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Original Article

Effect of in-situ application of simvastatin gel in surgical management of osseous defects in chronic periodontitis–A randomized clinical trial

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ABSTRACT

Background: The present randomized controlled clinical study was designed to investigate the effect of in situ application of 1.2 mg Simvastatin (SV) gel in the surgical management of Intrabony defects in chronic periodontitis patients.
Methodology: 20 patients contributing 40 sites were categorized into two treatment groups: Open flap debridement plus 1.2 mg SV gel (Group 1) and Open flap debridement plus Placebo gel (Group 2). Gingival index (GI), Plaque index (PI), Pocket depth (PD) and clinical attachment level (CAL) were recorded at baseline, 3 months, 6 months and 9 months. At baseline and at the end of 6 and 9 months Radiographic evaluation of Intrabony defect fill was done using Image j software.
Results: Significant reduction of GI, PD and gain in CAL was observed at the end of 9 months in both groups. Amount of bone fill and percentage of original defect fill in Group 1 was statistically highly significant than Group 2 at the end of 6 and 9 months.
Conclusion: Higher amount of decrease in GI and PD along with more amount of CAL gain was observed in treatment group than control group. Radiological assessment confirmed that significant intrabony defect fill and percentage fill of original defect in treatment group than controlled group.

1. Introduction

Periodontitis, an inflammatory disease of periodontium is considered to be caused by bacterial biofilm (Dental plaque), and its onset and progression are modulated by a variety of risk factors, such as systemic conditions and smoking. If Periodontitis left untreated, results into periodontal attachment loss and subsequently tooth loss. Various methods are effective in repairing these periodontal defects by creating space and host bone formation through the use of various periodontal regenerative materials.1 Autologous bone graft is ideal grafting material for the treatment of periodontal defects and fracture repair.2 However, need for a second surgical site is the most important drawback which has led to the development of alternative materials. Growth factors (e.g.: bone morphogenetic proteins) are expensive, may degrade with rapid rate at the treated site and sometimes may elicit immune responses, thus limiting their use.3

Not satisfied with traditional weapons to restore lost alveolar bone support, researchers have turned towards new contemporary methods for periodontal regeneration.4 The newer approaches e.g. Extracorporeal shock wave therapy, Photodynamic therapy, polishing with glycine powder to prevent subgingival plaque formation, topical and systemic administration of Simvastatin etc are still in infancy but show promise nonetheless. Pharmacologic compounds e.g. Simvastatin stimulate bone growth by inducing growth factors. This newer contemporary approach may prove to be a cost-effective, non-space occupying way to correct bone defects.5

Statins block conversion of hydroxy-3-methyl-glutaryl coenzyme A (HMG-CoA) to Mevalonic acid, required for cholesterol biosynthesis. By this, it reduces cardiovascular mortality and morbidity and helpful in prevention of primary and secondary coronary artery disease.6 Other than this primary effect, few cholesterol independent effects have also been shown by statins, called as pleiotropic effect. It consists of effects on vascular tissue, heart, kidney, glucose and bone metabolism.7

Recent literatures have shown that SV assists in bone regeneration as well as has the anti-inflammatory effect when delivered systemically or applied locally.8 SV also increases the expression of osteocalcin, Type I collagen and bone sialoprotein

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with significant amount of anti-inflammatory effect by reducing the production of interleukin-6 and interleukin-8.9 SV is reported to increase vascular endothelial growth factor (VEGF) in dose dependent manner and the authors have suggested that statins may promote osteoblast differentiation by stimulating VEGF expression in bone tissue.10

Various controlled drug releasing vehicles have been mentioned in literature such as Carbopol, hydroxylpropyl methylcellulose etc.11,12 Traditionally in the management of mild to moderate pockets tetracycline fiber, metronidazole gel, chlorhexidine chip etc have been used as local drug delivery agents. Vehicles used for this type of drug delivery should be bio compatible with easy fabrication and predictable biodegradable kinetics. Carbopol has been used extensively in pharma industry, such as the solution of various ophthalamic drug deliveries.13

SV is a new pharmacological agent introduced as a host modulatory agent in periodontal therapy. Very few clinical trials have been reported using SV as a local host modulatory agent in the management of periodontal diseases. Keeping the above facts in mind, the present study was carried out as randomized controlled split mouth placebo control single centered clinical trial to investigate clinically and radiologically (bone fill) the effect of in-situ gel application of 1.2 mg SV in the surgical management of osseous defects in chronic periodontitis. Aim of the present study was to evaluate whether SV used in-situ gel after surgical debridement will have any added value in Clinical (Gingival index, Plaque index, Pocket Probing depth, Clinical attachment level) and Radiographic parameter (Bone fill) over the period of 9 months.

2. Materials and methods

2.1. Source of data

Patients for this study were recruited from the outpatient section of the Department of Periodontics, KLE Society's institute of Dental Sciences, Bangalore, Karnataka. Twenty patients, aged between 25–55 years (10 males and 10 females) diagnosed with generalized chronic periodontitis, contributing 40 sites were enrolled for the study by convenience sampling method. It was made clear to the all subjects that participation was voluntary. Written informed consent was obtained from each and every patient, and ethical clearance for the study was received from the university ethical Committee and registered with clinical trial registry of India. (CTRI/2016/11/007428).

2.2. Selection criteria

Patients without any systemic illness having periodontal probing depth of $\geq$5 mm clinically and radiographic evidence of vertical bone loss in the mandibular molar region bilaterally without any history of periodontal therapy and antiobiotic administration in last 6 months were included for this study. Patients with history of administration of NSAID drugs, patients with aggressive periodontitis, current smokers patients, patient on systemic statin therapy, patients with immunocompromised medical status, patients with bleeding disorders, pregnant and lactating female patients and patients indicated for multiple extractions or undergone multiple extractions were excluded from the study.

All selected patients, following an initial examination and treatment planning discussion, were given detailed instructions regarding plaque control measures and received preliminary periodontal therapy consisting of scaling and root planing. Clinical parameters, including Gingival Index (GI),14 Plaque index,14 Probing pocket depth (PPD) and Clinical Attachment Level (CAL) were recorded full mouth as well as site specific at baseline and at the end of 3, 6 and 9 months post operatively.

For Probing Pocket Depth (PPD) measurements, a customized acrylic stent was fabricated to reduce the measurement error using cold cure acrylic resin on each patient's study cast to fit over the teeth selected for the study. A metal wire was adapted 1 mm above the gingival margin on the buccal surface of the selected teeth and fused to the stent. The pocket depth was measured using a University of North Carolina No 15 (UNC-15) probe.15 The customized acrylic stents on the prepared study casts were stored in water to minimize distortion and to record the measurement at 3 months, 6 months and 9 months post –operatively. Clinical Attachment Level (CAL) was measured by considering fused metal wire of customized acrylic stent as the fixed reference point. The distance from the metal wire [Fixed reference point (FRP)] to the free gingival margin (FGM) was recorded. The level of attachment was determined by adding this distance to the probing pocket depth (PPD).16

2.3. Radiographic assessment of intrabony defects: (Fig. 1)

Intraoral direct digital periapical Radiovisiograph (RVG-Suni Medical Imaging, Inc.) of each defect site was exposed using long cone paralleling technique. The mandibular molar regions with bilateral intrabony defects were the selected site for the study. Exposures were made at 70 KVp, 7 ma for 0.2 s. The focus to film distance was 20 cm and film holder (Troll byte plus) was used. The radiographs were taken by the same clinician throughout the study to minimize errors. To estimate magnification, an orthodontic wire with known diameter (0.8 mm) and length (10 mm) was incorporated in a customized occlusal splint.17 On the digitized images Linear measurements were made using Image J software (Wayne Rasband, National institute of health-USA). Intrabony defect depths were determined by linear measurement analysis of RVG. The following two distances were assessed by RVG for each defect :

- Cementoenamel junction (CEJ) to Alveolar crest (AC)
- Cementoenamel junction (CEJ) to Base of defect (BD)

Base of the defect was defined as the most coronal point where the periodontal ligament showed a continuous width. If identification of periodontal ligament is difficult then the point where the projection of the alveolar crest crossed the root surface was used. If both the structures could be identified at one defect, the landmark defined by the periodontal ligament was taken as the base of the

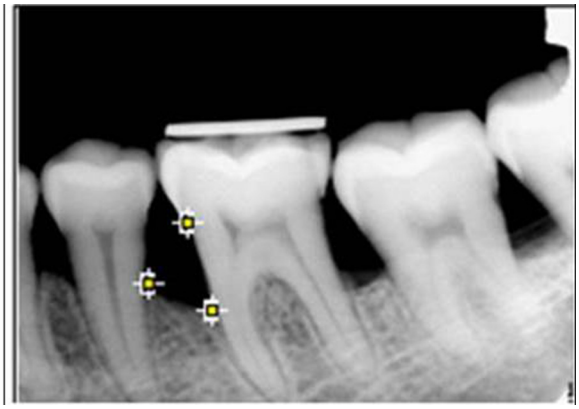

Fig. 1. Amount of bone fill was measured by Linear measurement analysis of RVG, considering three landmarks: Cementoenamel junction (CEJ), Alveolar crest (AC) and Base of the defect (BD).