The use of Autologous Concentrated Growth Factors in Osseous Regeneration after Periapical Curettage: A Clinical Study

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ABSTRACT

Introduction: The contemporary research interest in autologous platelet concentrates is backed by an emerging evidence of their promising regenerative potential in number of clinical applications. Periapical inflammatory lesions represent a chronic pathology of the periapical tissues that result in considerable bone resorption and worsen the overall tooth prognosis. With this background, the present study was designed to evaluate the effect of the most recent platelet concentrate preparation, concentrated growth factors (CGF) on osseous regeneration after surgical management of periapical lesions.

Material and methods: A prospective study was done in twenty patients where CGF was used to fill the periapical defects after periapical curettage. Area of radiolucency and mean gray values were assessed at baseline, 1 month, 3 months and 6 months after surgery using Image J software. Paired t-test was used to evaluate changes occurring between baseline and 1 month and baseline and 6 months.

Results: And early and enhanced healing was evident form the substantial decrease in area of radiolucency, and mean grayscale values indicated a progressive increase in bone density during the observational period. These changes were highly significant ($P< 0.05$).

Conclusion: CGF can be used as an efficacious and cost-effective alternative to conventional bone substitutes for promoting healing after the surgical debridement of periapical defects.

Keywords: Periapical Surgery, Concentrated Growth Factors, Bone Density

INTRODUCTION

Traditional surgical approaches to treat periapical defects include debridement of apical lesions along with reshaping of the surrounding bone, resection, and retro filling of root apex, where healing is almost always by repair.[1] Repair is defined as the healing of a wound by tissue that does not fully restore the architecture or the function of the part.[2] Since this is not ideal, newer approaches such as regenerative procedures that aim to restore lost tissue have been introduced. Conventionally, bone grafts and bone substitute materials have been used for this purpose; their use being loomed by concerns of higher costs, biocompatibility, cross-reactivity and disease transmission. These inhibitions have led to the quest for autogenous sources of bone substitutes.

Recent advances in haematological technology have led to the development of autogenous platelet derived, growth factor rich fibrin scaffolds, known as the autologous platelet concentrates.[3] These have been shown to have a promising potential for promoting wound healing and regeneration, which is ascribed to the sequestration and degranulation of activated platelets. This releases a number of growth factors crucial for initial wound healing processes such as vascular proliferation, mesenchymal cell recruitment and activation, as well as osteogenesis.[3]

Prepared by centrifugation, these platelet concentrates have classically evolved through generations, the first being represented by PRP, the second by PRF and the third by CGF (Concentrated Growth Factors). Described by Sacco in 2006,[4] CGF is an aggregate of WBC's, CD34+ stem cells and activated platelets along with indigenous growth factors in a cross linked meshwork of fibrin, which is denser and tougher than PRF, besides having higher growth factor concentrations.[5]

The regenerative potential of CGF has been demonstrated in a number of applications, e.g. sinus and ridge augmentation,[6,7] neurosurgery and sports medicine.[8,9] On these lines it was foreseen that this platelet concentrate could also potentially optimize the healing of inflammatory periapical lesions.

Hence the present study was designed to evaluate the effect of CGF on healing and resolution of periapical inflammatory lesions when used in conjunction with periapical surgery.

MATERIAL AND METHODS

The study was designed as a prospective cohort study, conducted at the Department of Periodontology, Government Dental College and Hospital Srinagar, with prior ethical clearance. Twenty patients in the age group of 20-40 years were included based on the presence of (i) periapical radiolucency >1cm diameter (ii) normal platelet count. Patients were excluded if they had a history of any systemic illness/medication/condition that might affect healing or coagulation.

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How to cite this article: Huda Hussain, Suhail Majid Jan, Roobal Behal. The use of autologous concentrated growth factors in osseous regeneration after periapical curettage: a clinical study. International Journal of Contemporary Medical Research 2019;6(6):F5-F8.

DOI: http://dx.doi.org/10.21276/ijcmr.2019.6.6.45

Informed consent was obtained from the patients and they were prepared by thorough phase I therapy to control any existing periodontal inflammation.

Surgical treatment

Periapical surgery was performed following the standard surgical technique using crevicular and two releasing incisions for thorough debridement, periapical curettage, root end resection and retrograde filling using glass ionomer cement. CGF was prepared using 10 ml of blood centrifuged according to the protocol by Rodella et al.[10] At the end of the process, blood was separated into three phases: (i) upper Platelet Poor Plasma (ii) middle CGF (iii) lower RBC layer. The CGF phase was isolated and used to fill the periapical defects. Primary closure was obtained and standard postoperative instructions and medications (diclofenac sodium 50 mg TID + amoxicillin-clavalunic acid 625mg TID for 5 days) were prescribed. The patients were recalled at 1 week for suture removal, and at 1 month, 3 months and 6 months thereafter, when they were examined clinically regarding postoperative discomfort, pain, sensitivity to percussion, and presence/absence of swelling.

STATISTICAL ANALYSIS

Radiographic assessment using standardized radiographs was done at baseline, 1 month, 3 months and 6 months after surgery to evaluate defect resolution and density changes using Image J software version 1.8.0, (National Institute of Health, US) in terms of area of radiolucency and mean gray values. Paired t-test was performed using SPSS for windows (version 20) to evaluate changes between baseline and 1 month and baseline and 6 months.

RESULTS

13 male and 7 female patients were followed for the study. There were no signs of infection or rejection, untoward reaction, wound dehiscence, extrusion of material in any of the patients, and an uneventful soft tissue healing was achieved. Follow-up radiographic examination by area and mean grayscale study revealed progressive, predictable, and significant radiographic osseous regeneration and an increase in bone density ($p<0.05$) (Table1) (Fig 2,3). Radiographically, all patients showed that CGF promotes faster osseous regeneration within the 1st postoperative

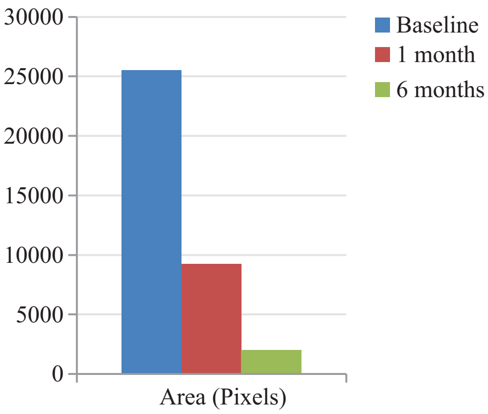

Figure-1: Change in Average area of Radiolucencyy

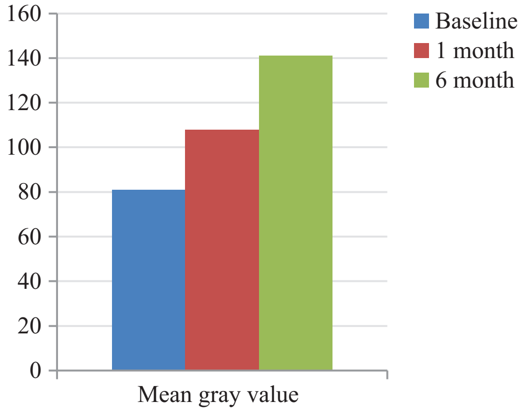

Figure-2: Change in Average Bone density

Figure-3: Case1-Baseline clinical defect, CGF prepared and filled in defect. Radiographic appearance at baseline, 3 months and 6 months

Figure-4: Case2-Radiographic appearance at baseline, 1 month and 6 months

Parameter	Between baseline and 1 month	Between baseline and 6 months
Area of radiolucency	0.021	0.017
Mean gray value	0.010	0.007

Table-1: P value of parameters

month, and within 6th postoperative month, almost complete bone regeneration was seen.

DISCUSSION

Contemporary treatment standards focus on augmenting natural healing with bone substitutes in an attempt to optimize conditions for regeneration rather than repair. Though the spontaneous resolution of periapical defects after surgical curettage does occur, it is slow and unpredictable.[11] Recently, Lin et al.[12] have demonstrated that the healing of periapical tissues is a "programmed event." More than the size of the lesion, it is the microenvironment consisting of the progenitor/stem cells, extracellular matrix, and bioactive molecules that plays a crucial role in tissue regeneration or scar formation during wound healing. Conventionally used bone grafts provide a scaffold and may sometimes also provide inductive factors for bone formation. Conversely, platelet concentrates provide a fibrin scaffold with indigenous growth factors that are crucial for initial angiogenesis, fibroblast proliferation and extracellular matrix formation—without the concerns of cross-reactivity and biocompatibility.[3] Though the use of PRF has been demonstrated for this application in earlier studies,[13,14] the use of CGF for periapical defects has been reported only as subjective case reports,[15,16] where substantial healing of periapical defects was seen. With regard to CGF, besides these effects, a direct effect on osteoblast proliferation[17] has been shown which results in early bone healing.[18] The present study corroborates these findings, as evidence of changes in bone density and area of radiolucency were seen as early as 1 month with the use of CGF in the periapical defects. Pertinently, such changes occur after 1 year for small, and more than one year for large periapical lesions that are left to heal spontaneously.[11]

With regard to changes seen in bone density of the healing lesion, a progressive increase was noted throughout the observational period, which indicates a successive maturation of the newly formed tissue and confirms the regenerated tissue to be bone rather than reparative granulation tissue. These findings also implicate a shortening of the overall healing period with the use of CGF. Similar increase in bone density has been reported for postextraction implants[19] and alveolar grafting[20] using CGF, and may perhaps result from the documented osteopromotive effects of CGF.[21]

Overall, the present observations reflect an impression of accelerated healing with the use of CGF in periapical defects. As the CGF matrix has been shown to release growth factors uptil 28 days[22], concurrent with the decisive processes of angiogenesis, mesenchymal cell recruitment, and matrix formation, it can be postulated that these effects together facilitated a "regenerative microenvironment" for early resolution of the periapical defects.

CONCLUSION

Within the limits of this study, it can be concluded that CGF can be used as a safe, efficacious and cost-effective alternative to conventional bone substitutes for promoting early resolution of periapical defects. Further studies in comparison with other platelet concentrates are implicated to elicit possible mechanistic differences between these autologous products.

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Source of Support: Nil; **Conflict of Interest:** None

Submitted: 09-05-2019; **Accepted:** 01-06-2019; **Published:** 26-06-2019