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CLINICAL AND RADIOGRAPHIC COMPARISON OF 0.05% ZOLEDRONATE GEL (ZOMETA) ®AND 1% ALENDRONATE GEL (FOSAMAX) ® AS A LOCAL DRUG DELIVERY IN THE TREATMENT OF CHRONIC PERIODONTITIS- A SPLIT MOUTH STUDY

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ABSTRACT

Aim: The purpose of the study was to compare clinically and radiographically the efficacy of 0.05% zoledronate gel and 1% alendronate gel as a local drug delivery in the treatment of chronic periodontitis. **Materials & Method:** 45 surgical sites were selected in 15 patients and treated with SRP alone, SRP + 1% Alendronate gel and SRP + 0.05% zoledronate gel. Plaque index(PI), Gingival index(GI), Sulcus bleeding index(SBI), Probing Pocket Depth (PPD) Clinical Attachment Level Depth of defect (DOD) were recorded at baseline, 3months and 6 months postoperatively. The bone-fill was evaluated at baseline, 3 months and 6 months with the help of a PSP plate system. **Result:** Significant PI and GI reduction, probing pocket depth (PPD) reduction, clinical attachment level (CAL) gain and significant bone fill (BF) was observed in both Alendronate and Zoledronate treated sites. **Conclusion:** Both Alendronate and Zoledronate was effective in the treatment of intrabony defects with Zoledronate showing superior results.

KEYWORDS: Bisphosphonate, Intrabony defects, Local drug delivery.

INTRODUCTION

Chronic periodontitis is a microbial infectious disease which results due to inflammation within the supporting tissues of the teeth and leads to progressive attachment loss, bone loss, and periodontal pocket formation and gingival recession.[1] The goals of periodontal therapy are to preserve the natural dentition, periodontium and peri implant health, comfort, esthetics,

and function.[3] Mechanical debridement itself may not always reduce or eliminate the anaerobic infection at the base of the pocket, within the gingival tissues, and in both structures inaccessible to periodontal instruments.[4] To overcome this, systemic and local drug delivery of antimicrobials was initiated to enhance nonsurgical therapy by serving as an adjunct to scaling and root planing. However adverse effects such as drug toxicity, acquired bacterial resistance, drug interaction, and patient's compliance limit the use of systemic antimicrobials.[5] To complement the non-surgical therapy, there are multiple options of antimicrobials that can be locally delivered into the mucosa, such as metronidazole, chlorhexidine, minocycline, doxycycline and tetracycline. These drugs are used in periodontal pockets and can inhibit or eliminate the periodontopathogenic microorganisms as well as modulate the inflammatory response of the tissues (Greenstein and Tonetti, 2000). In periodontitis, the host is responsible for most of the tissue breakdown that occurs, leading to the clinical signs of disease. A variety of drug classes have been evaluated as host response modulators, including the nonsteroidal anti-inflammatory drugs, bisphosphonates, and tetracyclines.[7] Bisphosphonates (BP), the carbon-substituted pyrophosphate analogs are potent inhibitors of bone resorption and have been effectively used to control osteolysis or reduce bone loss in Paget disease, metastatic bone disease, hypercalcemia of malignancy and osteoporosis.[8] Alendronate (ALN) is an aminobisphosphonate that acts as a potent inhibitor of bone resorption. Recently, it has been demonstrated that local delivery of 1% Alendronate gel into periodontal pockets as an adjunct to scaling and root planing (SRP) in the treatment of chronic periodontitis and aggressive periodontitis (AgP) stimulates a significant increase in probing depth (PD) reduction, clinical attachment level (CAL) gain, and improved bone fill.[9] Zoledronate (ZLN), a third generation BP, is the most potent amongst all BPs known so far with the highest bone affinities. Studies have demonstrated that local and systemic treatments with ZLN can enhance the osseointegration and fixation of orthopedic implants as well as dental implants in rats.[10] These bone levels can be assessed through various radiographic modalities. Digital Radiography like Photostimulable phosphor (PSP) plates have been used in dentistry since the mid-1990. PSP plates have increased exposure latitude over conventional film and direct digital sensors, enabling them to accept a range of exposure without over- or underexposing the resulting radiographic image. An important advantage of this low exposure compensation is the ability to reduce patient dose. The reduction in dose is dependent upon the PSP plate system.[11] There are many studies in the literature which evaluates the clinical efficacy of 1% Alendronate and a few studies of 0.05% of Zoledronate separately in the treatment of chronic periodontitis but there is no study which compares the

clinical efficacy of Alendronate and Zoledronate in the treatment of chronic periodontitis patients. Hence, this study was done to compare the efficacy of 1% Alendronate and 0.05% Zoledronate gel in the treatment of chronic periodontitis patients both clinically and radiographically.

Methodology

A clinical and radiographic study was conducted to comparatively evaluate the efficacy of 1% alendronate gel and 0.05% Zoledronate gel as an adjunct to scaling and root planing in the treatment of chronic periodontitis.

Fifteen patients (Between 20 and 55 years of age) with chronic periodontitis were selected from outpatients visiting Department of Periodontology, D.A.P.M.R.V Dental College, Bangalore.

Subjects were selected from those diagnosed as having periodontitis stage III, Generalized, grade B and C, (BASED ON THE 2017 AMERICAN ASSOCIATION OF PERIODONTOLOGY AND EUROPEAN FEDERATION OF PERIODONTOLOGY) classification of periodontal diseases and conditions). A split mouth study was designed among all the selected subjects by randomly allocating SRP+ 1% alendronate, SRP+ 0.05% Zoledronate gel and SRP alone to different quadrants in each patient. Fifteen patients (between 20 and 55 years of age) with active periodontal sites were selected and treated with scaling and root planing. Three quadrants were selected from each patient and were allotted to three different groups randomly as follows.

GROUP A (N= 15) control group (CG) - received only Scaling and Root planing (SRP).
GROUP B (N=15) Alendronate group (AG) - received SRP + 1% alendronate gel.
GROUP C (N=15) Zoledronate group (ZG) - received SRP +0.05% Zoledronate gel.

Both 1% alendronate and 0.05% Zoledronate gels were prepared from KLE college of Pharmacy, Bengaluru.

The ethical clearance for the study was obtained from the ethical committee and review board of the institution. The nature of the study was explained verbally in a language comprehensible to the patient, information sheet was given, and informed consent was obtained from the patient.

Inclusion criteria

1. Patients diagnosed with periodontitis stage III, Generalized, grade B and C, (BASED ON THE 2017 AMERICAN ASSOCIATION OF PERIODONTOLOGY AND EUROPEAN FEDERATION OF PERIODONTOLOGY).
2. The sites should exhibit clinical evidence of periodontal probing depth of ≥5mm and radiographic evidence of vertical defects ≥3mm deep.
3. Age between 20 and 55 years of both sexes.
4. No systemic conditions that would contraindicate routine periodontal procedures.
5. Patients with no history of periodontal therapy or use of antibiotics in the preceding 6 months.

Exclusion criteria

1. Subjects who have known allergy to Alendronate and Zoledronate.
2. Patients on systemic Alendronate and Zoledronate therapy.
3. Pregnant and lactating patients.
4. Smokers.
5. Patients with aggressive periodontitis.

Pre-Treatment procedures

At first appointment case history, study casts and clinical photographs was taken. A standardized intraoral radiograph was taken using PSP plate system.

A customized acrylic stent was fabricated for each patient. The stent was grooved in an occlusal apical direction to produce a reproducible insertion axis for the probe.

Clinical parameters including Plaque index (Silness and Loe) (PI) (1964), Sulcus bleeding index (SBI) (1971) and gingival index (Loe and Silness) (GI) (1963) was recorded and probing pocket depth (PPD), clinical attachment levels (CAL) was recorded using customized acrylic stent and UNC 15 probe. Radiographic evaluation was done using PSP plate system.

Treatment procedure

Scaling and root planing (SRP) were performed in all the 15 patients, after which the quadrants were randomly allocated to one of the groups.

Group A (Control group): After recording the clinical and radiographic parameters at baseline, thorough scaling and root planing (SRP) was done using supragingival scalers, Gracey curettes and universal curettes. Group A received only SRP.

Group B: (SRP+ 1% Alendronate gel)-. This group received SRP followed by drug delivery of 1% Alendronate gel locally using 2 ml syringe and a preformed blunt cannula placed into the periodontal pocket, 0.5 ml of the gel was incorporated from the apical end of the periodontal pocket and moving coronally to avoid entrapment of air bubbles followed by the placement of periodontal dressing which was removed after 2 days.

Group C: (SRP + 0.05% Zoledronate gel)– This group received SRP followed by the drug delivery of 0.05% Zoledronate gel locally using 2 ml syringe and a preformed blunt cannula placed into the periodontal pocket. 0.5ml of gel was incorporated from the apical end of the periodontal pocket and moving coronally to avoid entrapment of air bubbles followed by the placement of periodontal dressing which was removed after 2 days.

Clinical parameters were re-recorded and radiographic evaluation was done using PSP plate system at 3 months and 6 months after the treatment. The data collected were tabulated and analyzed statistically.

Statistical test used: Repeated measures of anova.

RESULTS

The following parameters were assessed at baseline, 3 months and 6 months

- Plaque Index (Silness and Loe (1964)
- Gingival index (Loe and Silness (1963)
- Sulcus bleeding index (SBI) (Muhlemann H R and Son S in 1971)
- Probing Pocket Depth (PPD)
- Clinical Attachment Level
- Depth of defect (DOD)

The results of the study are as follows

1. **Gender distribution:**- Total 15 patients were selected, of which 10 were male patients (66.7%) and 5 were female patients (33.3%).

2. **Age distribution**- Of the selected 15 patients, mean age distribution of patients was 43.6 years. (41- 50 years).

Age and gender distribution are shown in table 1 and graph 1 and 2.

3. **Plaque index (PI)**

Intra group Comparison- Group A

The plaque index scores in Group A at baseline, 3 months and 6 months were 1.40 ± 0.12, 1.28 ± 0.10 and 1.18 ± 0.10 respectively. The mean difference between the values at baseline to 3 months, baseline to 6 months and between 3 to 6 months was 0.12, 0.22 and 0.1 respectively. The difference in the mean PI was found to be statistically significant between all the time intervals (P<0.05).

Intra group Comparison- Group B

The mean plaque index scores at baseline, 3 months and 6 months were 1.40 ± 0.12, 1.09 ± 0.11 and 0.92 ±0.12 respectively. The mean difference in the values between baseline and 3 months, baseline and 6 months, 3months and 6 months were 0.31, 0.48 and 0.17. The difference in the mean PI was found to be statistically significant between all the time intervals (P<0.05).

Intra group Comparison- Group C

The plaque index scores in Group A at baseline, 3 months and 6 months were 1.39 ± 0.14, 1.02 ± 0.11 and 0.83 ± 0.06 respectively. The mean difference between the values at baseline to 3 months, baseline to 6 months and between 3 months and 6 months was 0.37, 0.56 and 0.19 respectively. The difference in the mean PI was found to be statistically significant between all the time intervals (P<0.05).

Inter- Group comparison

Comparison of mean plaque index scores between three groups at different time intervals has been shown in Table 2 and Graph, 3, 9, 11.

When mean plaque index scored were compared at baseline among Control group, Alendronate group and Zoledronate group, there was no statistically significant difference seen. (P value 0.96).

When mean plaque index scores were compared at 3 months among Control group, Alendronate group and Zoledronate group, a statistically significant difference was seen. (P value <0.001*).

The mean difference in plaque index scores between Control group and Alendronate group, Control group and Zoledronate group, Alendronate group and Zoledronate group were 0.19, 0.26 and 0.07 respectively. There was statistically significant difference between Control group and Alendronate group, Control group and Zoledronate group. However, there was no statistically significant difference between Alendronate group and Zoledronate group. (P>0.05).

When mean plaque index scores were compared at 6 months among Control group, Alendronate group and Zoledronate group, a statistically significant difference was seen (P value <0.001*).

The mean difference in plaque index scores between Control group and Alendronate group, Control group and Zoledronate group, Alendronate group and Zoledronate group were 0.26, 0.35 and 0.09 respectively. The differences were statistically significant between all the groups. (P<0.05).

4. Gingival index (GI)

Intra group Comparison- Group A

The mean gingival index scores at baseline, 3 months and 6 months were 1.46±0.36, 1.35±0.32 and 1.22± 0.26 respectively. The mean difference in the values between baseline and 3 months, baseline and 6 months, 3 months and 6 months were 0.11, 0.24 and 0.13 respectively. The difference in the mean GI was found to be statistically significant between all the time intervals (P<0.05).

Intra group Comparison- Group B

The mean gingival index scores at baseline, 3 months and 6 months were 1.46±0.36, 1.16±0.12 and 1.07± 0.14 respectively. The mean difference in the values between baseline and 3 months, baseline and 6 months, 3 months and 6 months were 0.3, 0.39 and 0.09 respectively. The difference in the mean GI was found to be statistically significant between all the time intervals (P<0.05).

Intra group Comparison- Group C

The mean gingival index scores at baseline, 3 months and 6 months were 1.43±0.37, 1.07±0.15 and 0.89± 0.07 respectively. The mean difference in the values between baseline and 3 months, baseline and 6 months, 3 months and 6 months were 0.36, 0.54 and 0.18 respectively. The difference in the mean GI was found to be statistically significant between all the time intervals (P<0.05).

Inter- Group comparison

Comparison of mean gingival scores between three groups at different time intervals has been shown in Table 3 and Graph, 4, 9, 11, 13.

When mean Gingival index scores were compared at baseline among Control group, Alendronate group and Zoledronate group, there was no statistically significant difference seen. (P value 0.96).

When mean Gingival index scores were compared at 3 months among Control group, Alendronate group and Zoledronate group, a statistically significant difference was seen. (P value <0.003*).

The mean difference in Gingival index scores between Control group and Alendronate group, Control group and Zoledronate group, Alendronate group and Zoledronate group were 0.19, 0.28 and 0.09 respectively. There was statistically significant difference between Control group and Alendronate group, Control group and Zoledronate group. However, there was no statistical significant difference between Alendronate group and Zoledronate group. (P>0.05).

When mean Gingival index scores were compared at 6 months among Control group, Alendronate group and Zoledronate group, a statistically significant difference was seen. (P value <0.001*).

The mean difference in Gingival index scores between Control group and Alendronate group, Control group and Zoledronate group, Alendronate group and Zoledronate group were 0.15, 0.33 and 0.18 respectively. The differences were statistically significant between all the groups. (P<0.05).

5. Sulcus bleeding index

Intra group Comparison- Group A

The mean sulcus bleeding scores at baseline, 3 months and 6 months were 1.55±0.32, 1.37±0.25 and 1.28± 0.22 respectively. The mean difference in the values between baseline and 3 months, baseline and 6 months, 3 months and 6 months were 0.18, 0.27 and 0.09 respectively. The difference in the mean SBI was found to be statistically significant between baseline and 3 months, and between baseline and 6 months. The difference in the mean SBI was not found to be statistically significant between 3 months and 6 months. (P value 0.24).

Intra group Comparison- Group B

The mean sulcus bleeding scores at baseline, 3 months and 6 months were 1.55±0.32, 1.16±0.17 and 1.10± 0.20 respectively. The mean difference in the values between baseline and 3 months, baseline and 6 months, 3 months and 6 months were 0.39, 0.45 and 0.06 respectively. The difference in the mean SBI was found to be statistically significant between baseline and 3 months, and between baseline and 6 months. The difference in the mean SBI was not found to be statistically significant between 3 months and 6 months. (P value 0.32).

Intra group Comparison- Group C

The mean sulcus bleeding index scores at baseline, 3 months and 6 months were 1.52±0.34, 1.10±0.14 and 0.89± 0.13 respectively. The mean difference in the values between baseline and 3 months, baseline and 6 months, 3 months and 6 months were 0.42, 0.63 and 0.21 respectively. The difference in the mean SBI was found to be statistically significant between all the time intervals ($P<0.05$).

Inter- group comparison

Comparison of mean sulcus bleeding scores between three groups at different time intervals has been shown in Table 4 and Graph, 5, 9, 11, 13.

When mean sulcus bleeding scores were compared at baseline among Control group, Alendronate group and Zoledronate group, there was no statistically significant difference seen. (P value 0.96).

When mean sulcus bleeding scores were compared at 3 months among Control group, Alendronate group and Zoledronate group, a statistically significant difference were seen. (P value <0.001*).

The mean difference in sulcus bleeding scores between Control group and Alendronate group, Control group and Zoledronate group, Alendronate group and Zoledronate group were 0.21, 0.27 and 0.06 respectively. There was statistically significant difference between Control group and Alendronate group, Control group and Zoledronate group. However, there was no statistically significant difference between Alendronate group and Zoledronate group. (P>0.05) 40.

When mean sulcus bleeding scores were compared at 6 months among Control group, Alendronate group and Zoledronate group, a statistically significant difference was seen (P value <0.001*).

The mean difference in sulcus bleeding scores between Control group and Alendronate group, Control group and Zoledronate group, Alendronate group and Zoledronate group were 0.18, 0.39 and 0.21respectively. The differences were statistically significant between all the groups. (P<0.05).

6. Probing pocket DEPTH

Intra group Comparison- Group A

The mean Probing pocket depth index scores at baseline, 3 months and 6 months were 6.60±0.51, 5.73±0.46 and 5.20± 0.78 respectively. The mean difference in the values between baseline and 3 months, baseline and 6 months, 3 months and 6 months were 0.87, 1.4 and 0.53 respectively. The difference in the mean PPD was found to be statistically significant between all the time intervals (P<0.05).

Intra group Comparison- Group B

The mean Probing pocket depth index scores at baseline, 3 months and 6 months were 6.53±0.52, 4.60±0.51 and 3.93± 0.59 respectively. The mean difference in the values between baseline and 3 months, baseline and 6 months, 3months and 6 months were 1.93, 2.6 and 0.67 respectively. The difference in the mean PPD was found to be statistically significant between all the time intervals (P<0.05).

Intra group Comparison- Group C

The mean Probing pocket depth index scores at baseline, 3 months and 6 months were 6.87±0.83, 4.40±0.63 and 3.33± 0.49 respectively. The mean difference in the values between baseline and 3 months, baseline and 6 months, 3 months and 6 months were 2.47, 3.54 and

1.07 respectively. The difference in the mean PPD was found to be statistically significant between all the time intervals (P<0.05).

Inter- group comparison

Comparison of mean probing pocket depth between three groups at different time intervals has been shown in Table 5 and Graph, 6, 10, 12, 14.

When mean probing pocket depth scores were compared at baseline among Control group, Alendronate group and Zoledronate group, there was no statistically significant difference seen. (P value 0.33).

When mean probing pocket depth scores were compared at 3 months among Control group, Alendronate group and Zoledronate group, a statistically significant difference were seen. (P value <0.001*).

The mean difference in probing pocket depth scores between Control group and Alendronate group, Control group and Zoledronate group, Alendronate group and Zoledronate group were 1.13, 1.33 and 0.2 respectively. There was statistically significant difference between Control group and Alendronate group, Control group and Zoledronate group. However, there was no statistically significant difference between Alendronate group and Zoledronate group. (P>0.05).

When mean probing pocket depth scores were compared at 6 months among Control group, Alendronate group and Zoledronate group, a statistically significant difference was seen (P value <0.001*).

The mean difference in probing pocket depth scores between Control group and Alendronate group, Control group and Zoledronate group, Alendronate group and Zoledronate group were 1.27, 1.87 and 0.6 respectively. The differences were statistically significant between all the groups. (P<0.05).

7. Clinical attachment level

Intra group Comparison- Group A

The mean Clinical attachment level index scores at baseline, 3 months and 6 months were 6.27±0.59, 5.80±0.68 and 5.33± 0.82 respectively. The mean difference in the values between baseline and 3 months, baseline and 6 months, 3 months and 6 months were 0.47, 0.94 and

0.47 respectively. The difference in the mean CAL was found to be statistically significant between baseline and 3 months, and baseline and 6 months. The difference in the mean CAL was not found to be statistically significant between 3 months and 6 months. (P value 0.09).

Intra group Comparison- Group B

The mean Clinical attachment level index scores at baseline, 3 months and 6 months were 6.47±1.13, 5.07±0.80 and 4.40± 0.63 respectively. The mean difference in the values between 43 baseline and 3 months, baseline and 6 months, 3 months and 6 months were 1.4, 2.07 and 0.67 respectively. The difference in the mean CAL was found to be statistically significant between all the time intervals (P<0.05).

Intra group Comparison- Group C

The mean Clinical attachment level index scores at baseline, 3 months and 6 months were 6.13±0.99, 4.53±0.64 and 3.47± 0.52 respectively. The mean difference in the values between baseline and 3 months, baseline and 6 months, 3 months and 6 months were 1.6, 2.66 and 1.06 respectively. The difference in the mean CAL was found to be statistically significant between all the time intervals (P<0.05).

Inter- group comparison

Comparison of mean clinical attachment level between three groups at different time intervals has been shown in Table 6 and Graph, 7, 10, 12, 14.

When mean clinical attachment level scores were compared at baseline among Control group, Alendronate group and Zoledronate group, there was no statistically significant difference seen. (P value 0.62).

When mean clinical attachment level scores were compared at 3 months among Control group, Alendronate group and Zoledronate group, a statistically significant difference were seen. (P value <0.001*).

The mean difference in clinical attachment level scores between Control group and Alendronate group, Control group and Zoledronate group, Alendronate group and Zoledronate group were 0.73, 1.27 and 0.54 respectively. There was statistically significant difference between Control group and Alendronate group, Control group and Zoledronate group. However, there was no statistically significant difference between Alendronate group and Zoledronate group. (P>0.05).

When mean clinical attachment level scores were compared at 6 months among Control group, Alendronate group and Zoledronate group, a statistically significant difference was seen (P value <0.001*).

The mean difference in clinical attachment level scores between Control group and Alendronate group, Control group and Zoledronate group, Alendronate group and Zoledronate group were 0.93, 1.86 and 0.93 respectively. The differences were statistically significant between all the groups. (P<0.05).

8. Depth of defect (DOD)

Intra group comparison-Group A

The mean DOD index scores at baseline, 3 months and 6 months were 3.87±0.83, 3.67±0.72 and 3.60± 0.74 respectively. The mean difference in the values between baseline and 3 months, baseline and 6 months, 3 months and 6 months were 0.2, 0.27and 0.07 respectively. The difference in the mean DOD was not found to be statistically significant between all the time intervals (P>0.05).

Intra group comparison-Group B

The mean DOD index scores at baseline, 3 months and 6 months were 4.20±0.56, 3.13±0.35 and 2.67± 0.49 respectively. The mean difference in the values between baseline and 3 months, baseline and 6 months, 3 months and 6 months were 1.07, 1.53 and 0.46 respectively. The difference in the mean DOD was found to be statistically significant between all the time intervals (P<0.05).

Intra group comparison-Group C

The mean DOD index scores at baseline, 3 months and 6 months were 4.00±0.38, 2.93±0.59 and 2.27± 0.46 respectively. The mean difference in the values between baseline and 3 months, baseline and 6 months, 3 months and 6 months were 1.07, 1.73 and 0.66 respectively. The difference in the mean DOD was found to be statistically significant between all the time intervals (P<0.05).

Inter- group comparison

Comparison of mean depth of defect between three groups at different time intervals has been shown in Table 7 and Graph, 8, 10, 12, 14.

When mean depth of defect scores were compared at baseline among Control group, Alendronate group and Zoledronate group, there was no statistically significant difference seen. (P value 0.34).

When mean depth of defect scores were compared at 3 months among Control group, Alendronate group and Zoledronate group, a statistically significant difference was seen. (P value <0.004*).

The mean difference in depth of defect scores between Control group and Alendronate group, Control group and Zoledronate group, Alendronate group and Zoledronate group were 0.54, 0.74 and 0.2 respectively. There was statistically significant difference between Control group and Alendronate group, Control group and Zoledronate group. However, there was no statistically significant difference between Alendronate group and Zoledronate group. (P>0.05).

When mean depth of defect scores were compared at 6 months among Control group, Alendronate group and Zoledronate group, a statistically significant difference was seen (P value <0.001*).

The mean difference in depth of defect scores between Control group and Alendronate group, Control group and Zoledronate group, Alendronate group and Zoledronate group were 0.93, 1.33 and 0.4 respectively. There was statistically significant difference between Control group and Alendronate group, Control group and Zoledronate group. However, there was no statistically significant difference between Alendronate group and Zoledronate group. (P<0.05).

DISCUSSION

Periodontitis is a chronic progressive disease of bacterial origin involving the loss of supporting tissues of the teeth. It results from host inflammatory and immunologic reactions to one or more bacterial pathogens and is characterized by the loss of periodontal attachment on the root surface and alveolar bone.[1] The standard approach to the prevention and treatment of periodontal diseases for a number of years has been mechanical therapy and if required surgical intervention for regeneration of the structures lost due to periodontal disease.[2,3,4]

The concept of reducing the plaque bacteria by standard approaches was changed when investigators began to document the host's contribution to disease pathogenesis.[5] Host response is a protective mechanism but concomitantly induce tissue damage, alveolar bone resorption viz breakdown of connective tissue fibers in the periodontal ligament. Consequently, a treatment modality where in by altering the host response, the destructive host mechanisms could be interfered by altering the outcome of the disease process. A great interest has been generated in this field with the development of host modulatory therapy against periodontal disease.[5] A number of host modulatory agents have been investigated in clinical trials. A better understanding of the role of host immune inflammatory mediators in the progression of the disease has directed investigations towards the potential use of modulating agents as adjuncts to routine periodontal treatment.[10]

Among those, bisphosphonates are a unique class of pharmacological agents which are potent inhibitors of bone resorption and have been effectively used to treat metabolic bone diseases in humans such as Paget's disease, hypercalcaemia of malignancy, osteoporosis and estrogen deficiency.[6,7]

It is logical to hypothesize that any therapeutic agent that can cause suppression of bone resorption can protect against alveolar bone loss in periodontitis. Bisphosphonates suppress osteoclast- mediated bone resorption as it is well taken up by the skeleton. Among the various bisphosphonates, Alendronate (4 - amino 1 - hydroxybutylidine bisphosphonate), is a very persuasive inhibitor of bone resorption.[8] A number of animal and human studies have proved the efficacy of bisphosphonates in treating metabolic bone diseases.[9,10]

Zoledronate (ZLN), a third-generation BP, is the most potent amongst all BPs known so far with the highest bone affinities.[23] Studies have demonstrated that local and systemic treatments with ZLN can enhance the osseointegration and fixation of orthopedic implants.[24,25,26] as well as dental implants in rats.[27]

In the present trial, ZLN has been used as a LDD system for treating periodontal intrabony defects. It acts by inhibiting the key enzyme (farnesyl pyrophosphatase)[28] of mevalonate pathway that regulates many cellular activities in osteoclasts, consequently leading to its apoptosis and reduced bone resorption.[29]

These unique pharmacokinetic characteristics can thus enable small doses of ZLN which can be utilized as a LDD system in osseous defects with minimal unwanted side effects.

However, no allergic complications were observed because of ZLN and ALN, because they were used locally at very low concentrations and dosage. Further long-term studies are required to see the incidence of such adverse effects after the local drug delivery.[47,49]

These subgingivally delivered drugs enhance the bone formation in various periodontal intraosseous defects. These bone levels can be assessed through various radiographic modalities. Digital Radiography like Photostimulable phosphor (PSP) plates have been used in dentistry since the mid-1990.

Photostimulable phosphor (PSP) plates

The PSP plates consist of a flexible polyester base coated with a crystalline emulsion of europium activated barium fluorohalide48 compound.

Storage phosphor plates (SPPs) includes a

1. Reusable photo stimulated screen
2. A readout scanner
3. A photomultiplier tube
4. A digital interface card
5. A computer and software.

When X-ray photons strike the phosphor layer included on the plate, a latent image is formed. PSP plate system has the following advantage of being reused indefinitely, wide exposure range, fewer retakes and less radiation is required. No chemical processing is required, image processing is available, images can be transferred & retrieved, and computed aided diagnosis can be achieved.

Some of the disadvantages include, Phosphor plates must be packaged in sterile envelopes due to possibility of transfer of contaminated material to patient's mouth if integrity of plate's protective envelope is jeopardized and is quite expensive.[51] It was well-recognized that patients who received bisphosphonate may develop osteonecrosis of the jaw bone (ONJ) as one of the long-term side effects of bisphosphonate therapy and duration of bisphosphonate therapy is a significant factor associated with an increased likelihood of ONJ.[52]

There are many studies in the literature which evaluates the clinical efficacy of 1% Alendronate and a few studies of 0.05% of Zoledronate separately in the treatment of chronic periodontitis but there is no study which compares the clinical efficacy of Alendronate and Zoledronate in the treatment of chronic periodontitis patients. Hence, this study was conducted to compare the efficacy of 1% Alendronate and 0.05% Zoledronate gel in the treatment of chronic periodontitis patients both clinically and radiographically.

A total of 15 patients in the age range of 35-55 years were enrolled for this study, of which 10 were male patients and 5 were female patients.

Of the selected 15 patients, mean age distribution of patients was 43.6 years. (41- 50 years)
The properties of alveolar bone do not remain constant with age; rather, they change throughout life. Hence, in this study, patients with similar age groups were considered to avoid bias.[53]

Following the Inclusion and Exclusion criteria the patients were randomly divided into three groups

GROUP A (N=15) Control group (CG) who received only Scaling and Root planing (SRP).
GROUP B (N= 15) Alendronate group (AG) who received SRP + 1% alendronate gel.
GROUP C (N=15) Zoledronate group (SG) who received SRP +0.05% zoledronate gel.

All the patients were followed for a period of 6 months[52]

The present study has included only those sites that have shown Interproximal probing depth ≥ 5mm following phase I therapy and radiographic evidence of angular bone loss ≥3mm deep.

This was in accordance with study done by Abhaya Gupta et al. and A. R. Pradeep et al. who has shown that to benefit from LDD for the intrabony defects in chronic periodontitis patients in their 6-month follow-up study.

The parameters and variables assessed were Plaque index (PI), Gingival index (GI),Sulcus bleeding index, Periodontal Probing Depth (PPD), Clinical Attachment Level (CAL) and Depth of defect (DOD) at baseline, 3 months and 6 months. Probing pocket depth (PPD) and Clinical Attachment Level (CAL) were assessed using a UNC 15 probe positioned along the grooves on a customized acrylic stent which was fabricated for each patient for providing a

reproducible insertion axis for the probe. Similar technique has been adopted in other studies.[54]

The stent had the advantage of providing an unchangeable insertion axis during the reevaluation period.

It has been shown in a study by Payne et al that Probing pocket depth (PPD) and Clinical Attachment Level (CAL) measurement reflect changes in the underlying bone level over time and hence are good clinical parameters to assess the potential effects of regenerative materials in the treatment of intrabony defects. The Probing pocket depth and Clinical Attachment Level have been measured as the basic clinical parameters in other studies.[53]

This study assessed Plaque index, Gingival index and Sulcus bleeding sulcus at baseline, 3 months and 6 months. The results of the study showed statistically significant decrease in the plaque index, Gingival index and Sulcus bleeding sulcus from baseline to 3 months and baseline to 6 months in Control group, Alendronate as well as Zoledronate group.

In intergroup comparison, at baseline, there was no statistically significant difference among all the three groups. At 3 months there was statistically significant difference between control and alendronate group and control and zoledronate group. There was no statistically significant difference between zoledronate and alendronate group. At 6 months there was statistically significant decrease in the plaque index, Gingival index and Sulcus bleeding sulcus between all the three groups and zoledronate showed greater decrease in the plaque index and Gingival index followed by alendronate group and control group.

The improvement in plaque status, Gingival index and Sulcus bleeding sulcus may be patients were given oral hygiene instructions before start of the study.

These results were consistent with the studies conducted by Abhay Gupta et al. and A. R. Pradeep et al. Their study showed improvement in plaque status, Gingival index and Sulcus bleeding sulcus in all the patients who maintained good oral hygiene.[8,10]

This study assessed Probing pocket depth (PPD) at baseline, 3 months and 6 months. The results of the study showed statistically significant decrease in the Probing pocket depth (PPD) from baseline to 3 months and baseline to 6 months in Control group, Alendronate as well as Zoledronate group.

In intergroup comparison, at baseline, there was no statistically significant difference among all the three groups. At 3 months there was statistically significant difference between control and alendronate group and control and zoledronate group. There was no statistically significant difference between zoledronate and alendronate group. At 6 months there was statistically significant decrease in the Probing pocket depth (PPD) between all the three groups and zoledronate showed greater reduction in the Probing pocket depth(PPD) followed by alendronate group and control group.

Most of the studies show reduction in probing pocket depth. In, this study also significant reduction in probing pocket depth was observed between different time intervals. The results were in accordance with studies done by Abhay Gupta et al, A. R. Pradeep et al. and Bernardo Carvalho Dutra.[8,10,55]

This study assessed Clinical attachment level (CAL) at baseline, 3 months and 6 months. The results of the study showed statistically significant decrease in the Clinical attachment level from baseline to 3 months and baseline to 6 months in Control group, Alendronate as well as Zoledronate group.

In intergroup comparison, at baseline, there was no statistically significant difference among all the three groups. At 3 months there was statistically significant difference between control and alendronate group and control and zoledronate group. There was no statistically significant difference between zoledronate and alendronate group. At 6 months there was statistically significant decrease in the Clinical attachment level between all the three groups and zoledronate showed greater reduction in the Clinical attachment level followed by alendronate group and control group.

The results were in accordance with studies done by A. R. Pradeep et al and Abhaya Gupta et al.[9,10] The decrease in PPD and gain in CAL may be due to the affinity of Alendronate and[55] zoledronate for binding to the hydroxyappetite crystals of bone and their promotion of osteoblast differentiation.

This study assessed Depth of defect (DOD) at baseline, 3 months and 6 months. The results of the study showed statistically significant decrease in the Depth of defect from baseline to 3 months and baseline to 6 months in Control group, Alendronate as well as Zoledronate group.

In intergroup comparison, at baseline, there was no statistically significant difference among all the three groups. At 3 months there was statistically significant difference between control and alendronate group and control and zoledronate group. There was no statistically significant difference between zoledronate and alendronate group. At 6 months there was statistically significant difference between control and alendronate group and control and zoledronate group. There was no statistically significant difference between zoledronate and alendronate group and zoledronate showed greater reduction in the Depth of defect followed by alendronate group and control group.

The results were in accordance with studies done by A. R. Pradeep et al and Abhay Gupta et al and Bernardo Carvalho Dutra.[9,10,55]

Increase in bone fill can be because of the physiological osseous remodeling process once all osteoclasts near the resorptive bone surface get apoptosed by the ALN and ZLN.

The significant findings in mean PI, GI, SBI, PPD, CAL and Bone fill were in accordance with the previous studies,[8] in which 1% ALN gel was utilized as a LDD for the intrabony defects in chronic periodontitis patients in their 6-month follow-up study. However, in contrast, another study did not observe any improvement in PD measurements in periodontitis of monkey model treated with systemic ALN for duration of 10 weeks.

The lack of such effects can be explained by the short duration of treatment and mode of administration of drug.

However long-term studies are required, to evaluate the radiographic bone gain of these locally delivered drugs to explore their potential and to exploit them for further treatment of chronic periodontitis.

List of tables

Age and gender distribution among study subjects (Table 1)

Variable	Category	N	%
Sex	Males	10	66.7%
	Females	5	33.3%
Age	< 40 years	5	33.3%
	41- 50 years	8	53.3%
	> 50 years	2	13.3%
		Mean	SD

	Mean & SD	43.6	5.2
	Range	37 – 52	

Plaque index

Inter group comparison

Comparison of mean values of Plaque index between 3 groups at different time intervals using One-way ANOVA and Tukey's Post hoc Test (TABLE 2)

Time	Groups	N	Mean	Sd	P value[a]	Mean diff	P-value[b]
Baseline	Group a	15	1.40	0.12	0.96		
	Group b	15	1.40	0.12			
	Group c	15	1.39	0.14			
3months	Group a	15	1.28	0.10	<0.001*	G1 vs g20.19	<0.001*
	Group b	15	1.09	0.11		G1 vs g30.26	<0.001*
	Group c	15	1.02	0.11		G2 vs g30.07	0.26
6months	Group a	15	1.18	0.10	<0.001*	G1 vs g20.26	<0.001*
	Group b	15	0.92	0.12		G1 vs g30.35	<0.001*
	Group c	15	0.83	0.06		G2 vs g30.09	0.03*

* - Statistically Significant

Note: a. P-value derived by One-way ANOVA test; b. P-value derived by Tukey's Post hoc Test

Gingival index

Inter group comparison

Comparison of mean values of Gingival index between 3 groups at different time intervals using One-way ANOVA and Tukey's Post hoc Test (TABLE 3)

Time	Groups	N	Mean	Sd	P value[a]	Mean diff	P-value[b]
Baseline	Group a	15	1.46	0.36	0.96		
	Group b	15	1.46	0.36			
	Group c	15	1.43	0.37			
3months	Group a	15	1.35	0.32	0.003*	G1 vs g20.19	0.04*
	Group b	15	1.16	0.12		G1 vs g30.28	0.003*
	Group c	15	1.07	0.15		G2 vs g30.09	0.48
6months	Group a	15	1.22	0.26	<0.001*	G1 vs g20.15	0.04*
	Group b	15	1.07	0.14		G1 vs g30.33	<0.001*
	Group c	15	0.89	0.07		G2 vs g30.18	0.02*

- Statistically Significant

Note: a. P-value derived by One-way ANOVA test; b. P-value derived by Tukey's Post hoc Test

Gingival index

Inter group comparison

Comparison of mean values of Gingival index between 3 groups at different time intervals using One-way ANOVA and Tukey's Post hoc Test (Table 3)

Time	Groups	N	Mean	Sd	P value[a]	Mean diff	P-value[b]
Baseline	Group a	15	1.46	0.36	0.96		
	Group b	15	1.46	0.36			
	Group c	15	1.43	0.37			
3months	Group a	15	1.35	0.32	0.003*	G1 vs g20.19	0.04*
	Group b	15	1.16	0.12		G1 vs g30.28	0.003*
	Group c	15	1.07	0.15		G2 vs g30.09	0.48
6months	Group a	15	1.22	0.26	<0.001*	G1 vs g20.15	0.04*
	Group b	15	1.07	0.14		G1 vs g30.33	<0.001*
	Group c	15	0.89	0.07		G2 vs g30.18	0.02*

* - Statistically Significant

Note: a. P-value derived by One-way ANOVA test; b. P-value derived by Tukey's Post hoc Test

Sulcus bleeding index

Inter group comparison

Comparison of mean values of Sulcus bleeding index between 3 groups at different time intervals using One-way ANOVA and Tukey's Post hoc Test (TABLE 4)

Time	Groups	N	Mean	Sd	P value[a]	Sig diff	P-value[b]
Baseline	Group a	15	1.55	0.32	0.96		
	Group b	15	1.55	0.32			
	Group c	15	1.52	0.34			
3months	Group a	15	1.37	0.25	0.001*	G1 vs g20.21	0.01*
	Group b	15	1.16	0.17		G1 vs g30.27	0.001*
	Group c	15	1.10	0.14		G2 vs g30.06	0.65
6months	Group a	15	1.28	0.22	<0.001*	G1 vs g20.18	0.03*
	Group b	15	1.10	0.20		G1 vs g30.39	<0.001*
	Group c	15	0.89	0.13		G2 vs g30.21	0.01*

* - Statistically Significant

Note: a. P-value derived by One-way ANOVA test; b. P-value derived by Tukey's Post hoc Test

Probing pocket depth

Inter group comparison

Comparison of mean values of Probing pocket depth scores between 3 groups at different time intervals using One-way ANOVA and Tukey's Post hoc Test (TABLE 5)

Time	Groups	N	Mean	Sd	P value[a]	Sig diff	P-value[b]
Baseline	Group a	15	6.60	0.51	0.33		
	Group b	15	6.53	0.52			
	Group c	15	6.87	0.83			
3months	Group a	15	5.73	0.46	<0.001*	G1 vs g21.13	<0.001*
	Group b	15	4.60	0.51		G1 vs g31.33	<0.001*
	Group c	15	4.40	0.63		G2 vs g30.2	0.57
6months	Group a	15	5.20	0.78	<0.001*	G1 vs g21.27	<0.001*
	Group b	15	3.93	0.59		G1 vs g31.87	<0.001*
	Group c	15	3.33	0.49		G2 vs g30.6	0.03*

* - Statistically Significant

Note: a. P-value derived by One-way ANOVA test; b. P-value derived by Tukey's Post hoc Test

Clinical attachment level

Inter group comparison

Comparison of mean values of CAL between 3 groups at different time intervals using One-way ANOVA and Tukey's Post hoc Test (TABLE 6)

Time	Groups	N	Mean	Sd	P value[a]	Sig diff	P-value[b]
Baseline	Group a	15	6.27	0.59	0.62		
	Group b	15	6.47	1.13			
	Group c	15	6.13	0.99			
3months	Group a	15	5.80	0.68	<0.001*	G1 vs g20.73	0.02*
	Group b	15	5.07	0.80		G1 vs g31.27	<0.001*
	Group c	15	4.53	0.64		G2 vs g30.54	0.11
6months	Group a	15	5.33	0.82	<0.001*	G1 vs g20.93	0.001*
	Group b	15	4.40	0.63		G1 vs g31.86	<0.001*
	Group c	15	3.47	0.52		G2 vs g30.93	0.001*

* - Statistically significant

Note: a. P-value derived by One-way ANOVA test; b. P-value derived by Tukey's Post hoc Test

Depth of defect

Inter group comparison

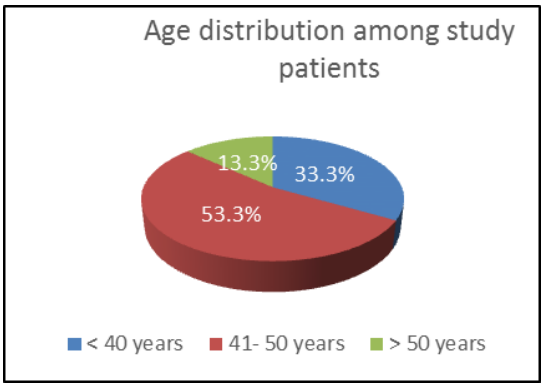
Comparison of mean values of DOD between 3 groups at different time intervals using One-way ANOVA and Tukey's Post hoc Test (TABLE 7)

Time	Groups	N	Mean	Sd	P value[a]	Sig diff	P-value[b]
Baseline	Group a	15	3.87	0.83	0.34		
	Group b	15	4.20	0.56	0.34		
	Group c	15	4.00	0.38	0.34		
3months	Group a	15	3.67	0.72	<0.004*	G1 vs g20.54	0.04*
	Group b	15	3.13	0.35	<0.001*	G1 vs g30.74	0.003*
	Group c	15	2.93	0.59	<0.001*	G2 vs g30.2	0.61
6months	Group a	15	3.60	0.74	<0.001*	G1 vs g20.93	<0.001*
	Group b	15	2.67	0.49	<0.001*	G1 vs g31.33	<0.001*
	Group c	15	2.27	0.46	<0.001*	G2 vs g30.4	0.15

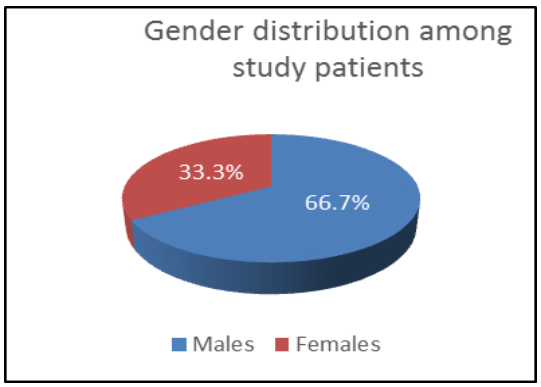
* - Statistically Significant

Note: a. P-value derived by One-way ANOVA test; b. P-value derived by Tukey's Post hoc Test

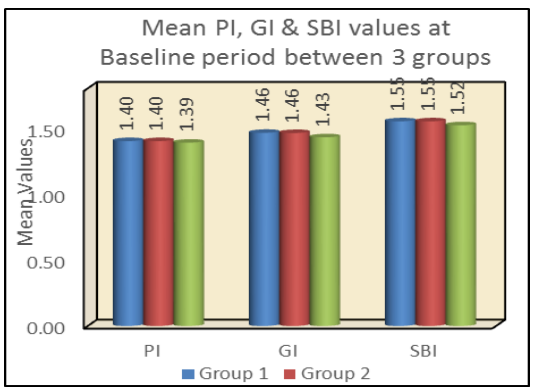
List of graphs



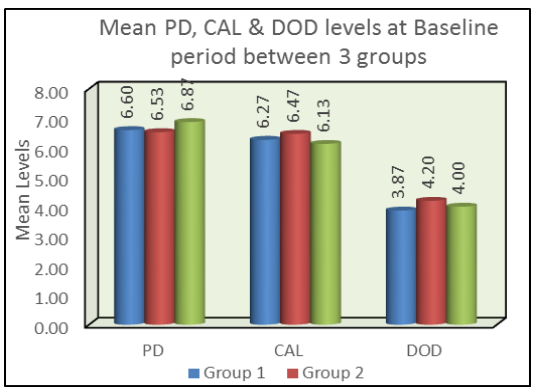
Graph 1



Graph 2



Graph 9



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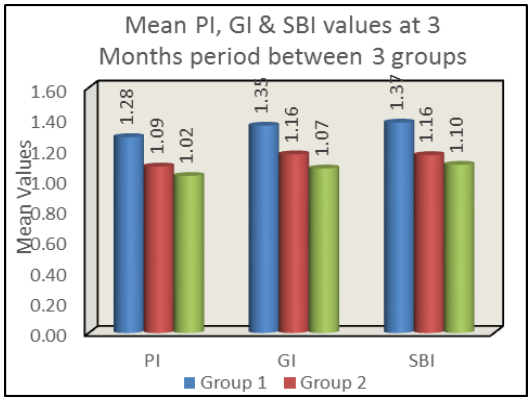
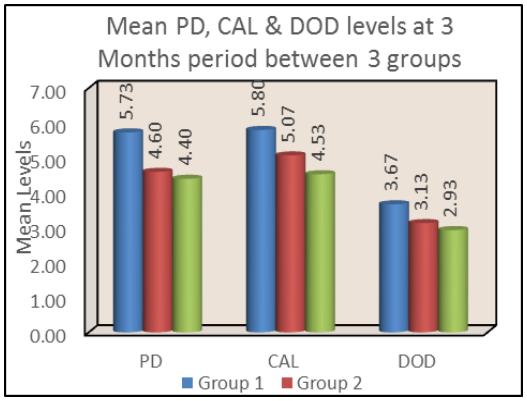
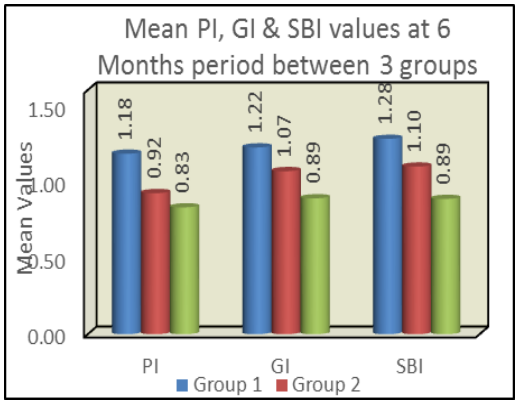


Graph 11



Graph 12



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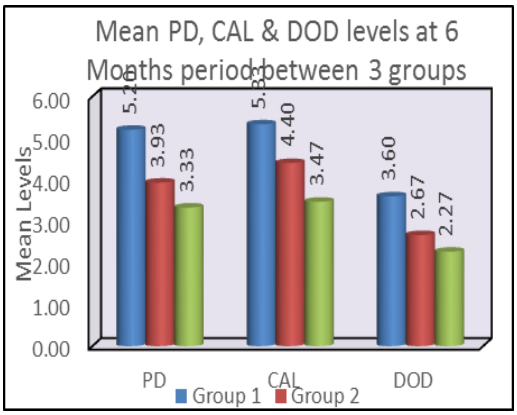

Graph 14

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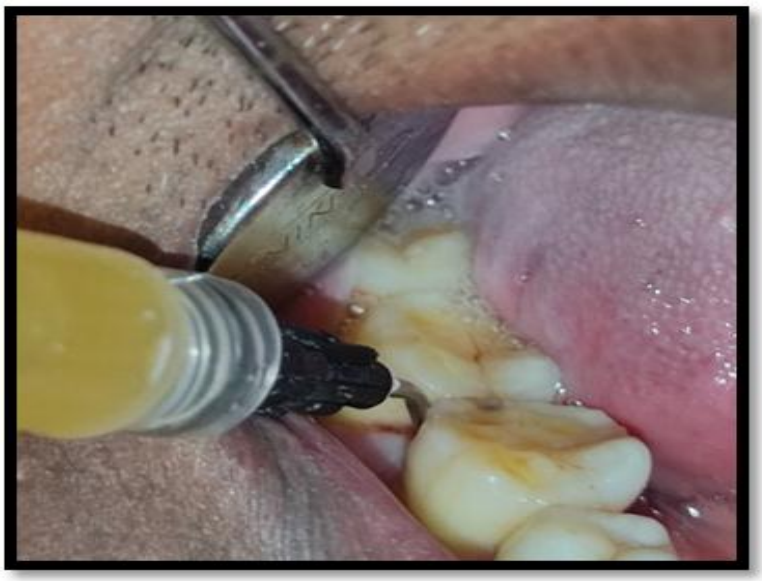

Figure 6: Delivering 1% alendronate gel using blunt canula.

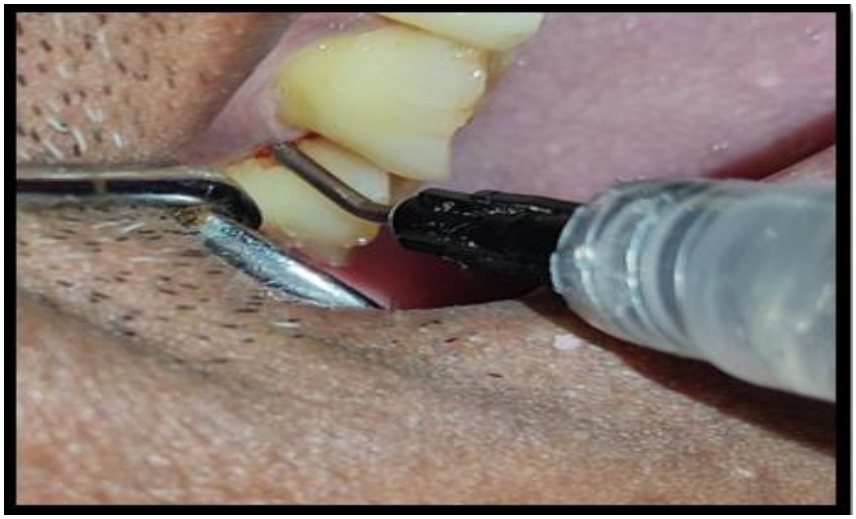

Figure 7: Delivering 0.05% zoledronate gel using blunt canula.

Case clinical photographs

Clinical photographs showing measurement of probing pocket depth (group a)

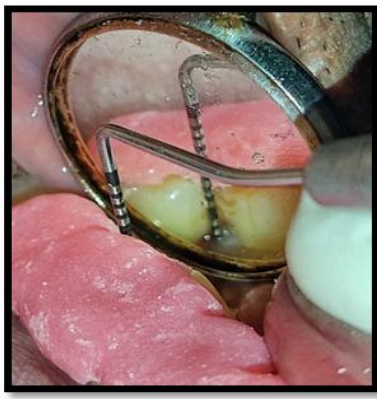

Figure 8: (Baseline).

Figure 9: (3 Months).

Figure 10: (6 Months).

Clinical Photographs Showing Measurement of Probing Pocket Depth (Group B)

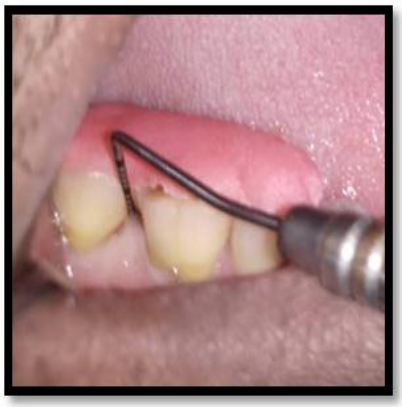

Figure 8: (Baseline).

Figure 9: (3 months).

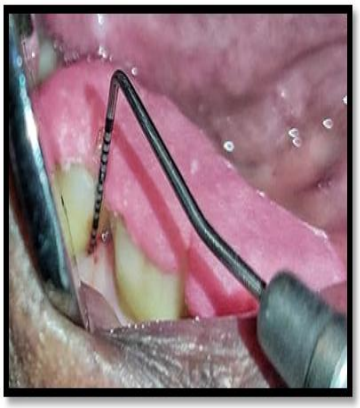

Figure 10: (6 months).

Clinical photographs showing measurement of probing pocket depth (group c)

Figure 8: (Baseline).

Figure 9: (3 Months).

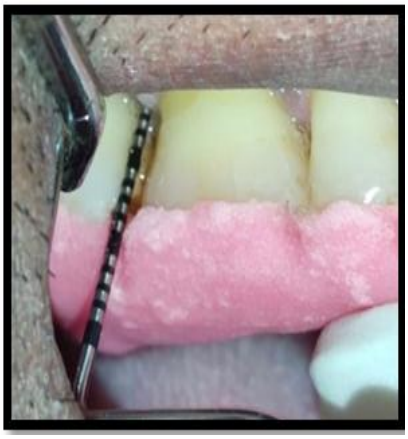

Figure: 10: (6 months).

Radiographs showing measurement of bone defect (Group- A)

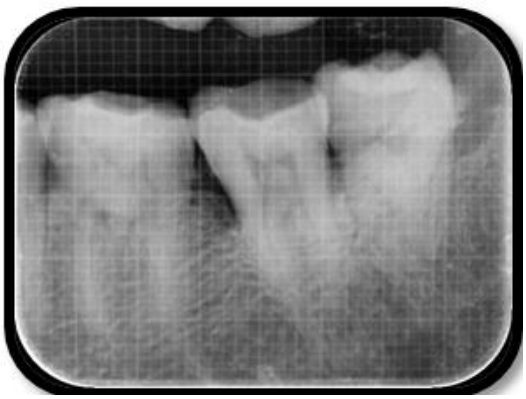

Figure 17: (Baseline).

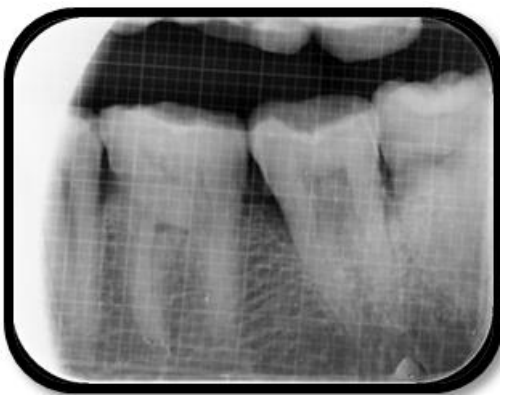

Figure 18: (6 Months).

Radiographs showing measurement of bone defect (Group- B)

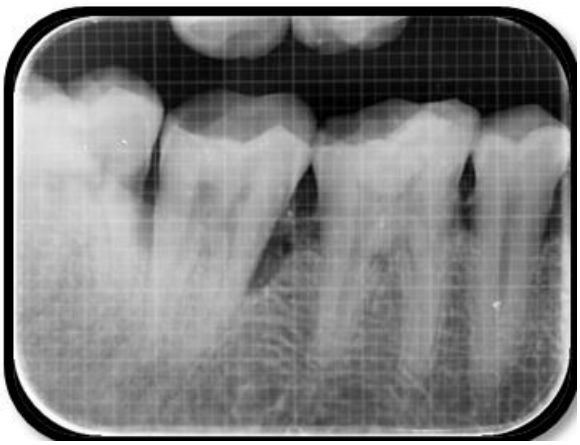

Figure 19: (Baseline).

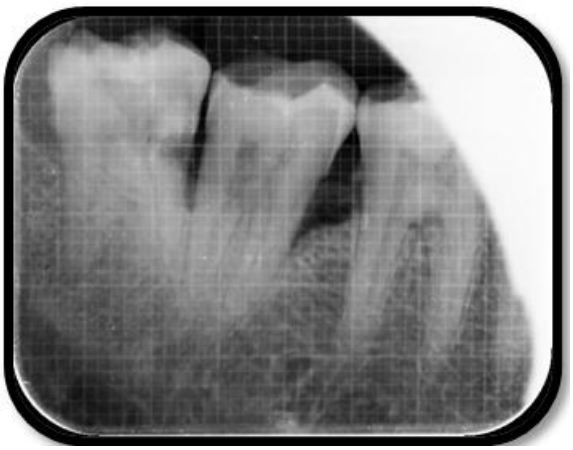

Figure 20: (6 Months).

Radiographs showing measurement of bone defect (Group- C)

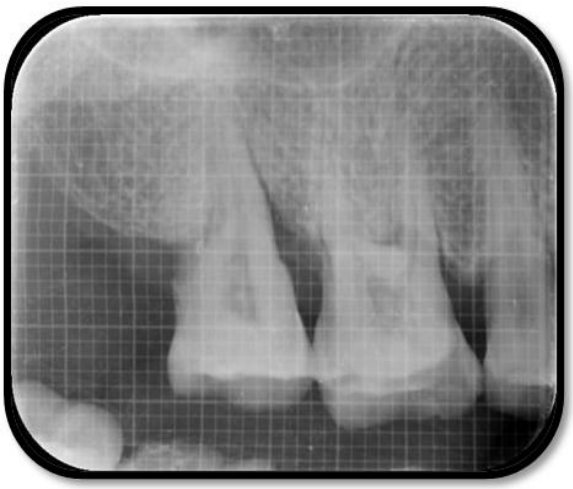

Figure 21: (Baseline).

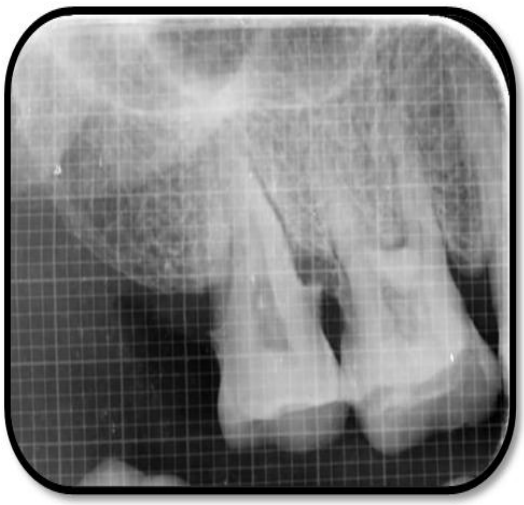

Figure 22: (6 Months).

CONCLUSION

The present study showed that the local delivery of 0.05% zoledronate into periodontal pockets associated with intrabony defects resulted in significant reduction in PPD, CAL gain, radiological defect depth reduction at the end of 6 months.

The present study showed that the local delivery of 1% Alendronate into periodontal pockets associated with intrabony defects resulted in significant reduction in PPD, CAL gain, radiological defect depth reduction at the end of 6 months.

Alendronate gel and Zoledronate gel have shown better results in comparison to SRP alone in the treatment of chronic periodontitis. Zoledronate gel seems to have slight advantage over Alendronate gel with respect to clinical and radiographic parameters. However, long term randomized clinical trial and histomorphometric studies are required to arrive at definitive conclusion.

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