 (UNC-15, Hu-Friedy, Chicago, IL, USA) periodontal probe.

Radiographic Assessment: Intraoral periapical (IOPA) radiographs were obtained by long cone paralleling technique to obtain standardized radiographs at baseline and 9 months postsurgery. The anatomical landmarks of the defects were selected based on the criteria set by Schei *et al*.[22] which include CEJ, alveolar crest (AC), and base of the defect (BOD). For measurement of bone defect, distance from the crest of the alveolar bone to the base of the defect (AC-BOD) was considered.

Surgical Therapy

After administration of Local anesthesia (2% lidocaine with 1:80000 adrenaline) bone sounding was done to identify the extension of the defect. Intrasulcuar incisions were given buccally and lingually involving one tooth mesial and distal to the intrabony defect and mucoperiosteal flaps were reflected. Vertical incisions were avoided. After performing meticulous defect debridement, direct measurement of the osseous defect was obtained with UNC-15 periodontal probe.

CGF preparation[23]: The CGF was produced as follows: 9 mL of blood was drawn into 2 sterile test tubes. These tubes were then immediately centrifuged in a special machine using a program with the following characteristics: 30 seconds acceleration, 2 minutes at 2,700 rpm, 4 minutes at 2,400 rpm, 4 minutes 2,700 rpm, 3 minutes at 3,000 rpm and 36 seconds deceleration and stopped. At the end of the process, three blood fractions were identified: (1) the upper layer, representing the liquid phase of plasma named platelet poor plasma (PPP), (2) the lower layer, at the bottom of the tube, consisting in free red blood cells (RBC); (3) the middle layer, representing the solid CGF, consisting in three parts: the upper white part (WP), the downer red part (RP) and the middle "buffy coat" (BC), interface between white and red part. After centrifugation, CGF was removed from each tube, using sterile tweezers. The solid CGF was obtained by cutting and discarding the lower fraction of the red part of CGF, 0.5 cm under the white part.

In the CGF group the defects were filled with GCF. The control group defects were treated with OFD only. The flaps were secured with interrupted 3-0 black braided silk sutures.

Post Operative Care

Systemic antibiotic (Augmentin 625mg) 3 times daily for 5 days and analgesics (Diclofenac (Exudase DP) three times a day, for 5 days) were prescribed to the patients. Patients were also instructed to avoid brushing, flossing and chewing in the surgical area for a period of 2-3 weeks. All the patients were instructed to use 0.2% chlorhexidine rinses twice daily for 2 weeks. Sutures were removed 1 week postoperatively.

Statistical Analysis: The data were analyzed using statistical software SPSS (version 20.0) and Microsoft Excel (version 5.00). The results were averaged (mean standard deviation) for each clinical and radiographical parameter at baseline and 9 months. Inter group analysis of data was done by applying Student's independent t-test (also known as unpaired t-test) and for intra group analysis, Paired t-test was employed. A p-value of less than 0.05 was considered statistically significant.

Results

All participants were followed up for a period of 9 months. Postoperative healing of all the control and test sites were uneventful. Participant's age, gender, defect characteristics, and location are presented in table 1

Table 1 number, age, gender, osseous defect morphology, and defect location

Parameters	Group A (OFD only)	Group B (OFD+CGF)
No.of patients (sites)	10	10
Gender (m/f)	6/4	5/5
Mean age	45	44.5
Defect location(maxilla/mandible)	6/4	5/5
Osseous defect (2 wall/3 wall)	4/6	3/7

Clinical Parameters

A statistically significant reduction in the PI (table 2) and pocket depth(PD) (table 3) was seen in both the groups at 9 months postoperatively($p<0.05$). Mean reduction in PD was higher in group B compared to group A, however, the results were not statistically significant. Both the groups revealed significant ($p<0.05$) gain in the RAL(Table 3). Intergroup comparison showed a insignificant gain in RAL in group B compared to group A.

Table 2 PI scores in groups (A and B) at baseline and 9 months

Parameters	Group A (OFD) Mean ± SD P-value	Group B(OFD + CGF) Mean ± SD P-value
Plaque index		
Baseline	1.312±0.377 < .005	1.439±0.496 < .005
9 months	0.485±0.173 < .005	.582±0.207 < .005

Table 3 PD, RAL scores in groups (A and B) at baseline and 9 months

Parameters	Group a (ofd) Mean ± sd	P-value	Group b (ofd+ cgf) mean ± sd	P - value
Pocket depth (pd) Baselin*				
e	5.6 ± 1.0747	0.0004	5.4 ± 0 .965	0.000007
9 months	3.1 ± 0.7348		2.5 ± 0.5263	
Relative attachment level (ral)				
Baseline	9.2 ± .6324	0.000005	9.5 ± 1.0798	0.000002
9 months	7.1 ± 0.5676		6.7 ± 0.8228	

Radiographic parameters+

Both the groups showed a significant reduction in Defect depth (AC-BOD) at 9 months postoperatively ($P < 0.05$). Inter-group analysis revealed a statistically significant ($P < 0.05$) mean Defect depth reduction in group B compared to group A. (Table 4)

Table 4 Radiographic defect depth over 9 month period

Parameters	Group a (ofd) Mean ±sd	p-value	Group b (ofd + cgf) Mean ±sd	p-value
Defect depth Alveolar crest (ac) – base of defect (bod)				
Baseline	3.5 ±0.4711	0.00002	3.55± 0.4377	0.000007
9 months	2.39 ± 0.3025		1.7± 0.4189	

Table 5 Comparison of groups (A, B) with respect to mean changes in clinical parameters and radiographic DD over 9 month period

Parameters	Group a(ofd) Mean ± sd	Group b(ofd+ cgf) Mean ± sd
Mean pd change	2.5 ± 0.3399	2.9 ± 0.439
Mean ral gain	2.1 ± 0.316	2.8 ± 0.632
Mean dd reduction	1.11 ± 0.4444	1.85 ± 0.395

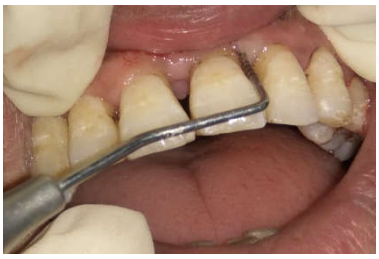

Figure 1, probing of defect

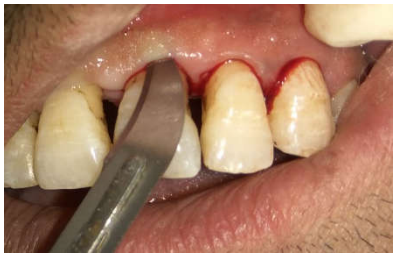

Figure 2, crevicular incision

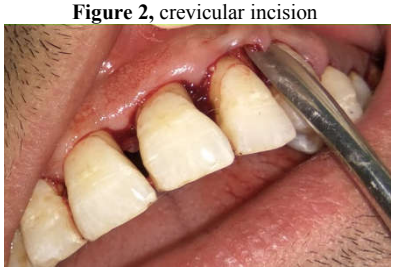

Figure 3, Reflection of Flap

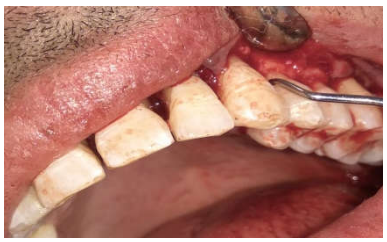

Figure 4, Debridement of defect

Figure 5, CGF prepared

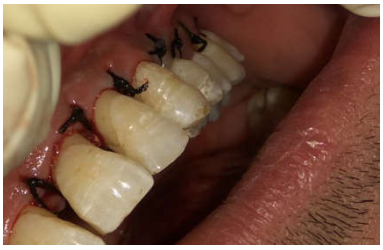

Figure 6, sutures placed

DISCUSSION

"Concentrated Growth Factors" (CGF) is one of the several types of platelet-rich plasma preparations (PRP) developed to date[24] representing a new generation of PRP, which exhibits an interesting clinical and biotechnological potential. PRPs are defined as preparations with a high concentration of platelets in a small volume of plasma,[25] containing also growth factors, leukocytes and fibrin matrix.[26-30] These 100% autologous preparations not only enhance tissue healing, but also improve the clinical outcomes of various surgical procedures, reducing complications such as pain, inflammation and morbidity.[31] CGF seems to possess a good regenerative capacity and versatility. For example, it has been reported that CGF has a positive effect for the following: sinus and alveolar ridge augmentation;[32] promotion of *in vitro* proliferation, osteogenic maturation and mineralization of mesenchymal stem cells and healing of critical-size bone defects *in vivo*;[33] promotion of *invitro* periodontal ligament stem cells proliferation,[34] management of chronic venous ulcers.

The present study evaluates the clinical efficacy of CGF in the treatment of IBD in patients with chronic periodontitis and shows a significant improvement in clinical and radiographic parameters. Only 2 or 3-wall IBDs were included because various wall defects have different potentials for regeneration. The number of remaining bony walls were found to be correlated positively with regeneration potential in grafting procedures.[35,36] In addition, 2 or 3 wall defects provide the best spatial relationship for defect bridging by vascular and cellular elements from the periodontal ligament and adjacent osseous wall. While monitoring changes in clinical and radiographic parameters, improved PD reduction was observed in CGF treated sites (groups B) compared to group A. An impressive

RAL gain (2.8 ± 0.632), was observed in CGF group compared to control group. Defect depth (DD) reduction (1.85 ± 0.395) was observed in group B. The improvement in PD, RAL, DD observed in CGF treated sites of present investigation are along the expected lines and in accordance with a recent systematic review.[37] Hence, the results of this trial add to the current evidence regarding the use of CGF with grafting material. The main limitations of our study are less sample size and inability to perform histological analysis due to ethical reason.

CONCLUSION

Within the limits of this study, it is concluded that treatment of intrabony defect with CGF appears to be associated with improvement in clinical and radiological parameters with uneventful healing. Considering the autologous nature, minimal cost and time, CGF can be incorporated as a regenerative material in intrabony defects.

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