EVALUATION OF 1.2% ATORVASTATIN AS AN ADJUNCT TO NON SURGICAL PERIODONTAL THERAPY IN CHRONIC PERIODONTITIS: A RANDOMIZED CONTROLLED CLINICAL TRIAL

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LIST OF ABBREVIATIONS

Sr. No.	Short Form	Full Form
1	CP	Chronic periodontitis
2	AAP	American Academy of Periodontology
3	LDD	Local drug delivery
4	3D	Three dimensional
5	2D	Two dimensional
6	CT	Computed tomography
7	CBCT	Cone beam computed tomography
8	ATV	Atorvastatin
9	SRP	Scaling and root planing
10	IBD	Intrabony defect
11	RVG	Radiovisiography
12	PPD	Probing pocket depth
13	CAL	Clinical attachment level
14	BP	Bleeding on probing
15	PI	Plaque index
16	GI	Gingival index
17	mSBI	Modified sulcus bleeding index
18	PBI	Papillary bleeding index
19	A. aspera	Achyranthesaspera
20	P. gingivalis	Porphyromonasgingivalis
21	GR	Gingival recession
22	BSAP	Bone specific alkaline phosphatase
23	NTx	Crosslinked N-telopeptides
24	PISA	Periodontal inflamed surface area
25	SMV	Simavastatin
26	CEJ	Cementoenamel junction
27	AC	Alveolar crest
28	BD	Base of the defect
29	DVT	Digital volume tomography

Sr. No.	Short Form	Full Form
30	IOR	Conventional intraoral radiography
31	UNC-15	University of North Carolina-15
32	mm	Millimeter
33	MD	Mesiodistal
34	BL	Buccolingual
35	FOV	Field of view
36	HMG-CoA	3-hydroxy-3-methylglutaryl coenzyme A
37	BMP	Bone morphogenic protein
38	RANKL	Receptor activator of nuclear factor kappa-B ligand
39	OPG	Osteoprotegerin
40	IL	Interleukin
41	MMPs	Matrix metalloproteinases
42	RSV	Rosuvastatin
43	OFD	Open flap debridement

INTRODUCTION

Periodontal diseases range from gingivitis, to chronic and aggressive forms of periodontal disease. Chronic inflammation present in inflammatory periodontal disease leads to destruction of the periodontal ligament and alveolar bone. Periodontal disease if left untreated; significant tissue damage occurs leading to the loss of affected teeth.[1]

Chronic periodontitis (CP) is defined as an inflammatory disease of the supporting tissues of the teeth caused by specific microorganisms or group of specific microorganisms resulting in progressive destruction of the periodontal ligament and alveolar bone with increased probing pocket depth formation, gingival recession or both. The clinical signs of periodontitis are changes in the morphology of gingival tissues, bleeding upon probing, as well as periodontal pocket formation.[2]

Nonsurgical periodontal therapy is the 'first line of defense' in periodontal therapy. It is effective in reducing the gingival inflammation as well as number and depth of periodontal pocket. Majority of patients with periodontitis can be treated by scaling and root planing combined with irrigation of periodontal pocket, systemic antibiotics and proper maintenance of oral hygiene by patients.[3]

According to the glossary of terms of the American Academy of Periodontology (AAP), an intrabony defect is defined as a ''periodontal defect within the bone surrounded by one, two or three bony walls or a combination thereof''.[4]Intrabony defects are usually classified according to the criteria presented by Goldman & Cohen:[5]

1. One-wall intrabony defects: defects limited by one osseous wall and the tooth surface;
2. Two-wall intrabony defects: defects limited by two osseous walls and the tooth surface; and
3. Three-wall intrabony defects: defects limited by three osseous walls and the tooth surface.

Nonsurgical periodontal therapy eliminates the microbial biofilm from the root surfaces of periodontally diseased teeth and removes diseased root cementum without surgical reflection of site. Furthermore it decreases gingival inflammation, periodontal pocket depth and gains clinical attachment level.[6]Local drug delivery (LDD) is used as an adjunct to non surgical periodontal therapy. Various local drug delivery systems used in treating periodontitis include fibers, film, gels, and strips. Gel formulations provide more advantages to the patient because of the relatively faster release of the incorporated drug and can be more easily prepared and administered. Moreover, they possess a higher biocompatibility and allow adhesion to the mucosa in the periodontal pocket.[7]

To achieve best results of nonsurgical periodontal therapy there is need of an agent, which not only acts as an adjuvant to the nonsurgical periodontal therapy but also helps effectively in gaining clinical attachment level, inhibits resorption of the alveolar bone and stimulates new bone formation. Dr. Max Goodson and coworkers introduced concept of LDD to the Periodontology. Goodson's first LDD devices involved hollow fibers of cellulose acetate filled with tetracycline.[8] From then onwards many other antimicrobial agents were introduced in LDD such as chlorhexidine, doxycycline, minocycline, metronidazole[9] and other class of drugs such as bisphosphonates[10] and statins.[11]The link between periodontitis and statins were first explored by J. Cunha-Cruz and coworkers.[12]Goes et.al. found that Atorvastatin decreased alveolar bone loss by over 47% and that the drug can prevent alveolar bone loss seen on a ligature induced periodontitis model.[13]Potential role of statins in periodontal regenerative therapy has been proven over the time. Statins are a group of drugs that reduce the blood cholesterol levels. Blood cholesterol reduction is achieved by blocking cholesterol producing enzyme in the liver. Nowadays, non cholesterol-dependent, pleiotropic effects of statins are gaining more attention. Anti-inflammatory pleiotropic effects result from the inhibition of isoprene modification of signal transducers of inflammation. Statins differ in several ways. They differ with respect to their ring structure and these differences in structure have an effect on the pharmacological properties of statins. [14]

One system to classify statins is by the method they are manufactured. Few of them are derived from microorganisms through biotechnology. These are called as fermentation derived or Type 1(Lovastatin, Simvastatin, Pravastatin, and Pitavastatin). Others are made through chemical synthesis. These are synthetic or Type 2 statins (Fluvastatin, Atorvastatin, and Rosuvastatin).

Amongst all the treatment modalities tried so far to treat periodontitis by gain in clinical attachment level and new bone formation; statins are one of the best family of drugs exhibiting anti-inflammatory and bone stimulating properties that may positively affect chronic periodontitis.[15]

There are various methods of assessing periodontal regeneration such as histological examination, surgical re-entry, probing depth examination, radiographic examinations. Although histological evaluation and surgical re-entry are gold standard but they are invasive methods. Probing depth examination is the easiest way to determine regeneration but all types of periodontal probing have some differences to the measurements due to variations in probing force, probe tip size and shape, angulation and recording errors. Also, the presence of gingival inflammation may allow the probe tip to penetrate the connective tissue attachment, thereby overestimating attachment loss. A decrease in inflammation after treatment could be misinterpreted as regeneration. Clinical attachment level along a root surface is a one-dimensional linear measurement, whereas the regenerative process is three dimensional (3D) in nature. In the case of bony destruction the visual interpretation of the radiograph often underestimates of the clinical situation. Thirty to sixty percent of the mineral content of the bone may be lost before a lesion is readily apparent with a conventional transmission radiograph which is 2 dimensional (2D) in nature.[16]

To tackle these issues, computed tomography (CT) has been introduced because it allows cross-sectional and 3D analysis without distortion. Unfortunately, CT is impractical because of machine cost, complexity, high radiation, and relatively low resolution. Another imaging technique i.e. cone beam computed tomography (CBCT) was introduced for head and neck applications. Divergent to CT, it consists of a conical radiographic source and a high-performance digital panel detector. In most CBCT

machines, the apparatus is analogous in size to a conventional panoramic machine, the examination takes 30 seconds, and radiation is within range of an intraoral full-mouth series. In addition, CBCT resolution can be as small as 0.2 mm, compared to 0.5 to 1 mm for CT.[17]

The literature search revealed that there are very few studies which have been carried out to check efficacy of Atorvastatin (ATV) in treating intrabony defects in CP along with the nonsurgical periodontal therapy. The preliminary results appear to be encouraging in terms of regeneration of the periodontal structures, and so, it was felt necessary to further study this material in the treatment of periodontal intrabony defects. Also, CBCT is one of the latest methods of evaluation and there are very few studies that have used CBCT to assess regeneration.

Considering the above fact, the current study was designed as a randomized clinical trial to evaluate and compare the efficacy of 1.2% ATV gel as an adjunct to scaling and root planing (SRP) and SRP with placebo gel in treatment of periodontal intrabony defects (IBDs) clinically and radiographically using radiovisiography (RVG) and CBCT.

AIM AND OBJECTIVES

The aim of the present study was to evaluate and compare the efficacy of 1.2% ATV gel as an adjunct to SRP and SRP with placebo gel in the treatment of periodontal IBDs.

Also, attached with this aim there were certain objectives:

1. To evaluate the efficacy of SRP in combination with placebo gel in treatment of periodontal IBDs.
2. To evaluate the efficacy of SRP in combination with 1.2% ATV gel in treatment of periodontal IBDs.

3. To assess and compare the efficacy of SRP with placebo gel and SRP with 1.2% ATV gel on the probing pocket depth (PPD) and clinical attachment level (CAL) at 3 and 6 months postoperatively.
4. To assess and compare the efficacy of SRP with placebo gel and SRP with 1.2% ATV gel on the radiographic bone fill at 3 and 6 months postoperatively by RVG.

To assess and compare the efficacy of SRP with placebo gel and SRP with 1.2% ATV gel on the radiographic bone fill at 6 months postoperatively by CBCT.

REVIEW OF LITERATURE

In CP alveolar bone loss is clearly associated with an alteration in the normal balance between bone resorption and formation. Non surgical periodontal therapy still remains the cornerstone of the treatment of periodontitis. Although after non surgical periodontal therapy reduction of the inflammation is obtained; for progressive bone loss in periodontitis adjunctive treatment along with SRP alone is required. It can be hypothesized that a pharmacological agent resulting in suppression of bone resorption or an acceleration of bone formation could protect against alveolar bone loss in periodontitis. This approach might provide a new mechanism by which periodontal disease could be arrested. Since locally delivered statins were discovered to be potent

stimulators of bone formation, the possibility of using these compounds as practical bone anabolic agents has been postulated.

The current study was designed to evaluate the effect of 1.2% ATV gel as LDD agent in CP patients as an adjunct to SRP and to compare changes in clinical parameters such as PPD,CAL and to evaluate radiographic IBD fill.

For the ease of understanding, the review of literature has been segregated into three parts

1. Review of studies on LDD in treatment of CP

2. Review of studies on ATV in treatment of CP

3. Review of studies on the methods of analysis of regeneration.

1. Review of studies on LDD in treatment of CP

Newman et al. (1994)[18]evaluated efficacy of SRP alone versus tetracycline fiber therapy used adjunctively with SRP in the treatment of localized recurrent periodontitis sites in maintenance patients. A total of 113 patients receiving regular supportive periodontal therapy were treated with SRP out of which 105 completed the study. Two non-adjacent sites in separate quadrants were selected in each patient for monitoring based on criteria that the sites were 5 to 8 mm deep and had a history of bleeding on probing (BP). The chosen sites were randomly assigned to one of the two treatment groups. PPD, BP and CAL were measured at baseline and 1, 3, and 6 months. At 1, 3 and 6 months, adjunctive fiber therapy was significantly better in reducing PPD and reducing BP than SRP alone. At 6 months, fiber therapy was significantly better in promoting CAL gain than SRP alone. Overall, these results indicate that fiber therapy significantly enhanced the effectiveness of SRP in the

management of localized recurrent periodontitis sites, in patients receiving regular supportive periodontal treatment.

Panwar et al. (2009)[19] carried out a case-control study on 30 patients suffering from CP. In each patient two quadrants with PPD of 5 mm were selected which were divided in two groups. Only SRP was carried out in 15 patients of Control Group and experimental Group of 15 patients was treated with SRP and tetracycline fiber.PPD was recorded preoperatively and after 30 and 90 days. The data was subjected to statistical analysis. The PPD after 30 and 90 days was subjected to general linear model. The results showed that decrease in PPD after 30 and 90 days following use of tetracycline as an adjunct to SRP was statistically highly significant. The study concluded that LDD with tetracycline fiber as an adjunct to SRP is highly effective in reducing the PPD.

Deo V et al. (2011)[20]in a randomized controlled clinical trial evaluated the efficacy of doxycylinehyclate 10% as an adjunct to SRP in the treatment of CP. Randomized clinical trial including 60 systemically healthy, CP patients was conducted for the 6 months. Test Group was treated by LDD of doxycycline hyclate 10% along with the SRP, while the Control Group was treated by SRP along with placebo. Significantly higher reduction in the mean PPD was demonstrated in the Test Group (3.03 ± 0.92 mm) when compared with the Control Group (2.3 ± 0.65 mm). It was concluded that the use of doxycyline hyclate 10% as an adjunct to SRP provides more favorable and statistically significant reductions in PPD and gain in CAL compared to SRP alone.

Jain R et al. (2012)[21] in a randomized controlled trial evaluated the long term efficacy of 2% minocycline gel as an adjunct to SRP for treating CP. Twenty two

pairs of sites with similar PPD were randomly assigned to Test and Control groups out of which only 13 pairs were evaluated at 9 months. All sites received thorough SRP. Minocycline gel application followed by SRP was carried out in the Test Group sites. PPD, CAL, plaque index (PI), and microbiological parameters using dark field microscope were recorded for both the groups over a 9-month period. The probing depth values in the Test Group at six (3.64±0.83 mm) and nine months (3.81±0.79 mm) were significantly less than Control Group (4.24±0.95 mm) at six and (4.63±0.94 mm) at nine months. At the end of nine months, the numbers of non-motile bacilli in Test Group were significantly less than Control Group. Results in this study did not show any statistically significant advantage of using 2% minocycline gel over scaling and root planing. Authors attributed this statistical insignificance to the small sample size of the study.

Kathariya R et al. (2014)[22]evaluated efficacy of subgingivally delivered 0.5% clarithromycin as an adjunct to SRP in the treatment of CP in a short term double blinded randomized controlled clinical trial. Ninety-eight patients were divided into two treatment groups: Test Group i.e. Group I was treated by SRP plus 0.5% clarithromycin and Control Group i.e. Group 2 was treated by SRP plus placebo. Clinical parameters recorded were gingival index (GI), PI, modified sulcus bleeding index (mSBI), PPD, and CAL at the interval of 4, 8 and 12 weeks. Gingival fluid concentration of 0.5% clarithromycin was estimated by reverse-phase high pressure liquid chromatography. Test Group showed enhanced reduction in GI, mSBI, and PPD, and gains in CAL over time, as compared with the Control Group. The mean concentration of clarithromycin was detected in gingival crevicular fluid for up to 7 weeks which proved its controlled-release. Study concluded that use of 0.5%

clarithromycin as a controlled drug delivery system as an adjunct to SRP enhanced the clinical outcome.

Babrawala I et al. (2016)[23] made use of natural 1% chitosan as LDD in the management of non-surgical periodontal treatment. This was randomized controlled split mouth study including ten patients with PPD ≥ 5 mm. They were categorized randomly by an envelope technique into two treatment groups: Test Group which had ten sites and was treated with SRP plus 1% chitosan membrane and Control Group which also had ten sites and was treated with SRP alone. GI, BP, PPD were the clinical parameters recorded at baseline before SRP and after 4 weeks. The Test Group showed significant improvement in all clinical parameters as compared to the Control Group with the mean difference of 1.4 mm between the outcomes of the Test and the Control groups for PPD and zero score for BP for the Test Group at the end of 4 weeks. Study concluded that chitosan membranes as a form of LDD can be used as an adjunct to SRP.

Vennila K et al. (2016)[24]used 10% neem oil chip as LDD to evaluate the efficacy in the periodontal disease management in a clinical and microbiological study. Twenty patients with the bilateral PPD of 5–6 mm were included in the study. After SRP, 10% nonabsorbable neem chip was placed in the periodontal pocket in one side of the arch while other side was treated with SRP only. Clinical parameters were recorded on the baseline, 7th day, and 21st day and plaque samples were obtained for microbiological evaluation on the baseline and 21st day. Quantitative and qualitative polymerase chain reaction assay was used for studying Porphyromonasgingivalis strains. On the neem chip site clinical parameters were statistically improved and presence of Porphyromonasgingivalis (P. gingivalis)

strains weresignificantly reduced. Study concluded that 10% neem oil LDD delivers desired effects on P. gingivalis and improves clinical parameters in CP.

Debnath K et al. (2016)[25] in a randomized controlled clinical trial evaluated efficacy of nano-bio-fusion gel as an adjunct to SRP in CP. Six chronic periodontitis patients with 76 sites and PPD between 5 and 7 mm were selected in this clinico-microbiological study and they were equally divided into Test and Control sites. SRP was performed in both Control and Test Group followed by nano-bio fusion gel application in 38 sites of the Test Group. Clinical parameters such as PI, GI, papillary bleeding index (PBI), PPD and CAL were recorded at baseline, 6 weeks, and 3 months. Supragingival microbial plaque analysis of 2 patients was done at baseline and 6 weeks interval by colony forming unit analysis in nutrient agar culture media. A statistically significant difference was observed between both groups for PPD, CAL along with the significant reduction of colony-forming units of aerobic periodontopathogens from baseline to a period of 3 months. Study concluded that Locally delivered nano-bio fusion gel exhibited a significant improvement in both clinical and microbiological parameters compared with SRP alone in CP.

Boyapati et al.(2017)[26] in a clinical study evaluated efficacy of LDD of Achyranthesaspera gel (A. asperagel) in the management of CP. Thirty patients with CP were included in the study and categorized into two equal groups. Group A was treated with SRP with A. asperagel and Group B was treated with SRP with placebo gel. A comparison of clinical parameters such as GI, PPD, and CAL were assessed at baseline and then again at 3 months after the treatment in both the groups. A.asperagel when delivered locally along with SRP showed a beneficial effect. The clinical parameter difference in both the Test and Control groups from baseline to 3

months showed that the mean GI in the Test and Control groups were 1.25 and 0.25, respectively, the mean PPDs in the Test and Control groups were 2.24 and 0.34,respectively, and the mean CAL in the Test and Control groups were 0.73 and 0.20, respectively, which showed statistically significant results.

Mahendra J et al. (2017)[27] evaluated the periodontal status of individuals and the presence of red complex microorganisms, such as Treponema denticola, P. gingivalis, and Tannerella forsythia in the subgingival tissues of periodontitis patients before and after the application of 4% mangostana gel as an adjunct to SRP. Twenty-five patients in the Test Group were treated with SRP, and the subgingival application of mangostana gel was used as LDD. Twenty-five patients in the Control Group were treated with SRP and placebo gel. Clinical parameters were recorded, and the presence of red complex microorganisms was analysed by polymerase chain reaction at baseline and at the third month.Clinical parameters, such as PI,GI,PPD,CAL and Treponema denticola were significantly reduced in the Test Group compared to the placebo group from baseline to the third month. P. gingivalis, and Tannerella forsythia were not detected in any of the samples at baseline and at the third month, and therefore, were not taken into statistical consideration. There was a significant improvement in the periodontal status with a reduction in Treponema denticola with the application of mangostana gel in periodontal pockets. Study concluded that, 4% mangostana gel can be used as an adjunct to SRP.

Agarwal E et al. (2012)[28] in a randomized controlled clinical trial locally delivered 0.5% Azithromycin, as an adjunct to SRP in CP with type 2 diabetes mellitus. This study included 63 patients which were categorized into two treatment groups. Group 1 was treated with SRP plus placebo gel and Group 2 was treated with SRP plus

0.5% Azithromycin. Clinical parameters such as PI, mSBI, PPD and CAL were recorded at baseline, 3, 6 and 9 months. Patients in Group 2 treated with non surgical periodontal therapy along with 0.5 % Azithromycin showed enhanced reduction in PI, mSBI, PPD and gain in CAL over a period of 9 months as compared to Group 1 which was treated with SRP along with placebo gel. Study concluded that although both treatment strategies seemed to benefit the patients, the adjunctive use of 0.5% Azithromycin as a controlled drug delivery system enhanced the clinical outcome.

Gupta A et al. (2018)[29] in a randomized controlled clinical trial evaluated the efficacy of LDD of zoledronate gel as an adjunct to SRP for the treatment of human periodontal IBDs clinically and radiographically. Forty intrabony defects in moderate to severely affected forty CP patients with the age range, 30–50 years were randomly divided into two groups and treated either with 0.05% zoledronategel or placebo gel after SRP. Clinical parameters such as PI, GI,PPD and CAL were assessed at baseline and at 3 and 6 months. Radiographic parameters were evaluated at baseline and 6 months. In intragroup comparisons, both groups showed significant PI and GI reduction after treatment at 3 and 6 months using dentascan. In intergroup comparisons, PPD reduction and CAL gain were significant only in zoledronate group at 6 months. Radiographically, significant reduction in defect depth and buccolingual width with volumetric defect gain of 40.24% ± 7.44% in zoledronate gel group compared to insignificant gain of 1.60% ± 4.06% in placebo gel group was observed at 6 months.

Singhal S et al. (2018)[30] in a randomized controlled clinical trial evaluated the efficacy of 0.75% boric acid gel as LDD adjunct to SRP for the treatment of class II furcation defects in comparison with placebo gel. Total 48 mandibular class II

furcation defects were randomized and treated with 0.75% boric acid gel at the Test site and placebo gel at the Control site. Clinical parameters were evaluated at baseline, 3 months, and 6 months and radiographic parameters were assessed at baseline and 6 months. Greater mean PPD reduction and mean vertical and horizontal CAL gain were shown to be greater in group treated with boric acid gel than in group treated with placebo gel at 3 and 6 months. Furthermore, a significantly greater mean percentage of bone fill was found in group treated with boric acid gel (16.98%±1.03%) than in the group treated with placebo gel (2.86%±0.92%) at 6 months. Study concluded that boric acid gel can also be used in treatment of class II furcations.

2. **Review of studies on ATV in treatment of CP**

J. Cunha-Cruz et al. (2006)[12] investigated statin use and tooth loss in CP patients. This study was designed to evaluate whether statin use by CP patients had any advantageous effect on tooth loss. This was a retrospective cohort study in which dental records were merged with pharmacy data. Conditions such as any type of statin use during 3 years, statin use during each of 3 regular years, and any statin use during the first 3 years after the initial periodontal examination were evaluated as predictors of tooth loss using negative binomial regression models with adjustment for potential confounding factors. They found that any statin use during 3 years was not associated with tooth loss rate in the year subsequent to the 3-year period. Regular statin use for consecutive 3 years was associated with a non-significant tooth loss rate of 37% in the subsequent years. Any statin use during the first 3 years after the initial periodontal examination was associated with a 48% decreased tooth loss rate in 4th and subsequent years. Although this study had lack of control for some potential confounders, particularly smoking, and evaluation of different

patterns of statin usage which hampered the interpretation of the results; exploration of these findings in additional epidemiological studies may be worthwhile.

Goes P et al. (2010)[13] studied the effect of ATV in radiographic density on alveolar bone loss in wistar rats. Periodontitis was induced in a total of 24 male wistar rats by ligature placement around the upper second left molar. Saline group was constituted by 6 rats. The animals received 0.5 mL of sterile saline by oral gavage, 30 min before ligature placement and then daily, during 11 days and at the 11th day, the animals were sacrificed. The other 18 rats were subdivided in 3 groups of 6 animals each, which received ATV dissolved in sterile saline by oral gavage at doses of 1, 3 and 9 mg/kg, for each respective group. ATV was administered 30 min before ligature placement and then daily, during 11 days, when the animals were sacrificed. After the animals were sacrificed, their maxillae were removed, defleshed, radiographed and latter stained to be photographed. Results found that ATV reduced alveolar bone loss by over 47% when compared to the group of untreated animals. Study concluded that ATV was able to prevent bone loss seen on a ligature induced periodontitis model.

Fajardo ME et al. (2010)[31] investigated the effect of ATV on CP in pilot study. Total 38 patients with CP were randomized into two group, paired by age to receive ATV (20mg) or placebo daily for 3 months. Both groups were treated by SRP at baseline. Clinical parameters such as PI, CAL, gingival recession (GR), BP and radiographic parameters i.e. distance from the crestal alveolar bone to the cement-enamel junction, bone mineral density also lipid profile as well as bone turnover markers such as serum bone-specific alkaline phosphatase (BSAP);a marker of bone formation, and serum crosslinked N-telopeptides (NTx);a marker of bone resorption were assessed at baseline and at 3 months. At the end of the study statistically

significant improvements were found in cholesterol levels, low density lipoprotein levels, dental mobility, the distance from the crestal alveolar bone to the cement-enamel junction and bone mineral density in the ATV group. Study concluded that ATV might have beneficial effects on bone alveolar loss and tooth mobility in subjects with periodontal disease.

Pradeep AR et al. (2013)[32] investigated the clinical efficacy of subgingivally delivered 1.2% ATV gel in CP in a randomized controlled clinical trial. Total 60 subjects were randomized into two treatment groups. Test Group received SRP plus 1.2% ATV gel and Control Group received SRP plus placebo gel. Clinical parameters, which included PI, mSBI, PPD, CAL were recorded at baseline,3,6 and 9 months. IBDs were measured on the radiograph by measuring the vertical distance from the crest of the alveolar bone to the base of the defect. Radiographically assessment of depth of bone fill was evaluated at baseline, 6 and 9 months using an image analyzer and computer aided software. Study results showed that mean PPD reduction and mean CAL gain were greater in the Test Group than the Control Group at 3, 6, and 9 months. A significantly greater mean percentage of radiographic bone fill was found in the ATV gel group compared to the placebo group after 9 months. Study concluded that ATV as an adjunct to SRP can provide a new direction in the management of IBDs.

Rosenberg D R et al. (2015)[33]investigated short term effects of 2% ATV dentifrice as an adjunct to SRP. This randomized, double masked clinical trial was performed with following two parallel groups: 1.ATV group which was treated with SRP plus medicated 2% ATV dentifrice and 2.placebo group which was treated with SRP plus placebo dentifrice. The effectiveness of these treatments was assessed using periodontal measurements obtained at baseline and 1 month later. The

measurements were BP, GI, PPD, CAL and periodontal inflamed surface area (PISA). Study found that the ATV group showed a decrease in PISA which was significantly greater than the reduction observed in the placebo group. There was also a significantly greater reduction in mean PD, percentage of sites with PD ≥ 5 mm, mean CAL, percentage of sites with CAL ≥ 5 mm, BP, and GI in the ATVgroup compared with the placebo group. Study concluded that SRP plus 2% ATV medicated dentifrice was more effective in improving clinical periodontal parameters than SRP plus a placebo dentifrice.

Kumari M et al. (2016)[34] evaluated the effectiveness of 1.2% ATV gel, as an adjunct to SRP in the treatment of IBDs in CP in subjects with type 2 diabetes mellitus. Seventy five patients were categorized into two treatment groups: SRP plus 1.2% ATV, and SRP plus placebo. Clinical parameters mSBI, PPD, CAL were recorded at baseline and at 3, 6 and 9 months. Percentage radiographic defect depth reduction was evaluated using computer-aided software at baseline, 6 months and 9 months. Mean PPD reduction and mean CAL gain was found to greater in ATV gel group than placebo group, at 3, 6 and 9 months. Furthermore, ATV group sites presented with a significantly greater percentage radiographic defect depth reduction at 6 and 9 months. Locally delivered ATV gel in was found to be effective in treatment of IBDs in CP in subjects with type 2 diabetes mellitus.

Martande SS et al. (2017)[35] in a randomized controlled trial compared effectiveness of 1.2% ATV gel and 1.2% simavastatin (SMV) gel, in addition to SRP, in the treatment of IBDs in patients with CP. Ninety-six individuals were categorized into three treatment groups: SRP plus 1.2% ATV gel, SRP plus 1.2% SMV gel and SRP plus placebo. Clinical parameters such as PI, mSBI, PPD, CAL were recorded at baseline before SRP and at 3, 6 and 9 months. Bone fill was

assessed using percentage radiographic defect depth reduction at baseline, 6 months and 9 months.Both ATV and SMV showed significant PPD reduction and CAL gain than placebo. ATV group showed greater mean PPD reduction and mean CAL gain as compared to SMV group at 3, 6 and 9 months. Furthermore, ATV group sites exhibited a significantly greater percentage of radiographic defect depth reduction (33.23 ± 3.11%; 34.84 ± 3.07%) as compared to SMV (30.39 ± 3.36%; 32.15 ± 3.37%) at 6 and 9 months. ATV resulted in greater improvements in clinical parameters with higher percentage of radiographic defect depth reduction as compared to SMV in the treatment of IBDs in CP subjects.

Masoumi S et al. (2017)[36]evaluated the effect of low dose doxycycline and ATVon gingival inflammation and alveolar bone loss in an experimental model of periodontitis in rats. Forty male Sprague Dawley rats were divided into four study groups as follows: (I) experimental periodontitis control, (II) rats with periodontitis treated with low dose ATV(10 mg/kg), (III) rats with periodontitis treated with low dose doxycycline (6 mg/kg) and rats with periodontitis treated with both doxycycline and ATV. Periodontitis was induced by ligature placement around the upper left second molar foe seven days. The periodontitis group received saline, doxycycline group received doxycycline by oral gavage, ATVgroup received ATV by oral gavage and doxycycline plus ATV group received both drugs simultaneously (6 and 10 mg/kg, respectively) for 21 days after ligature placement. Then, the rats were sacrificed and their maxillae were removed, defleshed, and prepared for histopathological examination. Results stated that using a combination of doxycycline and ATVcaused a significant decrease in gingival inflammation and alveolar bone loss (16.5%) and collagen degradation (13%) when compared to the Control Group (36.10% and 36.95%, respectively). It was concluded that Low dose

ATV and low dose doxycycline synergically prevented alveolar bone loss and collagen degradation in ligature-induced periodontitis in rats.

Kumari M et al. (2017)[37] investigated the effectiveness of a 1.2% ATV gel as as an adjunct to SRP in the treatment of IBDs in CP among smokers. Seventy one smokers with CP were categorized into two treatment groups: SRP + 1.2% ATV gel and SRP + placebo gel. Clinical parameters such as mSBI,PPD,CAL were recorded at baseline before SRP and at 3, 6, and 9 months. At baseline, 6 months, and 9 months, the percentage of radiographic defect depth reduction was determined using computer-aided software.The mean probing depth reduction and mean clinical attachment level gain were found to be greater in the ATV group than the placebo group at 3, 6, and 9 months. A significantly greater mean percentage of radiographic defect depth reduction was found in the ATV group compared to the placebo group after 9 months. Study concluded that the ATV as an adjunct to SRP can be used in the treatment of IBDs in CP among smokers.

3. Review of studies on the methods of analysis of regeneration.

Misch et al. (2006)[38] in a study did comparison between CBCT measurements of periodontal defects and measurements done by conventional methods. They created artificial osseous defects on dry skull mandibles. CBCT scanning, periapical radiography, and direct measurements using a periodontal probe were compared to an electronic caliper that was considered as a standard reference. There was no statistical difference between bone sounding, radiography, and CBCT in all the linear measurements. When isolated interproximal measurements using a probe versus the caliper were compared there was a significant difference but no significant difference was obtained for CBCT and radiography. Buccal and lingual

defects was not possible to be measured on radiographs. Overall, all the three techniques are useful for identifying interproximal periodontal defects. Study concluded that when compared to radiographs, the three-dimensional capability of CBCT offers a significant advantage.

Grimard et al. (2009)[39] did comparison between the measurements obtained from digital intraoral radiographs and CBCT images to direct surgical measurements for the evaluation of regenerative treatment outcomes. Digital intraoral radiographs and CBCT images were taken prior to initial bone grafting and at the 6 month reentry surgery for 35 intrabony defects. After carrying out defect debridement, direct bony defect measurements were done with a periodontal probe. These same measurements were made on the radiographs and CBCT images and then compared to the direct surgical values. CBCT correlated strongly with surgical measurements, whereas intraoral radiographs correlated less favorably. Intraoral radiographs measurements were significantly less accurate compared to CBCT for all parameters investigated and underestimated surgical measurements from 0.6 ± 2.3mm to 1.5 ± 2.3mm. No significant difference for the distance from the cementoenamel junction to the alveolar crest, defect fill, or defect resolution was seen between CBCT and surgical measurements. Overall, compared to direct surgical measurements, CBCT was significantly more precise and accurate than intraoral radiographs. Study concluded that CBCT may obviate surgical reentry as a technique for assessing regenerative therapy outcomes.

Vasconcelos K De Faria et al. (2012)[40] compared periapical radiographs with CBCT in detecting and localizing alveolar bone loss by comparing linear measurements of the height, depth and width of the defects as well as identifying combined bone defects in tomographic images. The images were selected from a

secondary database of patients referred for periodontal evaluation. There were 51 sites in study showing both horizontal and vertical bone loss, assessed by 3 trained examiners. The results showed that there were no statistically significant differences between the imaging methods in terms of recognition of the pattern of bone loss. However, there were differences between the two methods when the distance between the cementoenamel junction and the alveolar crest(CEJ-AC) was measured. The two methods differ in detecting the height of the alveolar bone crest but present similar views of the depth and width of bone defects. CBCT was the only method that allowed for an analysis of the buccal and lingual/palatal surfaces and improved visualization of the morphology of the defect.

Raichur et al. (2012)[41] compared the linear measurements of RVG and digital volume tomography (DVT) to direct surgical measurements of periodontal infrabony defects. RVG and DVT images were taken preoperatively for 28 infrabony periodontal defects. After debridement of the defect during surgery direct bony defect measurements were made from the cemento enamel junction to the base of the defect (CEJ-BD) and CEJ-AC with a periodontal probe. These same measurements were done on the RVG and DVT images and then compared to the direct surgical values. Correlation of DVT was stronger than RVG with surgical measurements. Study concluded that DVT technique is significantly more precise than RVG in the measurement of infrabony periodontal defects.

Pahwa et al. (2014)[42] compared the diagnostic values of RVG and CT images in comparison with direct surgical measurements for the determination of periodontal bone loss. Fifteen patients including10 female and 5 male with the age range 20 to 54 years participated in the study. The inclusion criteria were a diagnosis of generalized moderate to severe CP patients with at least one inter proximal site with

a minimum of 3 mm of CAL. Each defect was the unit of analysis in the present study. Total 31 vertical defects were included for direct measurements during surgery with a periodontal probe. At the beginning of the study, the patients were subjected to a baseline examination during which the PPD and CAL were assessed. RVG and CT images were taken preoperatively. Similar measurements were evaluated on RVG and CT and compared with the direct surgical values. Measurements included determination of alveolar bone level that is, CEJ-BD and CEJ-AC. Infrabony component was measured by subtracting CEJ-AC from CEJ-BD. Intra class correlation of CT scan was highest with the smallest length of 95% confidence interval. CT scan depicted maximum agreement with the surgical value. CT scan outscored over RVG in evaluation of the osseous defects and established more precise and clinically useful images of the osseous defects closer to the gold standard.

Banodkar et al. (2015)[43] evaluated the accuracy of CBCT measurements of alveolar bone defects caused due to periodontal disease, by comparing it with actual surgical measurements which is the gold standard. Total 100 IBDs in fifteen patients suffering from periodontitis and scheduled for flap surgery were included in the study. On the day of surgery prior to anesthesia, CBCT of the quadrant to be operated was taken. After reflection of the flap, clinical measurements of periodontal defect were made using a reamer and digital vernier caliper. In the case of horizontal defects, the defect depth was measured as distance between the CEJ-AC. In the case of vertical defects, the defect depth was measured as distance between the CEJ-BD. The CBCT measurements followed the same pattern as clinical measurements. The measurements taken during surgery were then compared to the measurements done with CBCT and subjected to statistical analysis. Overall

there was a very high correlation between the surgical and CBCT measurements. Hence CBCT is highly accurate in measurement of periodontal defects and proves to be a very useful tool in periodontal diagnosis and treatment assessment.

Chhabra et al. (2016)[44] determined the accuracy of CBCT in quantifying IBDs. Total 5 patients with IBDs were selected and 10 defects were assessed. A total of 60 measurements were performed. Periapical radiographs and CBCT images were taken. Height and depth of each defects was measured using proper software. Direct measurements were done during surgical interventions using a periodontal probe were considered the standard reference. Measurements made by all three techniques were compared to each other. Linear measurements for all defects revealed no statistical differences between CBCT and direct intra-surgical measurements with respect to the height and depth of the defect. There was a significant difference when comparing periapical radiographs to the other two techniques. Periapical radiograph measurements were only 74.3% accurate as compared to the standard intra surgical whereas the CBCT measurements showed accuracy of 86.5%. All three modalities were useful for identifying interproximal periodontal defect but CBCT took the front with better accuracy in reproducing the clinical measurement of IBDs and better visualization of the extent of the defect.

Yu-Jiao Guo et al. (2016)[45]assessed periodontal bone loss in CBCT images by 6 site method. Total 150 measuring points in 11 molars and 14 premolars from 6 patients i.e. 2 males and 4 females were included. Prior to periodontal surgery CBCT images of the teeth were acquired. Four observers evaluated the distances between CEJ-BD at the mesio–buccal, mid-buccal, disto-buccal, mesio-lingual/palatal, mid-lingual/palatal and disto–lingual/palatal sites in CBCT images. Direct surgical measurements of the six sites were obtained during periodontal

surgeries. Difference between the values of distances measured in the CBCT images and direct surgical measurements were checked. Interobserver and intraobserver differences were tested. Results showed that no statistically significant difference was found between the surgical and CBCT measurements. Diagnostic similarity rates of four observers were 86.7%, 87.3%, 88.7% and 88.0%, respectively. The interobserver and intraobserver variances were not statistically significant. Study concluded that the six-site measuring method implicated in study may be a useful 3-dimensional method for evaluation of periodontal defect.

Suphanantachat S et al. (2017)[46]compared evaluation of clinical values by CBCT and conventional intraoral radiography (IOR) in IBD assessment. The study included 25 patients suffering from periodontitis and presented at least two IBDs. All patients received clinical periodontal examination, IOR and CBCT. Three periodontists checked periodontal diagnosis and prognosis of each tooth. For teeth with presence of infrabony defects, the number of defect walls was determined. IOR and CBCT assessment was compared. There were total 666 teeth and 123 infrabony defects. The overall value similarity between IOR and CBCT for periodontal diagnosis, prognosis, infrabony defect type and infrabony defect treatment were 79.3%, 69.5%, 44.7% and 64.2%, respectively. Diagnosis, prognosis and the number of infrabony defect walls were underestimated by IOR at 16.4%, 24% and 37.4%, respectively. CBCT showed admirable interexaminer agreement and greater percentage of complete agreement among examiners than IOR for all assessments.IOR underrated the severity and prognosis of periodontal disease. CBCT was finer to IOR for valuation of infrabony defect morphology and treatment. The study concluded that CBCT provides excellent agreement among examiners on IBD assessment and hence is a reliable method to measure them.

MATERIALS AND METHODS

The present study was undertaken to evaluate and compare the efficacy of 1.2% ATV gel as an adjunct to SRP and SRP with placebo gel in treatment of periodontal IBDs. The evaluation was done clinically and radiographically using RVG and CBCT.

Present randomized controlled clinical study was conducted in Department of Periodontology of our institution. The study sample included 20 patients (10 males and 10 females) with generalized chronic periodontitis exhibiting bilateral intrabony defects. The patients were aged between 30 to 45 years.

The study was initiated after the clearance from the Institutional Ethics Committee of our institute. A special proforma was designed so as to have systematic and

methodological recording of observation and information. This included a detailed case history, clinical examination, radiographic evaluation, periodontal indices and written consent of the patient.

Inclusion Criteria

1. Patients with moderate to severe CP as assessed by PPD ≥ 5mm and CAL ≥ 5mm.
2. Patients with at least one pair of bilateral IBDs in either maxillary or mandibular arch.

Exclusion Criteria

1. Patients on systemic ATV /statin therapy.
2. Pregnant or lactating women.
3. Patient who has undergone periodontal treatment in previous 6 months.

Clinical parameters:

1. Plaque index (PI)[47]
2. Modified sulcus bleeding index (mSBI)[48]
3. Probing pocket depth (PPD)
4. Clinical attachment level (CAL)

Plaque index (PI)

It was examined in the scoring units of teeth: distofacial, facial, mesiofacial and lingual surfaces. A mouth mirror and dental explorer were used to assess PI.

Scoring Criteria

Score	Criteria
0	No plaque
1	A film of plaque adhering to the free gingival margin and adjacent area of the tooth. The plaque may be seen only by running a probe across the tooth surface.
2	Moderate accumulation of soft deposits within the gingival pocket,on the gingival margin and/or adjacent tooth surface, which can be seen by the naked eye.
3	Abundance of soft matter within the gingival pocket and/or on the gingival margin and adjacent tooth surface.

Calculation

PI per person was obtained by adding all of the plaque scores and dividing by the number of surfaces examined.

$$\text{PI} = \frac{\text{Total plaque score}}{\text{No of surfaces examined}}$$

Interpretation

Excellent	0
Good	0.1-0.9
Fair	1.0-1.9
Poor	2.0-3.0

Modified sulcus bleeding index (mSBI)

The severity of gingival bleeding, a sign of inflammation that is associated with periodontal disease. The tissues surrounding each tooth are divided into four gingival scoring units: disto-facial, facial, mesio-facial and the entire lingual gingival margin. To minimize examiner variability in scoring, the lingual surface was not subdivided because it is mostly likely being viewed indirectly with a mouth mirror. A periodontal probe was used and passed along the gingival margin to provoke bleeding, and the clinical findings were recording to the following scores and criteria.

Calculation

mSBI per person was obtained by adding all of the teeth scores and dividing by the number of teeth examined.

$$\text{mSBI} = \frac{\text{Total scores of all teeth}}{\text{Total number of teeth examined}}$$

Interpretation

Score	Criteria
0	No bleeding when a periodontal probe is passed along the gingival margin.
1	Isolated bleeding spots visible.
2	Blood forms a confluent red line on margin.
3	Heavy or profuse bleeding.

Stent Fabrication

A sterile, perforated stock metal impression tray was selected for each patient. An irreversible hydrocolloid impression material (alginate) was manipulated, carried into the tray and maxillary and mandibular impressions were made. Study casts were prepared for each patient. A customized acrylic occlusal stent was fabricated for each patient to fit over the selected sites. The PPD and CAL were measured by using UNC-15 (University of North Carolina-15) periodontal probe. A groove was made on the stent in relation to each involved tooth to guide the periodontal probe while taking measurements. This technique provided a fixed point and angulation for measurements with the probe at each site.

Probing pocket depth (PPD) and Clinical attachment level (CAL)

The PPD and CAL measurements were obtained using UNC -15 graduated probe with markings to the nearest millimeter (mm). PPD and CAL were measured at four sites around each tooth (mesial, midbuccal, distal and midlingual). PPD was measured from the free gingival margin (GM) to the bottom of the pocket. The distance of gingival margin to cemento-enamel junction (CEJ) was recorded. The distance from the gingival

margin to the bottom of the sulcus was measured in mm. The distance of gingival margin to CEJ was subtracted from the above measurements to obtain the CAL.

RVG analysis

RVG measurements were taken for each group i.e. the Test and the Control Group at baseline 3 and at 6 months. The RVG analysis included the measurement of bone defect height(CEJ –BD), bone defect depth (AC-BD) and the mesiodistal (MD) bone defect width.

CBCT analysis

CBCT measurements were taken for each group i.e. the Test and the Control Group at baseline and at 6 months. The CBCT analysis included the measurement of bone defect height (CEJ –BD), bone defect depth (AC-BD) and the mesiodistal (MD) bone defect width and buccolingual (BL) width.

Armamentarium

A.Diagnostic instruments

1. Mouth mirror

2. UNC-15 periodontal probe

3. Tweezers

4. Explorer

5. Kidney tray

6. Gloves, mouth mask & head Cap

B.Instruments for SRP

1. Scalers

2. Ultrasonic scalers

3. Gracey curettes

C. ForLDD

1. 1.2% ATV gel

2. Placebo gel

3. Disposable syringe

4. Blunt cannula

Preparation of 1.2% ATV gel

The gel base was prepared by adding accurately weighed methyl cellulose to a solution of sodium citrate in distilled water with continuous stirring. The vial was heated to 50ºC to 60º C and agitated using a mechanical shaker to obtain a clear solution. A weighed amount of ATV was added to the above solution and dissolved completely to obtain a homogeneous phase of polymer, solvent, and drug. Thus, the ATV gel was prepared with a concentration of 1.2%. The placebo gel contained the same methylcellulose gel without the ATV added.

Group I (Control Group)-Periodontal IBDs were treated with SRP and placebo gel placement subgingivally.

Group II (Test Group)-Periodontal IBDs were treated with SRP and 1.2% ATV gel placement subgingivally.

Clinical Procedure

Prior to initiating the study, its purpose and design was explained and informed consent was signed by patients in both groups. PPD and CAL was measured with the help of custom made acrylic stent using UNC 15 probe. Clinical procedure consisted of SRP with both hand and ultrasonic instruments. Group I patients were treated by SRP plus placebo gel placement subgingivally while Group II patients were treated by SRP plus 1.2% ATV gel placed subgingivally. For standardization, 0.1 ml placebo gel was injected into the periodontal pockets using a syringe with a blunt cannula in Group I and 1.2% ATV gel 0.1 ml prepared was injected into the periodontal pockets using a syringe with a blunt cannula in Group II. No periodontal dressing applied after delivery of the drug because the prepared formulation decreases in viscosity, which causes swelling and occlusion of the periodontal pocket. Patients were instructed to refrain from chewing hard or sticky foods, brushing near the treated areas, or using any interdental aids for 1 week.

Post operative evaluation

Patients were evaluated by RVG at baseline,3 and 6 months and by CBCT at baseline and 6 months intervals. Measurements of PPD, CAL were taken similar to the pre procedures using UNC-15 periodontal probe.

RVG measurements

A good quality IOPA radiograph with paralleling technique with film holder (XCP, Rinn) was taken using RVG and the linear measurements were done at baseline, 3 and at 6 months postoperatively to measure the defect height and width using software (Digora TM Optime RVG software, Finland).

The distance from CEJ to the base of the defect (CEJ-BD): The distance from the most apical point of the base of the defect to the CEJ was measured.

The distance from CEJ to the alveolar crest (CEJ-AC): The distance from CEJ to the most coronal level of AC along proximal root surface.

IBD Depth: The line perpendicular from the top of the alveolar crest to the root surface was drawn and was named as AC'.The distance from the point AC' to the bottom of the defect (AC'-BD).

MD width of the IBD (AC-AC'):The distance from the point AC' to the alveolar crest (AC).

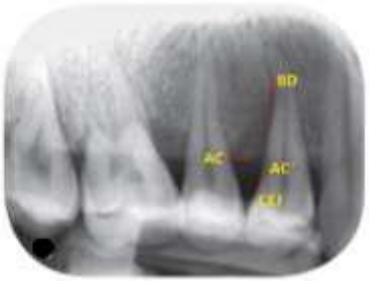


Figure 1: RVG showing different parameters

CBCT Measurements

All the sites in both Test and Control groups were subjected to CBCT assessment. The Orthophos® XG 3D manufactured by Sirona Dental Systems GmbH, Germany using 3Diagnosys 4.2 Imaging software was used for the CBCT assessment. Patient was asked to remove all metal objects and wear a lead apron. The patient was asked to bite gently and naturally on the bite block without joining the incisors. The upper incisors centered with the bite block. The patient was adjusted using two positional laser beams-

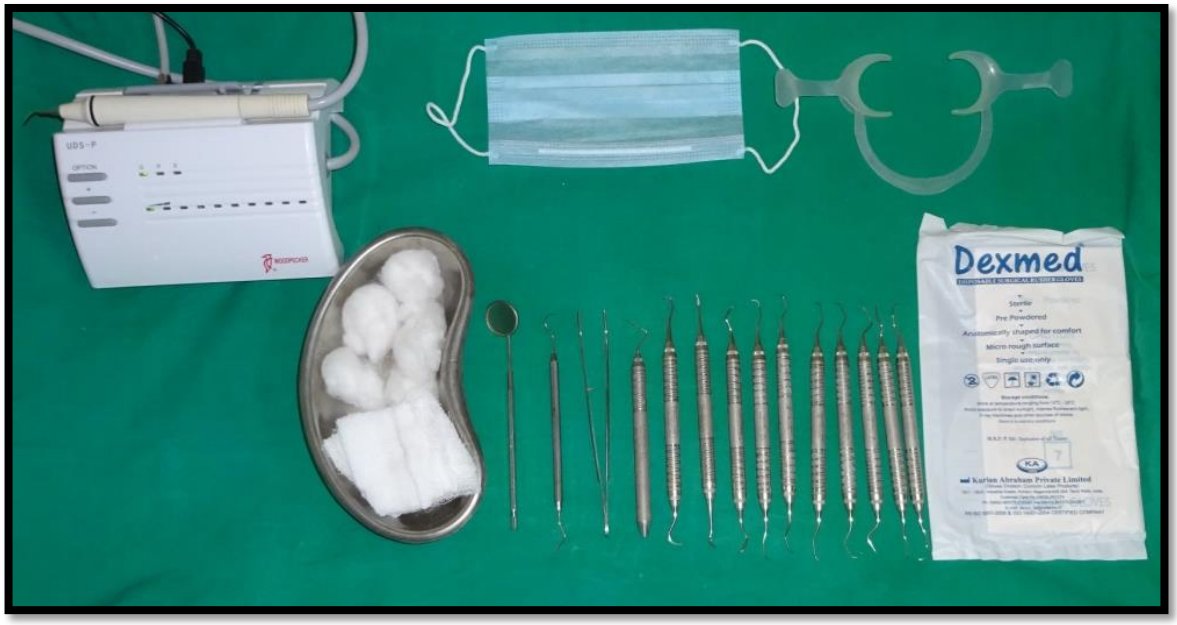
- The mid-sagittal positioning laser beam

- The 3D field of view (FOV) positioning laser beam

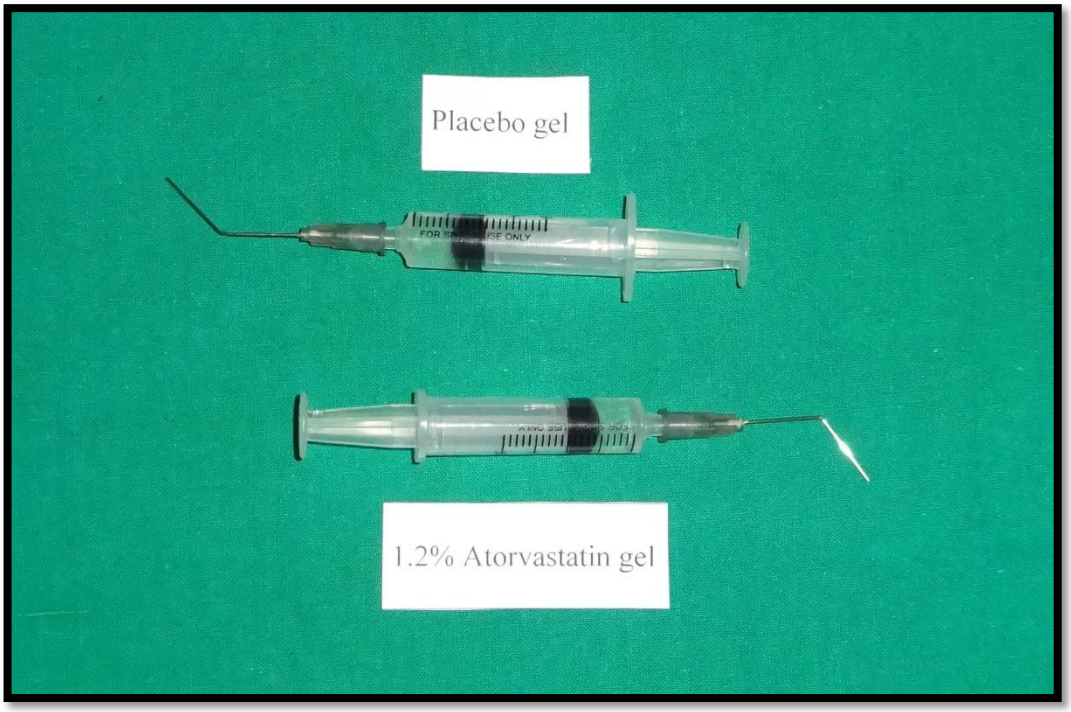
The digital readout was seen on the computer screen.

All the sites in both Test and Control groups were subjected to CBCT assessment at baseline and 6 months postoperatively.The parameters which were measured on CBCT included CEJ-BD, the depth of the defect (AC-BD) and the MD width of the intrabony defect. All parameters above were measured as the same as on the periapical radiographs. Additionally, the BL width of the defect was measured on the axial plane of the CBCT. When the BL width of the defect was measured, the innermost and the most coronal point for the buccal and lingual alveolar crest was chosen on the axial plane, and the horizontal distance of two points were measured. The linear measurements of CEJ to AC and CEJ to BD for each technique were used to determine IBD depth reduction.

ARMAMENTARIUM FOR SCALING AND ROOT PLANING



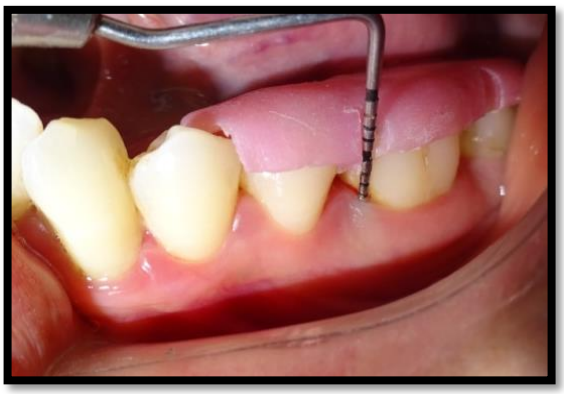
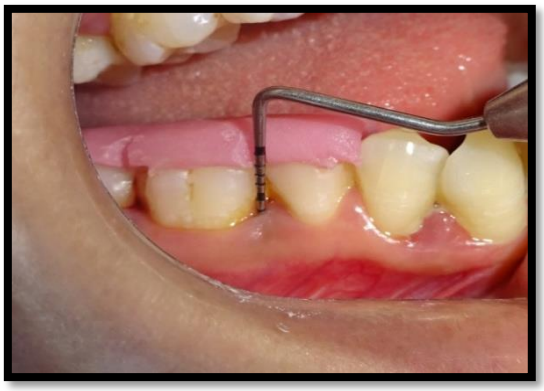
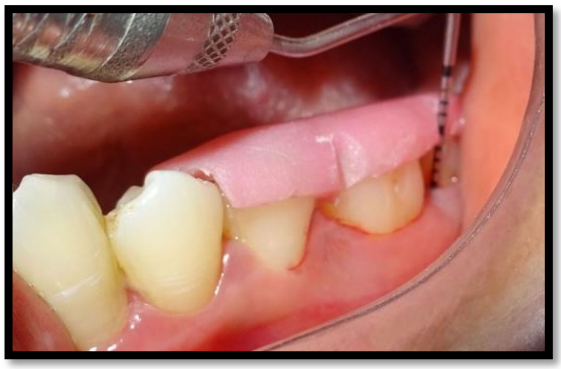
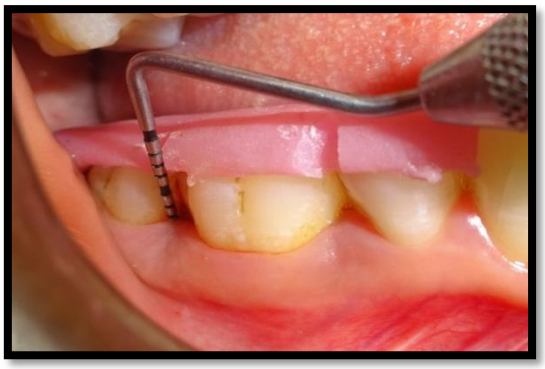
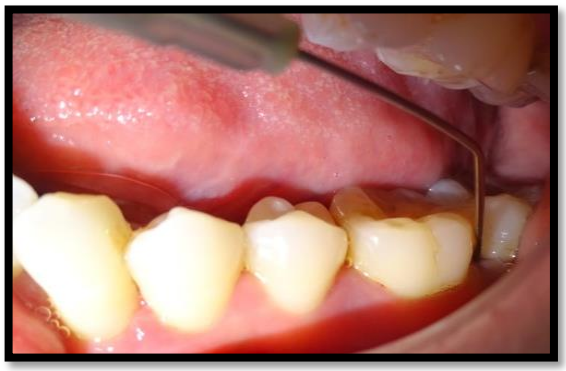
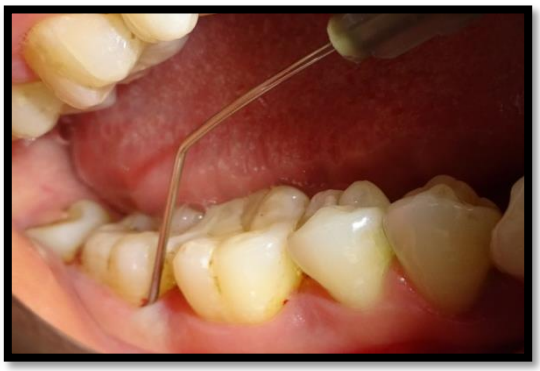
SYRINGE CONTAINING PLACEBO GEL AND 1.2% ATORVASTATIN GEL



CLINICAL RECORDS

BASELINE

GROUP I **GROUP II**

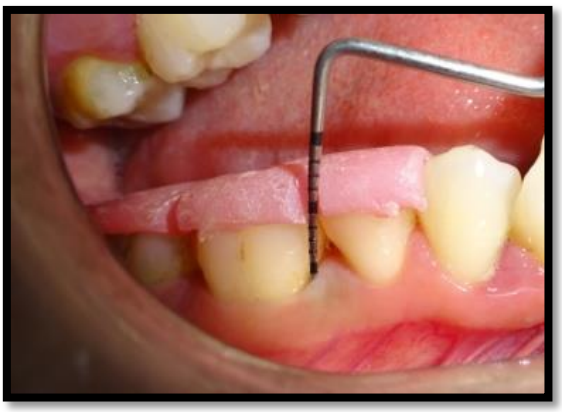







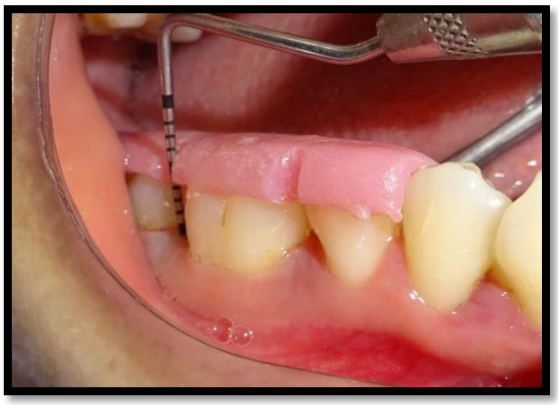
PLACEBO GEL **1.2% ATORVASTATIN GEL**

CLINICAL RECORDS

3 MONTHS RECALL

GROUP I **GROUP II**

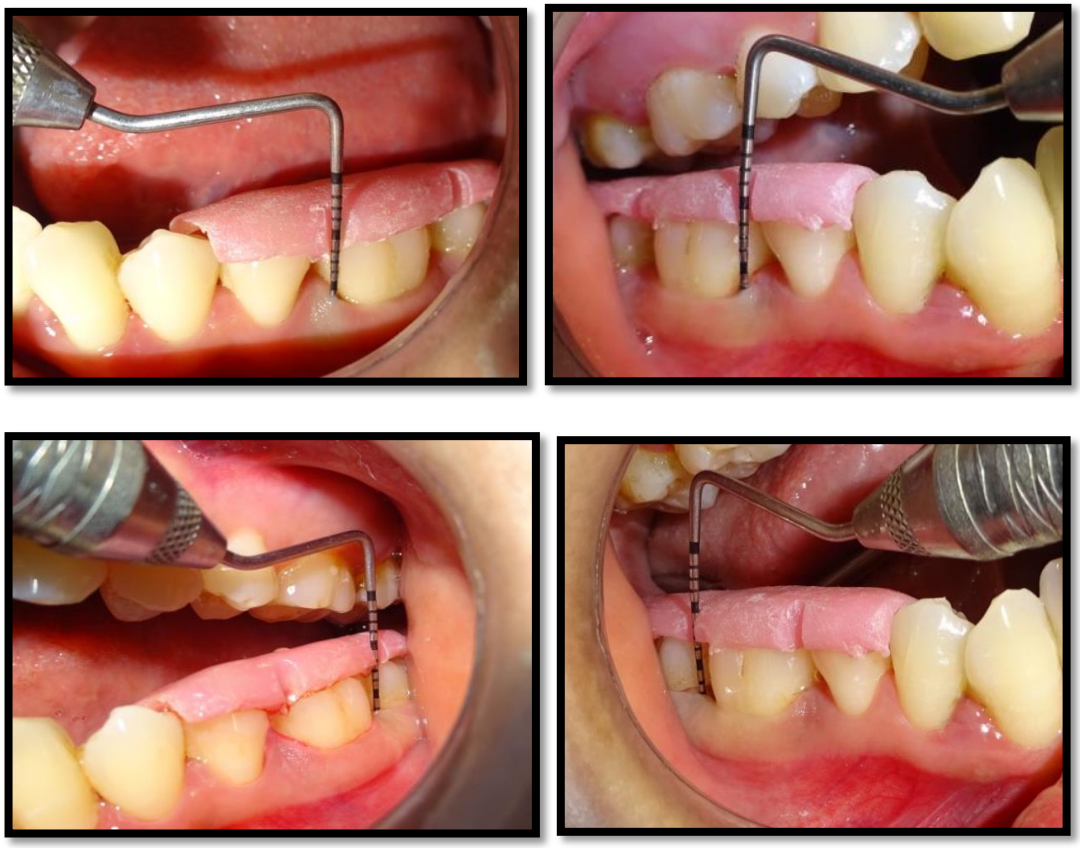





CLINICAL RECORDS

6 MONTHS RECALL

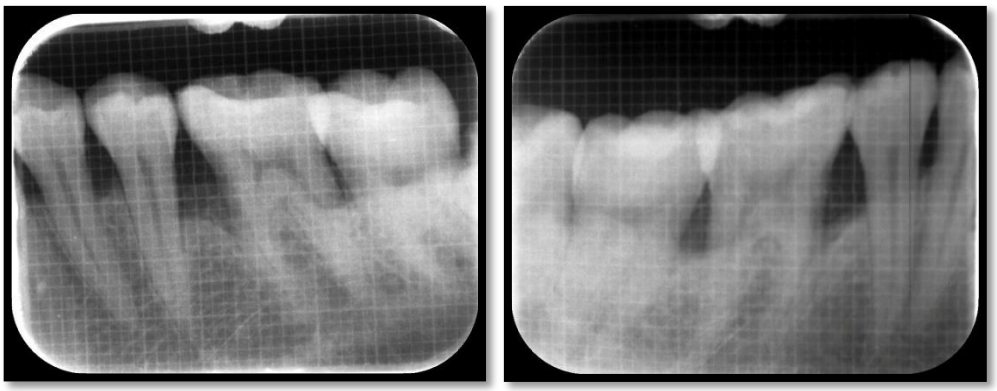
GROUP I **GROUP II**



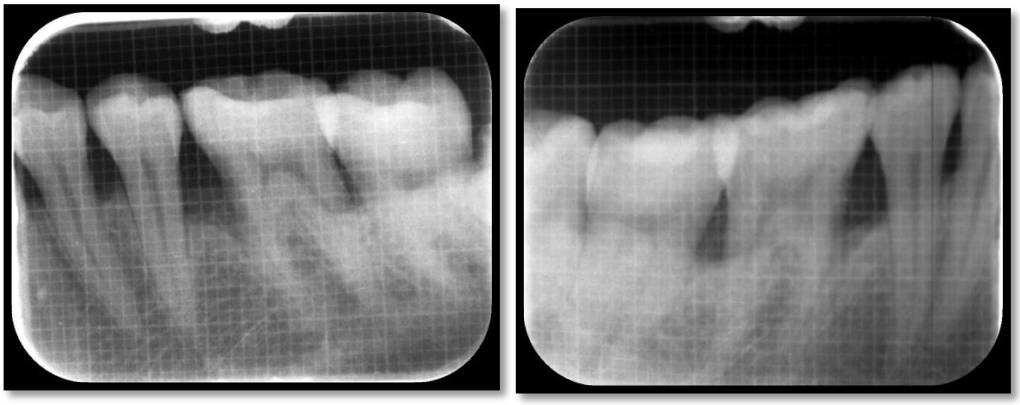
RADIOGRAPHIC RECORDS

RVG

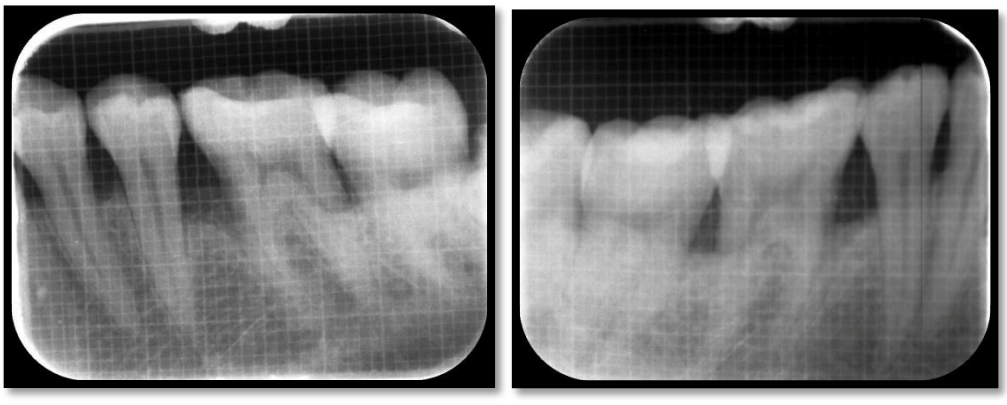
GROUP I **GROUP II**



BASELINE



3 MONTHS

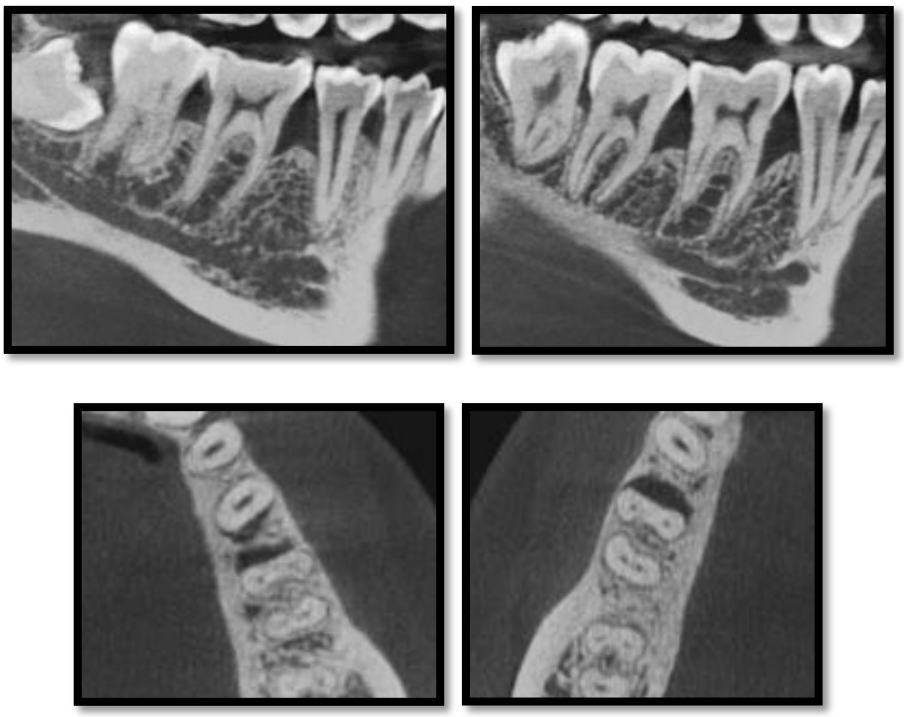


6 MONTHS

CBCT

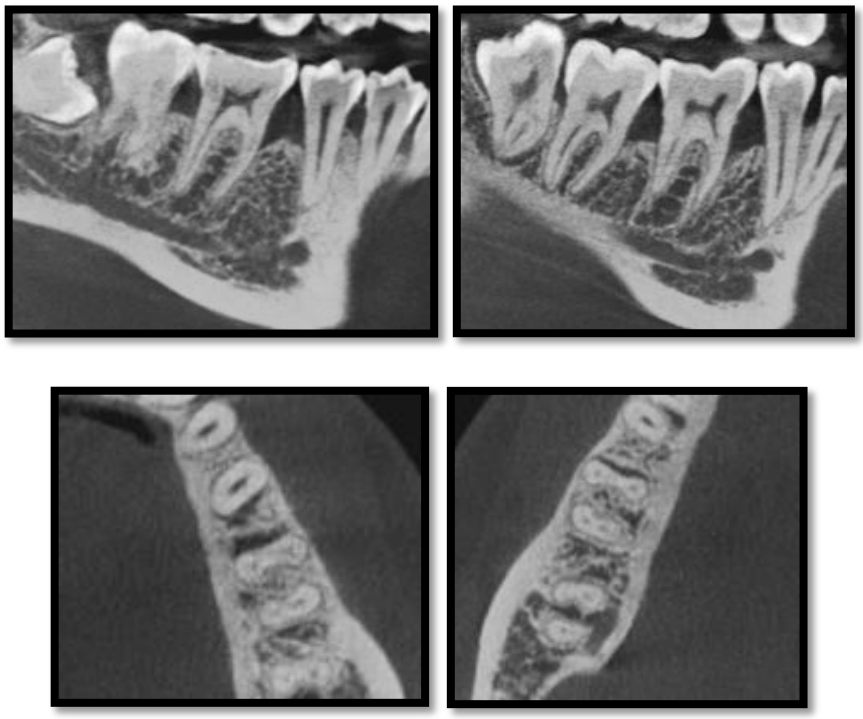
BASELINE

GROUP I **GROUP II**



6 MONTHS

GROUP I **GROUP II**



RESULTS

The present study was carried out to evaluate and compare the efficacy of 1.2% ATV gel as an adjunct to SRP and SRP with placebo gel in treatment of periodontal IBDs. The evaluation was done clinically and radiographically using RVG and CBCT.

At baseline the clinical parameters assessed were PI, mSBI, PPD, CAL and the intrabony defect parameters such as CEJ- BD, CEJ-AC, AC-BD, BL width, MD width were evaluated by CBCT and RVG for both the groups. PI, mSBI, PPD, CAL were measured at all recall visits of 3 and 6 months. Change in distance from CEJ-BD, CEJ-AC, AC-BD and MD width was measured at 3 and 6 months recall visit by RVG and 6 months recall visit by CBCT. CBCT evaluation at 6 months also included BL width dimension

Statistical analysis

The data was analyzed using the SPSS Version 20. The p value was taken as significant when less than 0.05.All clinical parameters were presented as mean ± SD**.** PI, mSBI was compared at different time interval by performing Friedman ANOVA. Change in index parameters between 2 groups were compared by performing wilcoxon rank sum test.PPD and CAL were compared at different time interval by performing one-way repeated measure ANOVA. Change in these clinical parameters at 3 and 6 months from baseline between 2 groups were compared by performing paired t-test. Comparison of CEJ-BD, CEJ-AC, AC-BD, MD, and BL by CBCT between baseline and 6 months was done by performing paired t-test. Mean change at 6 months from baseline between 2 groups were compared by performing paired t-test. Comparison of CEJ-BD,CEJ-AC,AC-BD,MD and BL by RVG at different time point (baseline, 3 and 6 months) by performing by performing one-way repeated measure ANOVA. Mean change at 6 months from baseline between 2 groups were compared by performing paired t-test.

The study sample comprised of 20 patients, which included 10 males and 10 females in the age range of 30 to 45 years, with CP exhibiting 20 pairs of bilateral IBDs. The selected sites were randomly divided to receive either a combination of SRP and placebo gel (Group I) or SRP and 1.2% ATV gel (Group II). The duration of study was 6 months. The study sample included 20 patients (10 males and 10 females) with bilateral IBDs. The patients were aged between 30 to 45 years.

In general, patients showed good oral hygiene through the complete duration of the study. Baseline full mouth PI was 1.76 ± 0.22 while at 3 months, it decreased to 1.04 ± 0.23 and at 6 months, the mean PI score was 0.61 ± 0.18. The difference in PI scores when compared with baseline measurements versus 3 months, showed statistically

highly significant decrease in PI score ($p<0.0001$). At 6 months post-surgical measurements showed statistically highly significant decrease ($p<0.0001$) when compared to baseline, also, the reduction of PI score from 3 to 6 months was statistically highly significant ($p<0.0001$). **(Table 1, 2)(Graph 1)**

The mean mSBI score dropped from 2.78 ± 0.66 at baseline to 1.39 ± 0.19 at 3 months and to 1.11 ± 0.08 at 6 months. mSBI scores when compared from baseline to 3 months showed statistically highly significant decrease ($p<0.001$) and also when compared at 6 months, the difference was statistically highly significant ($p<0.001$). The mean decrease in mSBI score from 3 to 6 months was also statistically highly significant ($p<0.001$). **(Table 1, 2)(Graph 2)**

Clinical outcomes

Probing pocket depth (PPD)

In Group I, the mean PPD at baseline was 7.45±0.51 mm and that at 3 months was 6.20±0.69 mm and in Group II, the mean PPD at baseline was 7.50±0.51 mm and that at 3 months was 5.60±0.59 mm. At 3 months, the mean PPD reduction was 1.25±0.44 mm for Group I and 1.90±0.31mm for Group II. There was a statistically highly significant reduction in PPD for Group I as well as Group II at 3 months compared to baseline ($p<0.0001$). In the Group I, the mean PPD at baseline was 7.45±0.51 mm and that at 6 months was 5. 65± 0.58 mm and in Group II the mean PPD at baseline was 7.50±0.51 mm and that at 6 months was 4.45±0.51 mm. At 6 months, the mean PPD reduction was 1.80±0.41 mm for Group I and 3.05±0.61 mm for Group II. There was statistically highly significant reduction in PPD for Group I and Group II at 6 months when compared to baseline ($p<0.0001$). **(Table 3,4) (Graph 3)**

Clinical attachment level (CAL)

In Group I, the mean CAL at baseline was 7.80±0.52 mm and that at 3 months was 6.50±0.76 mm. The mean CAL at baseline in Group II was 7.90±0.55 mm and that at 3 months was 5.80±0.62 mm. A mean CAL gain of 1.30±0.57 mm was observed in Group I and Group II exhibited a mean CAL gain of 2.10±0.64 mm. Both groups exhibited a statistically highly significant increase in CAL gain at the end of 3 months ($p<0.0001$).

In Group I, the mean CAL at baseline was 7.80±0.52mm and that at 6 months was 5.90±0.64 mm. Group II showed a mean baseline CAL of 7.90±0.55 mm and at 6 months, it was 4.55±0.51 mm. The mean CAL gain at 6 months in Group I was 1.90±0.55 mm and in Group II was 3.35±0.74 mm. There was statistically highly significant CAL gain for Group I and Group II at 6 months when compared to baseline ($p<0.0001$). There was a statistically highly significant CAL gain at 3 and 6 months in Group II when compared to Group I ($p<0.0001$). **(Table 3,4)(Graph 4)**

CBCT analysis of IBD parameters

Height of intrabony defect (CEJ-BD)

The mean CEJ-BD at baseline for Group I was 10.16±0.59 mm and for Group II it was 10.35±0.63 mm. At 6 months, the mean CEJ-BD for Group I was 9.96±0.64 mm, showing a mean reduction in CEJ-BD. The difference in the measurement values of CEJ –BD at baseline and 6 month denotes the bone fill. So bone fill of 0.20 ± 0.69 mm was noted after 6 months for Group I. The mean CEJ-BD at 6 months for Group II was 8.20 ± 0.61 mm thus exhibiting a reduction in CEJ-BD and giving a bone fill of 2.15 ± 0.49 mm. There was a statistically highly significant bone fill in both the groups ($p<0.0001$). When the reduction in CEJ-BD at 6 months was compared between the two groups it was higher in Group II as compared to Group I. **(Table 7) (Graph 5)**

Level of alveolar crest (CEJ-AC)

The mean CEJ-AC at baseline for Group I was 5.33±0.68 mm and for Group II it was 5.49±0.78 mm. The difference in the measurement values of CEJ –AC at baseline and 6 month denotes the change in level of alveolar crest. At 6 months, the mean CEJ-AC for Group I was 5.34±0.58 mm, showing a mean increase in CEJ-AC of 0.02 ± 0.89 mm. The mean CEJ-AC at 6 months for Group II was 5.04±0.58 mm thus exhibiting mean decrease in CEJ-AC of 0.44 ± 0.72 mm. There was statistically insignificant increase in CEJ-AC distance in Group I (p=0.940). There was significant decrease in CEJ-AC distance in Group II (p=0.012).When change in distance CEJ-AC was compared between the two groups was statistically not significant.(p=0.120) **(Table 8)**

Intrabony defect depth (AC-BD)

The mean defect depth (AC-BD) at baseline for Group I was 4.84 ± 0.37 mm and for Group II it was 4.87 ± 0.45 mm. The difference in the measurement values of AC- BD at baseline and 6 month denotes the reduction in IBD depth. At 6 months, the mean defect depth (AC-BD) for Group I was 4.62 ± 0.37 mm, showing a mean reduction in defect depth (AC-BD) of 0.22 ± 0.43 mm. The mean defect depth at 6 months for Group II was 3.16 ± 0.29 mm thus exhibiting a reduction in defect depth of 1.70±0.54 mm. There was a statistically highly significant defect depth reduction in group II (p<0.0001). When the reduction in defect depth at 6 months was compared between the two groups it was higher in Group II as compared to Group I and was statistically highly significant (p=<0.0001)**(Table 9)(Graph 6)**

Mesiodistal width (MD)

The mean MD dimension at baseline for Group I was 2.03±0.51 mm and for Group II it was 2.63±0.65 mm. At 6 months, the mean MD dimension for Group I was

1.81±0.53mm, showing a mean reduction in MD dimension of 0.29 ± 0.63 mm. The mean MD dimension at 6 months for Group II was 1.75±0.59 mm thus exhibiting a reduction in MD dimension of 0.68 ± 0.48 mm. There was a highly significant MD dimension reduction in Group II ($p<0.0001$). When the reduction at 6 months was compared between the two groups it was higher in Group II as compared to Group I and was statistically insignificant ($p=0.085$) **(Table 10)**

Buccolingual width (BL)

The mean BL dimension at baseline for Group I was 5.20±1.31 mm and for Group II it was4.89±1.63 mm. At 6 months, the mean BL dimension for Group I was 4.35±1.43 mm, showing a mean reduction in BL dimension of 0.85 ± 1.13 mm. The mean BL dimension at 6 months for Group II was 3.53±1.66 mm thus exhibiting a reduction in BL dimension of 1.36 ± 0.47 mm. There was a statistically highly significant BL dimension reduction in Group II ($p<0.0001$). When the reduction at 6 months was compared between the two groups it was higher in Group II as compared to Group I and was statistically not significant ($p=0.073$) **(Table 11)**

RVG analysis of IBD parameters

Height of intrabony defect (CEJ-BD)

In Group I, the mean CEJ-BD dimension at baseline was 10.18±0.64 mm and that at 3 months was 10.06±0.68 mm and in Group II, the mean CEJ-BD dimension at baseline was 10.35±0.66 mm and that at 3 months was 9.16±0.79 mm. At 3 months, the mean CEJ-BD reduction (bone fill) was 0.12±0.05 mm for Group I and1.19±0.47 mm for Group II. There was a statistically significant bone fill for Group I as well as Group II at 3 months compared to baseline. In Group I, the mean CEJ-BD dimension at baseline was 10.18±0.64 mm and that at 6 months was 9.96±0.67 mm and in Group II at baseline

it was 10.35±0.66 mm and that at 6 months it was 8.20±0.60 mm. At 6 months, the mean CEJ-BD reduction (bone fill) was 0.22±0.05 mm for Group I and 2.15±0.45mm for Group II. There was statistically significant bone fill for Group I and Group II (p <0.0001) at 6months when compared to baseline. **(Table 6,12)(Graph 7)**

Level of alveolar crest (CEJ-AC)

In Group I, the mean CEJ-AC dimension at baseline was 5.24±0.59 mm and that at 3 months was 5.30±0.64 mm and in Group II, the mean CEJ-AC dimension at baseline was 5.50±0.78 mm and that at 3 months was 5.17±0.58 mm. At 3 months, the mean CEJ-AC increase was 0.07±0.09 mm for Group I and CEJ-AC decrease 0.34±0.49 mm for Group II. There was a statistically significant difference for Group I as well as Group II at 3 months when compared to baseline.

In Group I, the mean CEJ-AC dimension at baseline was 5.24±0.59 mm and that at 6 months was 5.34±0.59 mm and in Group II at baseline it was 5.50±0.78 mm and that at 6 months it was 5.05±0.59 mm. At 6 months, the mean CEJ-AC increases was 0.10±0.19 mm for Group I and mean CEJ-AC reduction was 0.46±0.51 mm for Group II. There was statistically significant increase in CEJ-AC for Group I (p=0.033) and statistically significant decrease in CEJ-AC for Group II (p=0.001) at 6 months when compared to baseline as evaluated by RVG. There was statistically significant increase in CEJ-AC for Group I (p=0.004) and statistically significant decrease in CEJ-AC for Group II (p=0.007) at 3 months when compared to baseline as evaluated by RVG. **(Table 6,13)**

Intrabony defect depth (AC-BD)

In Group I, the mean AC-BD dimension (defect depth) at baseline was 4.95±0.42 mm and that at 3 months was4.76±0.46 mm and in Group II, the mean AC-BD dimension

(defect depth) at baseline was 4.85±0.47 mm and that at 3 months was 4.00±0.39mm. At 3 months, the mean defect depth reduction was 0.18±0.07 mm for Group I and 0.86±0.62 mm for Group II. There was a statistically significant defect depth reduction for Group I as well as Group II at 3 months compared to baseline ($p<0.0001$). In Group I, the mean AC-BD dimension (defect depth) at baseline was 4.95±0.42 mm and that at 6 months was4.63±0.39 mm and in Group II at baseline it was 4.85±0.47 mm and that at 6 months it was 3.15±0.29 mm. At 6 months, the mean defect depth reduction was 0.32±0.18 mm for Group I and 1.70±0.48 mm for Group II. There was statistically significant defect depth reduction for Group I and Group II ($p<0.0001$) at 6 months when compared to baseline. There was statistically significant defect depth reduction at 3 months and 6 months in Group I and Group II. **(Table 6,14) (Graph 8)**

Mesiodistal width (MD)

In Group I, the mean MD dimension at baseline was 2.35±0.77 mm and that at 3 months was 2.11±0.65 mm and in Group II, the mean MD dimension at baseline was 2.74±0.68 mm and that at 3 months was 1.87±0.70 mm. At 3 months, the mean MD dimension reduction was 0.34±0.23 mm for Group I and 0.47±0.52 mm for Group II. There was a statistically highly significant MD dimension reduction for Group I as well as Group II at 3 months compared to baseline. In Group I, the mean MD dimension at baseline was 2.35±0.77 mm and that at 6 months was 2.0±0.64 mm and in Group II at baseline it was 2.74±0.68 mm and that at 6 months it was 1.67±0.71 mm. At 6 months, the mean MD dimension reduction was 0.49±0.43 mm for Group I and 0.66±0.59 mm for Group II. There was statistically highly significant MD dimension reduction for Group I and Group II at 6 months when compared to baseline. There was no statistically significant MD dimension reduction at 3 months and 6 months in Group I ($p=0.15$) while group II

showed statistically significant MD dimension reduction (p=0.19) at 3 months and 6 months.**(Table6,15).**

DISCUSSION

Periodontitis is a chronic inflammatory disease, which if left untreated may lead to irreversible destruction of periodontal tissues. In periodontitis, host response has traditionally been considered to be mediated mainly by B and T lymphocytes, neutrophils and macrophages. These are triggered to produce inflammatory mediators including cytokines, chemokines, arachidonic acid metabolites and proteolytic enzymes which collectively contribute to tissue degradation and alveolar bone resorption. Non surgical periodontal therapy has focused on decreasing microbial challenge by mechanically disrupting and removing bacterial biofilms that form on tooth surfaces and adjacent soft tissue. A growing number of studies, however have indicated strong potential for adjunctive use of drugs as new therapeutic strategies in the management of periodontal disease.[49]

Various groups of pharmacologic agents are used in the treatment of periodontal diseases which offer wide variety of benefits. Statins are proven to be competitive inhibitors of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase. The enzyme HMG-CoA reductase catalyzes the conversion of HMG-CoA to mevalonate,that is the rate-limiting step in the synthesis of cholesterol.[50] Statins act by competitively inhibiting HMG-CoA reductase, the first committed enzyme of the HMG-CoA reductase pathway. Because statins are similar to HMG-CoA in molecular structure, they take the place of HMG-CoA in the enzyme and reduce the rate by which it is able to produce mevalonate, which eventually produces cholesterol. Hence these agents are widely used to lower cholesterol, and they provide an important and effective approach for the treatment of hyperlipidemia and arteriosclerosis. While reducing the hepatic biosynthesis of cholesterol by inhibiting mevalonate pathway, statins display a spectrum of pleiotropic effects like, anti-inflammatory, immunomodulatory, formation of bone morphogenic protein (BMP)-2, and promote osteogenesis by inhibiting osteoblast apoptosis and suppressing osteoclastogenesis. Therefore, statins could play a significant role as therapeutic agents in the treatment of periodontal IBDs.[14]

Effect of the statins on bone metabolism

Administration of the statins has been linked to beneficial effects on bone metabolism. Thus far three pathways have been identified that may explain the beneficial effects of statins on bone metabolism.

1. Statins directly stimulate osteoblast derived BMP-2 expression and subsequently enhance osteoblastic bone formation.

2. They directly affect osteoclasts. This effect depends upon inhibition of the formation of intermediates that are required to prenylate proteins, which block osteoclastic activity.
3. They act through osteoblast-osteoclast cross talks and involves the RANKL(Receptor activator of nuclear factor kappa-B ligand)/OPG(Osteoprotegerin) system. Lipohilic ATV enhances osteoblastic production of OPG, a crucial osteoblast derived cytokine that neutralizes RANKL and prevents the formation and activation of osteoclasts by promoting osteoblastic differentiation.ATV has also been found to enhance the expression of osteoblast differentiation markers, such as alkaline phosphatase and osteocalcin.[51]

It has been described that statins decrease the production of many proinflammatory cytokines, down regulating interleukin (IL)-1α-induced IL-6 and IL-8 production in epithelial cells in a dose-dependent manner. Moreover, statins have been found to decrease secretion of matrix metalloproteinases (MMPs) likeMMP-1, MMP-2, MMP-3 and MMP-9 in vitro. Thus, statins may reduce the fierce immune response, protecting periodontal tissue against destruction, possibly via some of the above mentioned anti-inflammatory mechanisms.[13]

Systemically delivered ATV has superior kinetics as compared to other statins. In a study to evaluate the pharmacokinetic profile and dose effectiveness of different statins in the reduction of oxidative stress in patients with type II diabetes mellitus, ATV 10 mg was found to attain target therapeutic concentrations as compared to 40 mg SMV. The study suggested that ATV reduced oxidative stress more effectively than simvastatin in patients with type II diabetes mellitus.[52]

Lindy et al.[53] suggested that CP patients taking statin medication had 37% lower number of periodontal pockets than those without statin medication. In animal models, statins have been suggested to prevent periodontal tissue breakdown.[54]Statins have beneficial effects on alveolar bone recovery after ligature induced alveolar bone resorption.[55]

In spite of beneficial effects of the statins described above; which can be effective in the treatment of CP; limited data exists about use of ATV in periodontal regeneration. Hence, the present study was carried out to evaluate and compare the efficacy of 1.2% ATV gel as an adjunct to SRP and SRP with placebo gel in treatment of periodontal IBDs. The evaluation was done clinically and radiographically. The study sample included 20 patients (10 males and 10 females) with the age range of 30-45 years with bilateral IBDs. In Group I IBDs were treated with SRP and placebo gel placement. In Group II IBDs were treated with SRP and subgingival delivery of 1.2% ATV gel.

PI, mSBI and clinical parameters such as PPD and CAL were evaluated at baseline, 3 months and 6 months postoperatively. For evaluation of regeneration, CBCT was taken at baseline and 6 months and RVG was taken at baseline at 3 and 6 months.

With regard to the dose of ATV used, 1.2 mg/0.1 mL per site was injected as in the previous study by Pradeep et al.[32]. The current study has considered the technique of subgingivally delivering ATV directly into IBDs in individuals with CP, as the LDD system provides the advantages of high concentrations at the required site with reduced dosage, fewer applications, and high patient acceptability. Compared to a systemic regimen, local delivery may offer important benefits in terms of adverse reactions and patient compliance.

Each patient participating in the study showed good oral hygiene level and a healthy clinical gingival condition throughout the duration of study. The PI score was low at the end of six months. This was the result of repeated oral hygiene instructions given to the patients throughout the study period. Plaque control is essential for the long term stability of clinical outcomes. Bacterial plaque is a major and important factor in the etiology of periodontal destruction and successful therapy depends upon its removal subsequent to treatment. Reduction in PI was statistically significant at the end of 6 months. This was in accordance with the study conducted by Pradeep et al.[31] in which 1.2% ATV gel was delivered to the IBDs of the patients with CP and patients were followed up to 3, 6 and 9 months.Also, same type of reduction in PI scores was observed by Pradeep et al.[56] in which 1.2% Rosuvastatin (RSV) gel was delivered to the IBDs of the patients with CP and patients were followed up to 1, 3, 4 and 6 months.

Researchers have used bleeding index as the way to measure the effectiveness of antiplaque and anti-gingivitis agents, to compare responses to various therapies (e.g., SRP versus periodontal surgery), and to correlate bleeding to disease activity. Clinicians have used BP in their diagnosis and treatment of periodontal diseases to record baseline data of disease, to screen patients before deciding on need for periodontal treatment, and to motivate patients to improve oral hygiene. In our study reduction in mSBI was statistically significant at the end of 6 months. Kumari et al.[34] obtained similar reduction in the values of mSBI where 1.2% ATV gel was delivered in CP with Type II diabetes mellitus and follow up was taken up to 3, 6 and 9 months. Also, same type of reduction in mSBI was observed by Surve et al.(2015)[57] who subgingivally delivered and compared efficacy of 1.2% ATV gel and 1.2% SMV gel as an adjunct to SRP and patients were followed up to 1 week and 1, 3, 6 months.

In contrast to a previous study by Saxlin et al.[58] which showed increased likelihood of deepened periodontal pockets with statin medication, our study found improvement in periodontal parameters in the Group II.

PPD and CAL changes following regenerative therapy is the most important clinical outcome variable in regenerative studies.In our study Group II showed more reduction in PPD as compared to Group I.This can be attributed to the fact that ATV inhibits inflammatory cells and MMPs, which play a role in the connective tissue breakdown in periodontal disease.[59]This was in accordance with the Pradeep et al.[32] and Kumari et.al.[34]According to Pradeep et al.[32] there was statistically significant reduction in PPD of the patients with CP treated with 1.2% ATV gel at the end of 6 months as compared to placebo group. Kumari et al.[34] obtained similar reduction in the values of PPD where 1.2% ATV gel was delivered in CP patients with type II diabetes mellitus and reduction in the PPD was more in ATV group than placebo group.

In our study Group II showed more gain in CAL as compared to Group I. This was in accordance with Rath et al.[60] and Pradeep et al.[56] Rath et al.[60] delivered 1.2% SMV gel in the patients with CP and CAL gain was achieved in both SMV gel group and placebo gel group at 6 month follow up. The difference from baseline was significant within the groups in CAL gain, but when compared there was no significant difference between the groups. This was in contrast with our study which showed statistically significant reduction in PPD in both the groups. Pradeep et al.[56]locally delivered 1.2% RSV gel in patients with CP. Mean CAL gain from baseline to 6 months was greater in RSV group and it was statistically significant. Our study found improvement in all the clinical parameters in the Group II which could be due to the anti inflammatory properties of

statins that could positively affect periodontitis. Improvement in the clinical parameters in Group I of our study can be attributed to the effect of SRP and patient compliance.

The results of our study were in accordance of the study carried by Rosenberg et al.[33] who used ATV in the form of dentifrice in Test Group and placebo dentifrice in Control Group in combination with SRP. They found SRP plus ATV medicated dentifrice was more effective in improving clinical parameters than that of SRP plus placebo dentifrice.

Reduction in the distance CEJ-BD signifies bone gain. In our study reduction in CEJ-BD was more in Group II as compared to Group I. This indicates role of ATV in periodontal regeneration. Change of distance CEJ-AC denotes change in the level of alveolar crest. In our study CEJ-AC distance increased in the Group I but decreased in the Group II at the end of 6 months. This indicates that alveolar crest resorption was more in Group I which was deprived of delivery of 1.2% ATV gel. This was in accordance with Fajardo et al.[31] who found that systemic ATV administration during a period of 3 months resulted in reduction in the distance of CEJ-AC, and reduction in the tooth mobility in individuals with periodontal disease signifying bone gain after 3 months. They found reduction in CEJ-AC distance after systemic administration of pharmacologic agent. On the contrary our study showed similar results by local drug delivery; hence increased the concentration of the drug at desired site at lower dose than systemic administration.

Reduction in the distance AC-BD denotes reduction in the defect depth.In our study defect depth reduction was more in Group II than in the Group I.This bone fill may be because of increased BMP-2 expression during bone regeneration,[61]anti-inflammatory

effects,[59] and angiogenesis during wound healing. ATV is a lipophilic statin that appears to have a more potent bone-sparing effect than hydrophilic statins.[62]Improvement in the Group I could be explained by the mechanical therapy and oral hygiene instructions provided at baseline.

Similar intrabony defect depth reduction was found using ATV in previous studies.[32,34,37] Pradeep et al.[32]subgingivally delivered 1.2% ATV gel in patients with CP. Kumari et al.[34]subgingivally delivered 1.2% ATV gel in the treatment of CP patients with type 2 diabetes mellitus. Kumari et al.[37]subgingivally delivered 1.2% ATV gel in the treatment of CP patients among smokers. In these clinical trials defect fill was evaluated on digital radiograph by software using an image analyzer. On the contrary our study used CBCT which offers better visualization of the bone defect and has higher accuracy than any other radiographic image modality.

Fei Li et al.[63] found that CBCT could provide relatively accurate measurements of MD width of the defect and the BL width of the defect which periapical radiograph could not show. Vasconcelos K De Faria et al.[40]compared periapical radiographs with CBCT imaging in detecting and localizing alveolar bone loss. The authors concluded that CBCT offers improved visualization of the morphology of the defect. CBCT allowed for an analysis of the buccal and lingual/palatal surfaces and an improved visualization of the morphology of the defect. We are also in agreement that CBCT allows better visualization of defect and helps in better preoperative decision making for treatment. Evaluation by CBCT in our study showed that reduction in MD and BL was more in Group II as compared to Group I.

Ong et al.[64] evaluated the use of bioactive glass for regenerating periodontal IBDs by performing re-entry procedure 9 to 13 months after surgical procedure. Authors reported more MD and BL fill in the Test Group where bioactive glass was used as compared to Control Group where only open flap debridement (OFD) was performed.

Variation in results can be attributed to the method of evaluation, treatment and selection of the defects.In our study regeneration therapy of IBDs was carried out non surgically using LDD of 1.2% ATV gel in the defects and evaluation of the regeneration was done at the end of 6 months by CBCT and surgical re entry procedure was not performed. This affirms finding by Grimard et al.[39] that CBCT may obviate surgical reentry as a technique for assessing regenerative therapy outcomes.

Our study affirms the finding of J. Cunha-Cruz et al.[12] and Goes et al.[13] who tried to associate the link between the use of statins and the periodontitis. J. Cunha-Cruz et al.[12] in a retrospective study stated that any statin use during 3 years was not associated with tooth loss rate in the year subsequent to the 3-year period. Although pharmacological effects of statins could be accountable for this result the observed association between statin use and decreased tooth loss could reflect confounding by unmeasured factors. Lack of control for some potential confounders such as smoking, and evaluation of different patterns of statin usage may have hampered the interpretation of the results.

Goes et al.[13] stated that ATV was able to prevent alveolar bone loss seen on a ligature-induced periodontitis model in wistar rats. Hence both of the above studies were unable to establish strong link between use of statins and periodontitis. Our study results affirm the finding of both the studies.

Martande SS et al.[35] in a comparative evaluation of 1.2% SMV gel and 1.2 % ATV gel in treatment of periodontal IBDs found that ATV gel resulted in greater improvements in clinical parameters with higher percentage of radiographic defect depth reduction as compared to SMV gel. This can be attributed to the fact that ATV has superior kinetics than SMV. In a study to evaluate the pharmacokinetic profile and dose effectiveness of different statins in the reduction of cholesterol, ATV (5 mg) was found to attain target therapeutic concentrations to bring about a 30% reduction in LDL cholesterol as compared to 10 mg SMV and 40 mg lovastatin.[65] A study also showed that compared with SMV, ATV exhibited more anti-inflammatory properties as suggested by markers of oxidative stress and inflammation in patients with type II diabetes mellitus.[66] Thus superior pharmacokinetic properties and potent antioxidant and anti-inflammatory properties can be considered as one of the reasons for superior results in the ATV group as compared to the SMV group. Pradeep et al.[67] compared 1.2% RSV gel with 1.2% ATV gel in the treatment of periodontal IBDs. Authors stated that LDD of 1.2% RSV gel results in significantly greater clinico-radiographic improvement compared to 1.2% ATV gel.In our study ATV gel was compared with the placebo gel and not with the other statins and hence appears to be the limitation of our study. Martande SS et al.[68] stated that PRF+1.2% ATV gel in the treatment of periodontal IBDs showed similar improvements in clinical parameters with greater percentage radiographic defect depth reduction as compared to PRF +OFD in treatment of intrabony defects in CP individuals. Thus 1.2% ATV gel failed to augment the regenerative potential of PRF alone in periodontal intrabony defects. Present study evaluated effects of 1.2% ATV gel nonsurgically hence ATV was not combined with any regenerative material to evaluate additional benefits of ATV in periodontal regeneration.

Present clinical trial proves the beneficial effects of the 1.2% ATV gel as an adjunct to SRP for the treatment of IBDs in CP in terms of both clinical and radiographic parameters and evaluated bone fill using CBCT after treating IBDs with 1.2% ATV gel in combination with SRP. Thus,1.2% ATV gel demonstrates a non invasive and attuned way to treat periodontal IBDs and enhance periodontal regeneration.

CONCLUSION

The present randomized, controlled clinical and CBCT study was undertaken to evaluate and compare the efficacy of 1.2% ATV gel as an adjunct to SRP and SRP with placebo gel in treatment of periodontal IBDs. The evaluation was done clinically and radiographically using RVG and CBCT.

Twenty systemically healthy subjects with 20 pairs of bilateral intrabony defects were selected for the study. Baseline measurements included clinical parameters such as PI, mSBI, PPD, CAL, and radiographic measurements included CEJ –BD, AC-BD, MD by CBCT and RVG also BL width by CBCT. PI, mSBI, PPD, CAL were assessed at 3 and 6 months while the CBCT analysis was done at 6 months.

The reduction in PI and mSBI indicated satisfactory maintenance of oral hygiene by patients throughout the study period. PPD reduction in Group I and Group II was significantly greater at 3 months and 6 months. The mean reduction in bone defect height, depth and width in Group II was statistically significantly greater than in Group I at 6 months evaluation. Bone fill was greater and statistically significant in Group II as compared to Group I.

From the analysis of results, following conclusions can be drawn:

1. SRP+1.2% ATV gel compared to SRP+ placebo gel resulted in statistically significant reduction of PPD at 3 months and 6 months compared to baseline.
2. SRP+1.2% ATV gel compared to SRP+ placebo gel resulted in statistically significant reduction of CAL at 3 months and 6 months compared to baseline.
3. SRP+1.2% ATV gel showed significantly better results in terms of reduction in bone defect height, depth and width at 6 months, compared to SRP+ placebo gel.

It can be concluded within the limits of study that the use of SRP+1.2% ATV gel could be more beneficial in achieving better results in terms of periodontal regeneration.

Attempting to identify the most accurate method for evaluating hard tissue changes after periodontal therapy is an important task. To date, re-entry procedure appears to be the gold standard and, while no single method can produce similar information consistently. The images obtained by CBCT, combined with clinical measurements, will definitely increase our ability to determine the treatment outcome without the use of re-entry procedure.

It should be noted that the differences in healing patterns, microbial pathogens, study designs, patient population, measurement techniques and human defect variations make

it difficult to compare clinical results. Also, different methods like clinical, histological and radiographic evaluations have been used in various studies for assessing the outcomes of treatments. This could be some of the reasons for variations observed amongst clinical trials.

The following were the limitations observed in the present study:

1. A larger sample size would be desirable so as to substantiate the results.
2. Long term analysis is needed to determine the stability of the results and to improve the radiographic assessment of the results.

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Table 1

Mean value of PI and mSBI at different time points

Parameters	Baseline		3 months		6 months		p- value
	Mean	SD	Mean	SD	Mean	SD	< 0.0001 (HS)
Plaque index	1.76	0.22	1.04	0.23	0.61	0.18	
mSBI	2.78	0.66	1.39	0.19	1.11	0.08	< 0.0001 (HS)

*Obtained using *Friedman ANOVA*; HS: Highly Significant

Table 2

Comparison of PI and mSBI between different time intervals

	Mean difference			
Comparison	Baseline vs 3 months	Baseline vs 6 months	3months vs 6 months	p- value
Plaque index	0.72	1.15	0.43	< 0.0001 (HS)
mSBI	1.39	1.67	0.28	< 0.0001 (HS)

*Obtained using *Friedman ANOVA*; HS: Highly Significant

Table 3

Mean values of PPD and CAL at different time points in two study groups (in mm)

	Mean ± SD			
Time points	PPD		CAL	
	Group I	Group II	Group I	Group II
Baseline	7.45±0.51	7.50±0.51	7.80±0.52	7.90±0.55
3 months	6.20±0.69	5.60±0.59	6.50±0.76	5.80±0.62
6 months	5.65±0.58	4.45±0.51	5.90±0.64	4.55±0.51
p- value	< 0.0001 (HS)		< 0.0001 (HS)	

*Obtained using *repeated measures ANOVA*; HS: Highly Significant

Table 4

Comparison of reduction of PPD and CAL gain between two groups at different time intervals (in mm)

	Mean ± SD					
Time points	PPD			CAL		
	Group I	Group II	p- value	Group I	Group II	p- value
Baseline vs 3 months	1.25±0.44 p< 0.0001	1.90±0.31 p< 0.0001	< 0.0001	1.30±0.57 p< 0.0001	2.10±0.64 p< 0.0001	< 0.0001
Baseline vs 6 months	1.80±0.41 p< 0.0001	3.05±0.61 p< 0.0001	< 0.0001	1.90±0.55 p< 0.0001	3.35±0.74 p< 0.0001	< 0.0001
3 months vs 6 months	0.55±0.51 p< 0.0001	1.15±0.58 p< 0.0001	< 0.0001	0.60±0.75 P=0.002(S)	1.25±0.72 p< 0.0001	< 0.0001

*Obtained using paired t-test;S:Significant; HS: Highly Significant(p< 0.0001)

Table5 : Mean values of different parameters by CBCT at baseline and 6 months (in mm)

CBCT	Parameters	Mean ± SD	
		Group I	Group II
Baseline	CEJ-BD	10.16±0.59	10.35±0.63
	CEJ-AC	5.33±0.68	5.49±0.78
	AC-BD	4.84±0.37	4.87±0.45
	MD	2.03±0.51	2.63±0.65
	BL	5.20±1.31	4.89±1.63
6 months	CEJ-BD	9.96±0.64	8.20±0.61
	CEJ-AC	5.34±0.58	5.04±0.58
	AC-BD	4.62±0.37	3.16±0.29
	MD	1.81±0.53	1.75±0.59
	BL	4.35±1.43	3.53±1.66

Table 6: Mean values of different parameters by RVG at baseline, 3 and 6 months (in mm)

RVG	Parameters	Mean ± SD	
		Group I	Group II
Baseline	CEJ-BD	10.18±0.64	10.35±0.66
	CEJ-AC	5.24±0.59	5.50±0.78
	AC-BD	4.95±0.42	4.85±0.47
	MD	2.36±0.77	2.74±0.68
3 months	CEJ-BD	10.06±0.68	9.16±0.79
	CEJ-AC	5.30±0.64	5.17±0.58
	AC-BD	4.76±0.46	4.00±0.39
	MD	2.11±0.65	1.87±0.70
6 months	CEJ-BD	9.96±0.67	8.20±0.60
	CEJ-AC	5.34±0.59	5.05±0.59
	AC-BD	4.63±0.39	3.15±0.29
	MD	2.0±0.64	1.67±0.71

Table 7: Comparison of CEJ-BD between two time points in each groups and comparison of change in CEJ-BD between two groups for time interval baseline to 6 months by CBCT (in mm)

Time point	Group I		Group II	
	Mean	SD	Mean	SD
Baseline	10.16	0.59	10.35	0.63
6 Months	9.96	0.64	8.20	0.61
p-value	<0.0001 (HS)		<0.0001 (HS)	
Change in CEJ-BD				
Baseline to 6 months	0.20	0.69	2.15	0.49
p-value*	<0.0001 (HS)			

*Obtained using paired t-test; HS: Highly Significant

Table 8: Comparison of CEJ-AC between two time points in each groups andcomparison of change in CEJ-ACbetween two groups for time interval baseline to 6 months by CBCT (in mm)

Time point	Group I		Group II	
	Mean	SD	Mean	SD
Baseline	5.33	0.68	5.49	0.78
6 Months	5.34	0.58	5.04	0.58
p-value	0.940 (NS)		0.012 (S)	
Change in CEJ-AC				
Baseline to 6 months	0.02	0.89	0.44	0.72
p-value*	0.120 (NS)			

*Obtained using paired t-test; NS: Not Significant

Table 9: Comparison of AC-BD between two time points in each groups andcomparison of change in AC-BDbetween two groups for time interval baseline to 6 months by CBCT(in mm)

Time point	Group I		Group II	
	Mean	SD	Mean	SD
Baseline	4.84	0.37	4.87	0.45
6 Months	4.62	0.37	3.16	0.29
p-value	0.337 (NS)		<0.0001 (HS)	
Change in AC-BD				
Baseline to 6 months	0.22	0.43	1.70	0.54
p-value*	<0.0001 (HS			

*Obtained using paired t-test; NS: Not Significant

Table 10: Comparison of MD between two time points in each groups andcomparison of change in MD between two groups for time interval baseline to 6 months by CBCT (in mm)

Time point	Group I		Group II	
	Mean	SD	Mean	SD
Baseline	2.03	0.51	2.63	0.65
6 Months	1.81	0.53	1.75	0.59
p-value	0.053 (NS)		<0.0001 (HS)	
Change in MD				
Baseline to 6 months	0.29	0.63	0.68	0.48
p-value*	0.085 (NS)			

*Obtained using paired t-test; NS: Not Significant

Table 11: Comparison of BL between two time points in each groups andcomparison of change in BL between two groups for time interval baseline to 6 months by CBCT (in mm)

Time point	Group I		Group II	
	Mean	SD	Mean	SD
Baseline	5.20	1.31	4.89	1.63
6 Months	4.35	1.43	3.53	1.66
p-value	0.003 (S)		<0.0001 (HS)	
Change in BL				
Baseline to 6 months	0.85	1.13	1.36	0.47
p-value*	0.073 (NS)			

*Obtained using paired t-test; NS: Not Significant

Table 12: Comparison of change in CEJ-BD between two time points in each group and between two groups for three time intervals by RVG (in mm)

Time points	Group I		Group II		Change in CEJ-BD
	Mean difference	p-value*	Mean difference	p-value*	p-value*
Baseline vs. 3 months	0.12±0.05	<0.0001 (HS)	1.19±0.47	<0.0001 (HS)	<0.0001 (HS)
Baseline vs. 6 months	0.22±0.05	<0.0001 (HS)	2.15±0.45	<0.0001 (HS)	<0.0001 (HS)
3 months vs. 6 months	0.10±0.00	<0.0001 (HS)	0.96±0.40	<0.0001 (HS)	<0.0001 (HS)

*Obtained using paired t-test; HS: Highly Significant

Table 13: Comparison of change in CEJ-AC between two time points in each group and between two groups for three time intervals by RVG (in mm)

Time points	Group I		Group II		Change in CEJ-AC
	Mean difference	p-value*	Mean difference	p-value*	p-value*
Baseline vs. 3 months	0.07±0.09	0.004 (S)	0.34±0.49	0.007 (S)	0.002 (S)
Baseline vs. 6 months	0.10±0.19	0.033 (S)	0.46±0.51	0.001 (S)	0.001 (S)
3 months vs. 6 months	0.04±0.21	0.472 (NS)	0.12±0.04	<0.0001 (S)	0.006 (S)

*Obtained using paired t-test; NS: Not Significant

Table 14: Comparison of change in AC-BD between two time points in each group and between two groups for three time intervals by RVG (in mm)

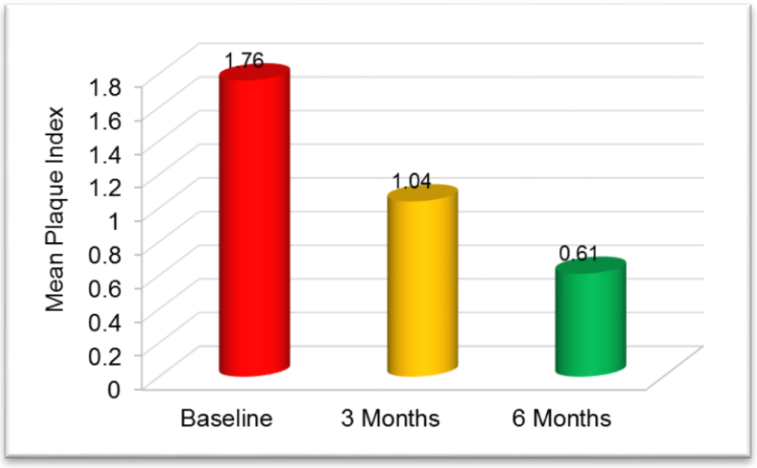
Time points	Group I		Group II		Change in AC-BD
	Mean difference	p-value*	Mean difference	p-value*	p-value*
Baseline vs. 3 months	0.18±0.07	<0.0001 (HS)	0.86±0.62	<0.0001 (HS)	<0.0001 (HS)
Baseline vs. 6 months	0.32±0.18	<0.0001 (HS)	1.70±0.48	<0.0001 (HS)	<0.0001 (HS)
3 months vs. 6 months	0.14±0.21	0.011 (S)	0.85±0.41	<0.0001 (HS)	<0.0001 (HS)

*Obtained using paired t-test; HS: Highly Significant

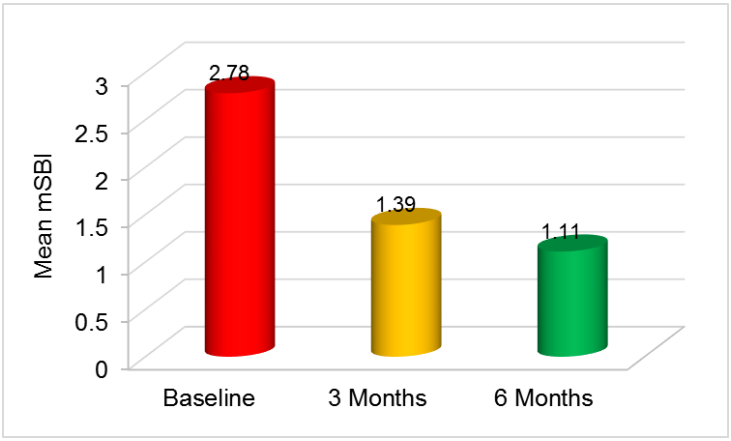
Table 15: Comparison of change in MD between two time points in each group and between two groups for three time intervals by RVG (in mm)

Time points	Group I		Group II		Change in MD
	Mean difference	p-value*	Mean difference	p-value*	p-value*
Baseline vs. 3 months	0.34±0.23	<0.0001 (HS)	0.47±0.52	<0.0001 (HS)	0.328 (NS)
Baseline vs. 6 months	0.49±0.43	<0.0001 (HS)	0.66±0.59	<0.0001 (HS)	0.421 (NS)
3 months vs. 6 months	0.15±0.32	0.052 (NS)	0.19±0.14	0.001 (S)	0.667 (NS)

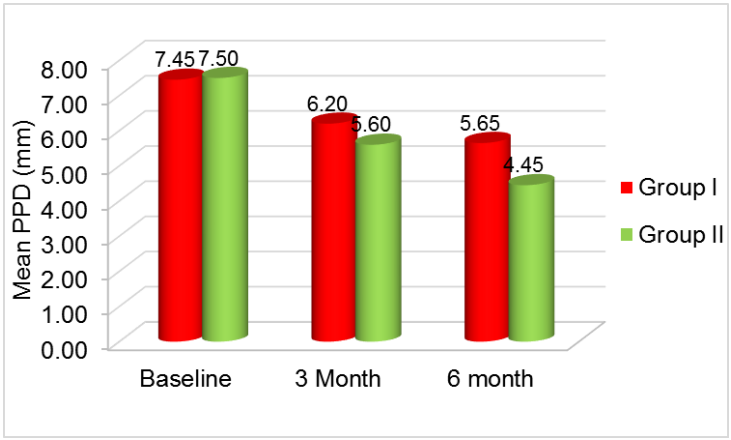
*Obtained using paired t-test; HS: Highly Significant



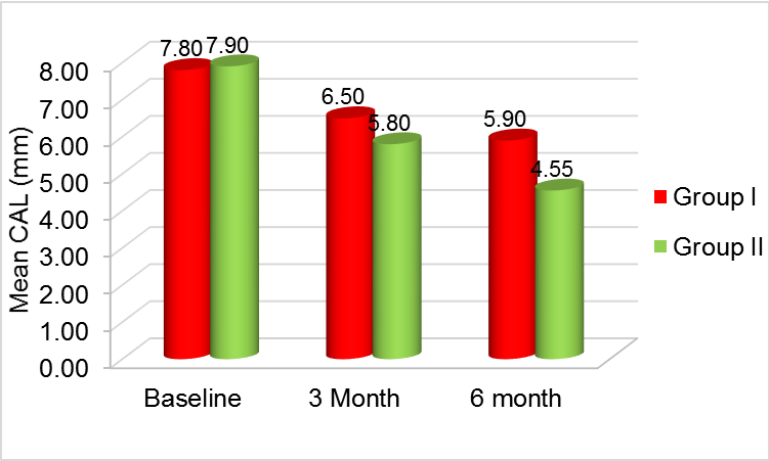
Graph 1: Mean PI at different time points



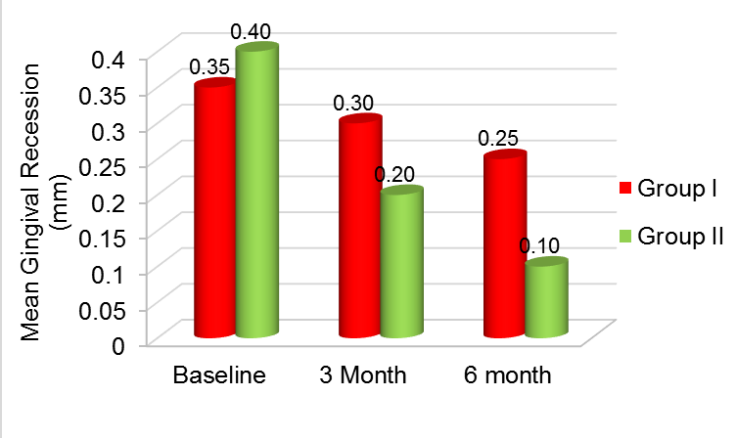
Graph2: Mean mSBI at different time points



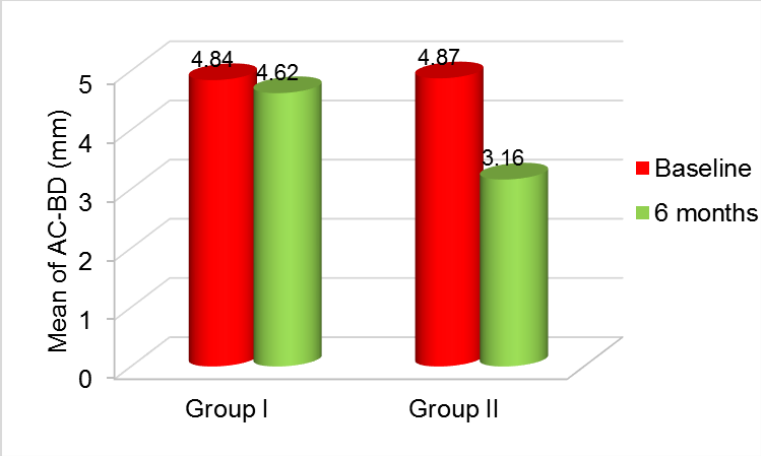
Graph 3: Mean PPD at different time points



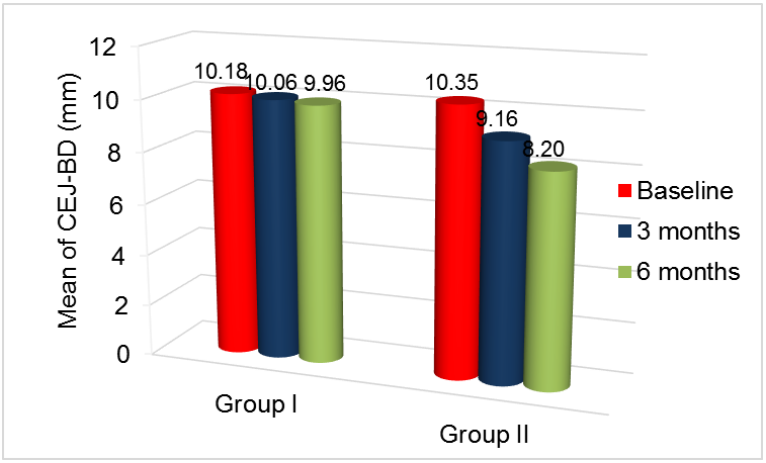
Graph 4: Mean CAL at different time points



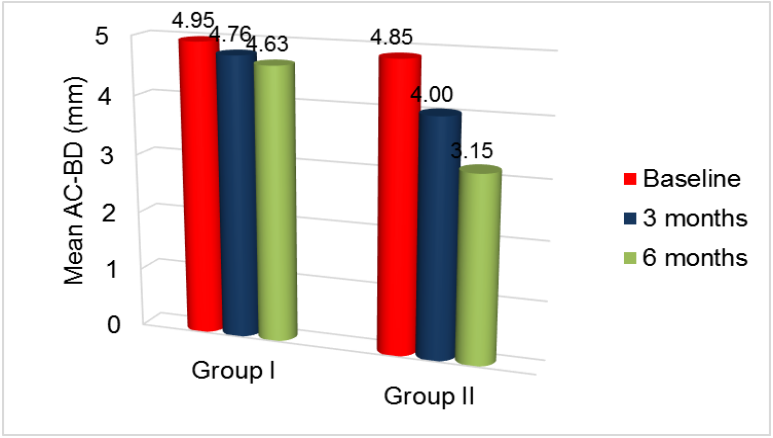
Graph 5: Mean CEJ-BD at baseline and 6 months (CBCT)



Graph 6: Mean AC-BD at baseline and 6 months (CBCT)



Graph 7: Mean CEJ-BD at baseline,3 and 6 months (RVG)



Graph 8: Mean AC-BD at baseline,3 and 6 months (RVG)

MASTER CHART

PLAQUE INDEX

Sr.no	Baseline	3 Months	6 Months
1	1.8	0.7	0.4
2	2.1	0.8	0.5
3	1.4	0.9	0.6
4	1.8	0.6	0.4
5	1.9	0.8	0.6
6	1.7	1.2	0.9
7	1.8	1.3	0.8
8	1.4	1.1	0.7
9	1.8	1.3	0.8
10	1.9	0.9	0.4
11	1.7	1.2	0.7
12	2.2	1.3	0.8
13	1.8	1.2	0.6
14	1.9	0.9	0.4
15	1.9	1.4	0.7
16	1.4	1.2	0.8
17	1.8	1.2	0.7
18	1.5	1.1	0.7
19	1.7	0.8	0.3
20	1.6	0.9	0.4

MODIFIED SULCUS BLEEDINGINDEX

Sr.no	Baseline	3 Months	6 Months
1	3.25	1.66	1.16
2	3.91	1.2	1.11
3	3.35	1.42	1.1
4	2.89	1.32	0.9
5	2.9	1.18	1.19
6	2.25	1.08	1.18
7	3.3	1.88	1.12
8	1.98	1.33	1.14
9	1.77	1.16	1.13
10	2.25	1.35	0.9
11	1.88	1.5	1.14
12	1.69	1.41	1.13
13	2.86	1.52	1.12
14	2.24	1.6	1.15
15	3.4	1.17	1.1
16	3.24	1.32	0.99
17	2.56	1.39	1.22
18	2.9	1.45	1.12
19	3.39	1.31	1.13
20	3.62	1.56	1.16

CLINICAL PARAMETERS (BASELINE)

Sr.no	GROUP I NSPT + PLACEBO		GROUP II NSPT + ATV	
	PPD (mm)	**CAL (mm)**	**PPD (mm)**	**CAL (mm)**
1	8	8	8	8
2	7	8	8	9
3	8	9	8	9
4	7	8	7	8
5	7	7	7	8
6	8	8	8	8
7	7	8	7	8
8	8	8	8	8
9	7	7	7	8
10	8	8	8	8
11	7	8	7	8
12	7	7	7	7
13	8	8	8	8
14	7	7	7	7
15	7	8	7	7
16	8	8	8	8
17	7	8	7	8
18	8	8	8	8
19	7	7	7	7
20	8	8	8	8

CLINICAL PARAMETERS (3 MONTHS RECALL)

Sr.no	GROUP I NSPT + PLACEBO		GROUP II NSPT + ATV	
	PPD (mm)	**CAL (mm)**	**PPD (mm)**	**CAL (mm)**
1	7	7	6	6
2	6	7	6	6
3	7	8	6	6
4	6	7	5	5
5	6	6	5	6
6	7	7	6	7
7	6	7	5	5
8	7	7	6	6
9	6	6	5	5
10	7	7	6	6
11	6	6	5	6
12	6	6	5	6
13	6	6	6	6
14	5	5	5	5
15	5	5	5	5
16	6	6	6	6
17	6	7	6	6
18	7	7	7	7
19	5	6	5	5
20	7	7	6	6

CLINICAL PARAMETERS (6 MONTHS RECALL)

Sr.no	GROUP I NSPT + PLACEBO		GROUP II NSPT + ATV	
	PPD (mm)	**CAL (mm)**	**PPD (mm)**	**CAL (mm)**
1	6	7	4	4
2	5	6	4	4
3	6	6	4	4
4	5	5	4	4
5	5	5	4	4
6	6	6	5	5
7	6	7	5	5
8	6	6	4	4
9	5	6	4	5
10	6	6	5	5
11	6	6	5	5
12	5	5	4	4
13	6	6	5	5
14	5	5	4	4
15	5	6	4	4
16	6	6	5	5
17	6	6	5	5
18	7	7	5	5
19	5	5	4	5
20	6	6	5	5

CBCT MEASUREMENTS OF INTRABONY DEFECT DIMENSION

AT BASELINE

Sr. no	GROUP I NSPT + PLACEBO					GROUP II NSPT + ATV				
	CEJ-BD	CEJ-AC	AC-BD	MD	BL	CEJ-BD	CEJ-AC	AC-BD	MD	BL
1	10	5.5	4.5	2.5	3.8	9.9	4.5	5.4	2.7	3.1
2	9.5	4.4	5.1	1.7	7.3	11.2	6.7	4.5	3.5	4.9
3	8.8	4.4	4.4	2.4	6	8.7	3.9	4.8	3.4	5.1
4	9.9	5.7	4.2	1.1	3	9.7	5.4	4.3	3.1	3.2
5	10.5	5.6	4.9	3.1	4.9	10.4	4.9	5.5	2.8	6.1
6	10.7	6	4.7	1.2	4.8	10.9	5.3	5.6	3.3	6.2
7	10.6	5.2	5.4	2	4.2	11.2	6.8	4.4	1.9	3.2
8	9.2	4.3	4.9	1.8	5.7	11.1	5.8	5.3	1.3	5.7
9	10.7	5.9	4.8	2.2	4	10.6	6	4.6	2.3	6
10	9.7	4.3	5.4	2.5	3	9.6	4.8	4.8	1.7	5.6
11	9.5	4.2	5.3	2.2	5.5	10.8	6.1	4.7	2.1	4.9
12	10.5	5.4	5.1	2.3	7.4	10.1	5	5.1	2.5	4.3
13	10.3	5.3	5	2.1	5.6	10.3	4.7	5.6	1.7	5.1
14	10.5	5.7	4.8	2.3	4.4	10.4	5.3	5.1	3.1	3
15	11	6.4	4.6	1.8	4.9	10.6	6.1	4.5	3.2	5.2
16	10.8	5.6	5.2	1.5	5.7	10.7	6.3	4.4	2.9	8.5
17	10.6	5.7	4.9	1.5	5.2	10.6	6.3	4.3	3.3	3.8
18	10.5	6.4	4.1	2.5	7.6	10.5	5.9	4.6	2.2	3.1
19	9.9	5.4	4.5	2.5	5.6	9.5	5	4.5	2.4	2.7
20	10	5.1	4.9	1.4	5.5	10.2	4.9	5.3	3.2	8

CBCT MEASUREMENTS OF INTRABONY DEFECT DIMENSION

AT 6 MONTHS

Sr. no	GROUP I NSPT + PLACEBO					GROUP II NSPT + ATV				
	CEJ-BD	CEJ-AC	AC-BD	MD	BL	CEJ-BD	CEJ-AC	AC-BD	MD	BL
1	9.5	5.2	4.3	2.4	2.6	8.5	5	3.5	2.3	2.5
2	10.9	6	4.9	1.6	5.8	8.8	5.3	3.5	2.9	4
3	8.4	4.2	4.2	2.2	4.4	7.5	4.1	3.4	2.7	4.8
4	9.2	4.9	4.3	0.9	1.7	6.9	4	2.9	2.6	2
5	10.1	5.5	4.6	2.9	2.9	8.7	5.8	2.9	1.9	4.8
6	10.3	5.1	5.2	1	3.1	8.9	5.7	3.2	2.3	4.5
7	10.8	6.1	4.7	1.8	2.7	8.8	5.9	2.9	1	1.6
8	10.6	5.8	4.8	1.3	4	8.5	5	3.5	0.9	4.3
9	10.2	5.5	4.7	1.9	4.3	8.7	5.6	3.1	1.9	5.1
10	9.9	5.1	4.8	2.4	4.2	7.7	4.8	2.9	1.3	4.3
11	10.4	5.9	4.5	2	6.5	9.4	5.9	3.5	1.4	3.7
12	9.9	4.9	5	2.1	5.8	7.9	5.2	2.7	1.3	3
13	9.1	4	5.1	1.9	3.9	7.6	4.1	3.5	1	4
14	10.1	5.5	4.6	2.2	4.7	8.1	4.8	3.3	2.3	1.6
15	10.5	5.4	5.1	1.4	4.2	8.6	5.4	3.2	1.7	3.1
16	10.3	5.8	4.5	1.3	4.5	8.1	4.7	3.4	1.6	6.9
17	10.1	6.2	3.9	1.2	6.9	7.9	4.7	3.2	1.3	2.5
18	10.2	5.6	4.6	2.1	6.8	7.7	5.1	2.6	1.6	1.1
19	9.1	5.2	3.9	2.3	4.1	7.6	4.7	2.9	1.4	0.7
20	9.5	4.9	4.6	1.3	3.9	8.1	5	3.1	1.6	6.1

RVG MEASUREMENTS OF INTRABONY DEFECT DIMENSION

AT BASELINE

Sr. no	GROUP I NSPT + PLACEBO				GROUP II NSPT + ATV			
	CEJ-BD	CEJ-AC	AC-BD	MD	CEJ-BD	CEJ-AC	AC-BD	MD
1	9.8	5.4	4.4	2	10	5	5	2.8
2	11.1	5.6	5.5	2	11.2	6.7	4.5	3.6
3	8.8	4.1	4.7	2.7	8.7	3.9	4.8	3.5
4	9.3	3.9	5.4	1.3	9.5	4.9	4.6	3
5	10.4	6.1	4.3	3.9	10.4	6	4.4	3.3
6	10.5	5.7	4.8	1.2	10.6	6	4.6	3.6
7	11.1	5.9	5.2	2	11.3	5.9	5.4	2.1
8	11	6	5	1.8	11.2	6.8	4.4	1.4
9	10.3	5.4	4.9	1	10.6	6.1	4.5	2.5
10	9.3	5.1	4.2	2.5	9.7	5.4	4.3	1.9
11	10.7	6	4.7	3.2	10.9	6.1	4.8	3
12	10	4.8	5.2	3.1	10.3	4.7	5.6	2.5
13	10.1	5	5.1	2.1	10.2	4.9	5.3	1.9
14	10.3	5.3	5	2.4	10.4	4.9	5.5	2
15	10.7	5.3	5.4	1.8	10.9	5.3	5.6	3.4
16	10.5	5	5.5	2.2	10.7	6.3	4.4	3.1
17	10.4	4.8	5.6	3.6	10.6	6.3	4.3	3.5
18	10.3	5.4	4.9	2.5	10.4	5.3	5.1	2.1
19	9.3	4.8	4.5	3	9.5	5	4.5	2.4
20	9.7	5.1	4.6	2.8	9.9	4.5	5.4	3.2

RVG MEASUREMENTS OF INTRABONY DEFECT DIMENSION

AT 3 MONTHS

Sr. no	GROUP I NSPT + PLACEBO				GROUP II NSPT + ATV			
	CEJ-BD	CEJ-AC	AC-BD	MD	CEJ-BD	CEJ-AC	AC-BD	MD
1	9.6	5.5	4.1	1.8	9.2	5.1	4.1	2.3
2	11	5.5	5.5	1.9	9.6	5.9	3.7	2.8
3	8.5	3.9	4.6	2.5	8.2	4.3	3.9	2.6
4	9.2	3.8	5.4	1.1	7.6	4.1	3.5	1.1
5	10.2	6.2	4	3	9.6	6	3.6	3.2
6	10.4	5.8	4.6	1.1	9.5	5.5	4	0.9
7	11	6	5	1.9	10.1	5.7	4.4	1.8
8	10.9	6.1	4.8	1.6	10.9	6	4.9	1.2
9	10.2	5.5	4.7	0.9	9.2	5.5	3.7	0.7
10	9.2	5.2	4	2.3	8.7	5.2	3.5	1.8
11	10.6	6.1	4.5	3	10.5	6	4.5	2.6
12	9.9	4.9	5	2.8	8.6	4.8	3.8	2.1
13	10	5.1	4.9	1.9	9.1	4.8	4.3	1.6
14	10.2	5.4	4.8	2.1	8.8	4.9	3.9	2.1
15	10.6	5.4	5.2	1.7	9.2	5.1	4.1	1.1
16	10.4	5.1	5.3	2.1	9.5	4.9	4.6	1.2
17	10.3	4.9	5.4	3.1	9.4	5.3	4.1	2.8
18	10.2	5.5	4.7	2.1	8.4	4.9	3.5	1.8
19	9.2	4.9	4.3	2.8	8.3	4.2	4.1	1.5
20	9.6	5.2	4.4	2.6	8.8	5.1	3.7	2.1

RVG MEASUREMENTS OF INTRABONY DEFECT DIMENSION

AT 6 MONTHS

Sr. no	GROUP I NSPT + PLACEBO				GROUP II NSPT + ATV			
	CEJ-BD	CEJ-AC	AC-BD	MD	CEJ-BD	CEJ-AC	AC-BD	MD
1	9.5	4.9	4.6	1.7	8.5	5	3.5	2.1
2	10.9	5.7	5.2	1.8	8.9	5.7	3.2	2.7
3	8.4	4.2	4.2	2.4	7.5	4.1	3.4	2.5
4	9.1	4	5.1	1	6.9	4	2.9	1
5	10.1	6.2	3.9	2.8	8.7	5.9	2.8	3
6	10.3	5.8	4.5	1	8.8	5.3	3.5	0.8
7	10.9	6	4.9	1.8	8.7	5.6	3.1	1.7
8	10.8	6.1	4.7	1.5	8.8	5.9	2.9	0.9
9	10.1	5.5	4.6	0.8	8.5	5.4	3.1	0.5
10	9.1	5.2	3.9	2.2	7.7	5.1	2.6	1.5
11	10.5	6.1	4.4	2.9	9.4	5.9	3.5	2.3
12	9.8	4.9	4.9	2.7	7.9	4.7	3.2	2
13	9.9	5.1	4.8	1.7	7.6	4.7	2.9	1.2
14	10.1	5.4	4.7	2	8.1	4.8	3.3	2
15	10.5	5.4	5.1	1.6	8.5	5	3.5	0.9
16	10.3	5.1	5.2	2	8.1	4.7	3.4	1.1
17	10.2	5.5	4.7	3	7.9	5.2	2.7	2.5
18	10.1	5.5	4.6	2	7.7	4.8	2.9	1.7
19	9.1	4.9	4.2	2.7	7.6	4.1	3.5	1.1
20	9.5	5.2	4.3	2.5	8.1	5	3.1	1.8

EVALUATION OF 1.2% ATORVASTATIN AS AN ADJUNCT TO NON SURGICAL PERIODONTAL THERAPY IN CHRONIC PERIODONTITIS: A RANDOMIZED CONTROLLED CLINICAL TRIAL

CASE HISTORY PROFORMA

NAME: **OPD NO.**

AGE/SEX: **DATE:**

OCCUPATION: **ADDRESS:**

CHIEF COMPLAINT:

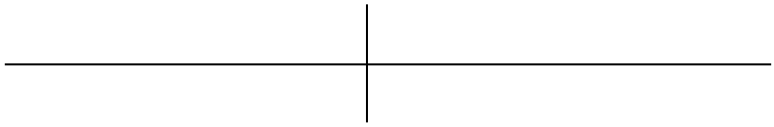
PAST DENTAL HISTORY:

PAST MEDICAL HISTORY:

FAMILY HISTORY:

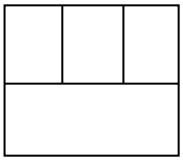
ORAL HYGIENE HABIT:

TEETH PRESENT:

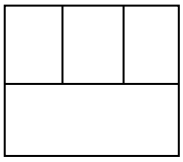


INDICES

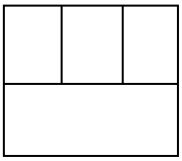
PLAQUE INDEX (Baseline)



16



12



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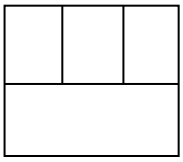

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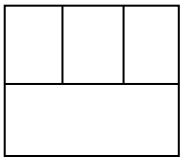

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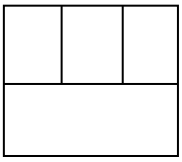
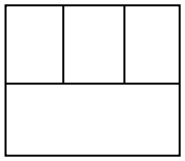


36

$$\frac{\text{Total scores of all teeth}}{\text{Total number of teeth examined}}$$

PLAQUE INSDEX (3 months)



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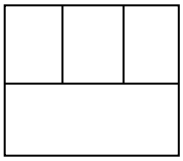

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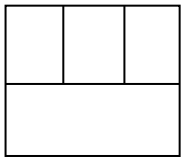

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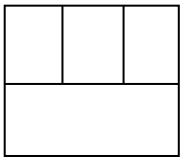

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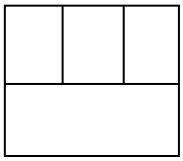
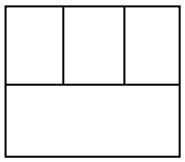


36

$$\frac{\text{Total scores of all teeth}}{\text{Total number of teeth examined}}$$

PLAQUE INDEX (6months)



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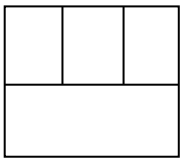

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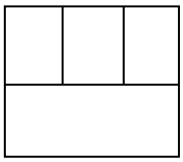

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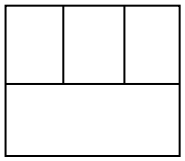

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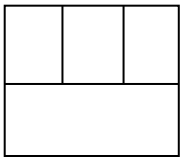

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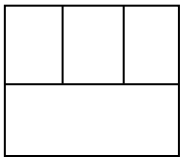


36

$$\frac{\text{Total scores of all teeth}}{\text{Total number of teeth examined}}$$

MODIFIED SULCUS BLEEDING INDEX (mSBI) (Baseline)

18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38

Total scores of all teeth =

Total number of teeth examined

MODIFIED SULCUS BLEEDING INDEX (mSBI)(3 Months)

18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38

Total scores of all teeth =

Total number of teeth examined

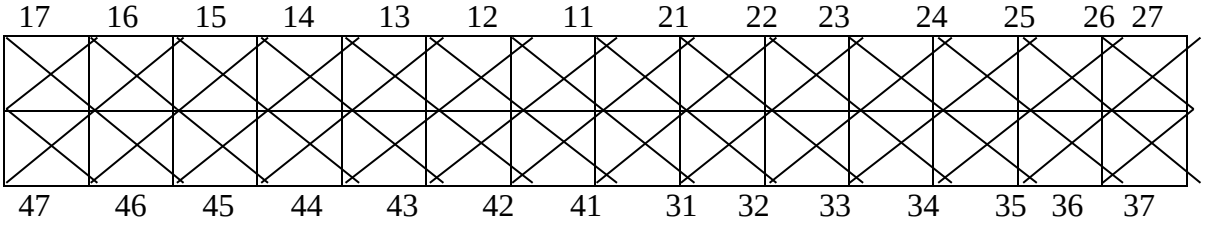
MODIFIED SULCUS BLEEDING INDEX (mSBI)(6 Months)

18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38

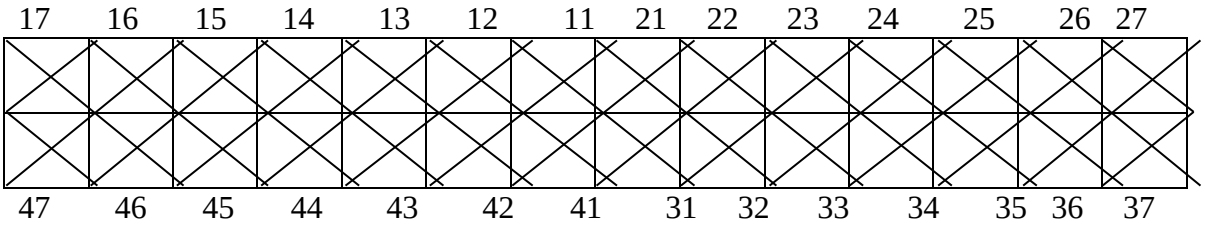
Total scores of all teeth =

Total number of teeth examined

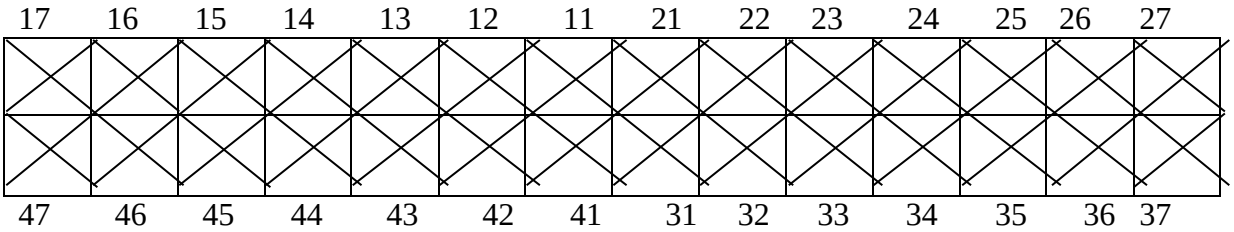
PROBING POCKET DEPTH (mm): Baseline



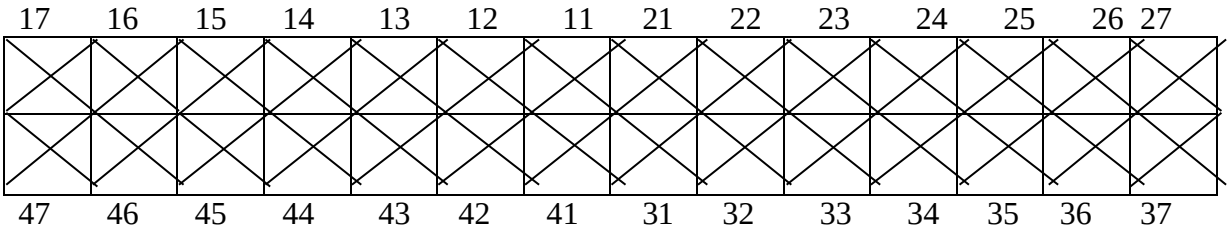
PROBING POCKET DEPTH (mm): 3 months



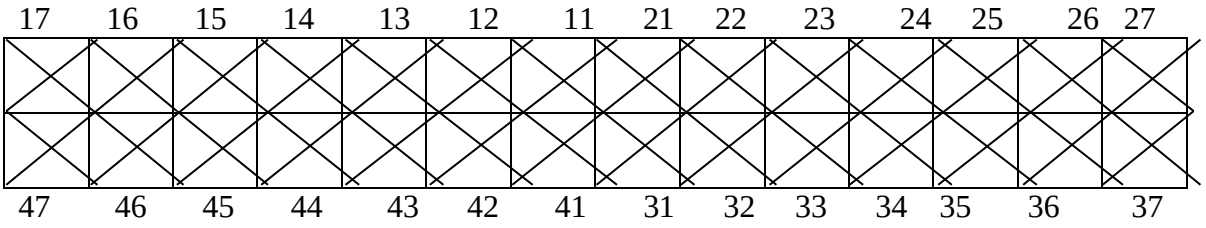
PROBING POCKET DEPTH (mm): 6 months



CLINICAL ATTACHMENT LEVELS (mm):Baseline

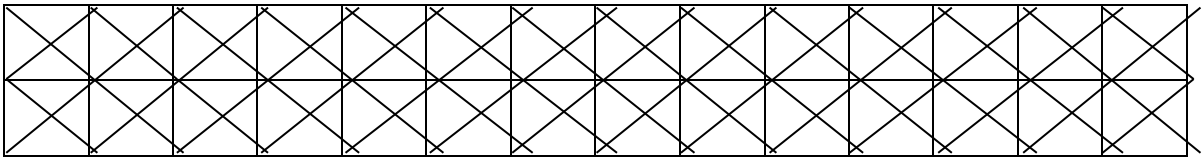


CLINICAL ATTACHMENT LEVELS (mm): 3 months



CLINICAL ATTACHMENT LEVELS (mm): 6 months

17 16 15 14 13 12 11 21 22 23 24 25 26 27



47 46 45 44 43 42 41 31 32 33 34 35 36 37

CLINICAL DIAGNOSIS:

RADIOGRAPHIC INVESTIGATIONS:

Intrabony Defect Dimensions (RVG) at baseline:

Site	**Tooth No.**	**Material Used**	**CEJ-BD dimension**	**CEJ-AC dimension**	**AC-BD dimension**	**MD width**
Control						
Test						

Intrabony Defect Dimensions (CBCT) at baseline:

Site	Tooth No.	Material Used	CEJ-BD dimension	CEJ-AC dimension	AC-BD dimension	MD width	BL width
Control							
Test							

Intrabony Defect Dimensions (RVG) at 3 Months:

Site	Tooth No.	Material Used	CEJ-BD dimension	CEJ-AC dimension	AC-BD dimension	MD width
Control						
Test						

Intrabony Defect Dimensions (RVG) at 6 Months:

Site	Tooth No.	Material Used	CEJ-BD dimension	CEJ-AC dimension	AC-BD dimension	MD width
Control						
Test						

Intrabony Defect Dimensions (CBCT) at 6 Months:

Site	Tooth No.	Material Used	CEJ-BD dimension	CEJ-AC dimension	AC-BD dimension	MD width	BL width
Control							
Test							

(Confidential)

Informed Consent Form

"Evaluation of 1.2% Atorvastatin as an Adjunct to Non Surgical Periodontal Therapy in Chronic Periodontitis: A Randomized Controlled Clinical Trial"

Mr./Master/Mrs./Miss._____

Resident of: _____

_____aged _____ years, excercising my free will/choice, without any pressure/lure of incentive in any form, hereby give my consent for the project to be conducted.

I acknowledge the receipt of "patient's information sheet", and also the doctor has informed me about this research project suitably and sufficiently to my satisfaction. I agree to let my X-rays, photographs, blood investigations, other investigations to be taken as required. I agree to take part in this project and will not mix any other projects during the period of this trial. I shall report to the dental hospital or other place where called on given appointment dates and time. I shall inform the doctor on any adverse effects or unusual symptoms noticed by me. I shall co-operate with the doctors and paramedical staff, in all respects. I permit to publishing the results of my participation in this study. I shall not be given any reimbursement or compensation. I have been informed of my right to opt out of this research project at any time without giving any reason for doing so. I hereby record my consent for participation in the said trial.

_____	_____	_____	_____
Patient's name	Signature/thumbprint	Date	Time

_____	_____	_____	_____
Investigator's name	Signature	Date	Time