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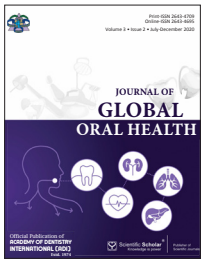

Research Article

Effects of statins as local drug delivery agents in treating chronic periodontitis and their antimicrobial effects using polymerase chain reaction

Ritunja Singh[1], Gangesh B. Singh[2], Soumya Gupta[3], Anil Agrawal[4]

[1]Department of Periodontology, New Horizon Dental College and Research Institute, Bilaspur, [2]Department of Orthodontics, GDC Raipur, Raipur, Departments of [3]Orthodontics and [4]Public Health Dentistry, New Horizon Dental College and Research Institute, Bilaspur, Chhattisgarh, India.

***Corresponding author:**
Ritunja Singh,
Post Graduate Student,
Department of Periodontology,
New Horizon Dental College
and Research Institute, Bilaspur,
Chhattisgarh, India.

ritunja21@gmail.com

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ABSTRACT

Objectives: The aim of the study was to evaluate the anti-inflammatory effect of statin medication in chronic periodontitis patients and to compare the change in periodontal probing depth and clinical attachment level using 1.2% atorvastatin (ATV) gel and scaling and root planning (SRP) compared to SRP alone.

Materials and Methods: This study was carried out on a sample size of 40 patients with equal male and female ratio between the age group of 40–60 years having chronic periodontitis with a minimum of 20 teeth that were selected for the study. Bilateral quadrants were selected and a split mouth study was conducted. Supragingival scaling was carried out in each patient in one long appointment. The patient was then recalled after 1 week for subgingival SRP. Root planing was carried out in two consecutive visits. Left side of the mouth on the 1st day followed by right side of the mouth on the next day. On the 2nd day, after completion of the root planning, followed by placement of 1.2% ATV gel and finally the Coe Pak was placed in one quadrant which was called the test site. In the other quadrant which was called control site placebo gel was placed and the treated site was covered by the Coe Pak. The recording of clinical parameters (plaque index [PI], gingival index [GI], probing pocket depth, and clinical attachment loss) was done at baseline, 1 month and 3 months. The selected site was sampled for subgingival microflora. The data obtained were subjected to statistical analysis. One-way ANOVA, Tukey's HSD test, and student *t*-test were used for intergroup and intragroup comparison.

Results: In our study, when intergroup comparison of mean value for PI at baseline, 1 month and 3 months was found to clinically insignificant for control and test groups, while for GI, periodontal pocket depth, and clinical attachment level it was found insignificant at baseline while significant at 1 and 3 months. Similarly, when comparison was made for microbial count it was found clinically insignificant between control and test group at baseline, while significant was noted at 3-month interval.

Conclusion: Our study evaluated the anti-inflammatory, osteoconductive and antimicrobial effects of atorvastatin giving significant reduction in PI, GI, PPD and gain in CAL along with significant decrease in the microbial load.

Keywords: Statins, Periodontitis, Polymerase chain reaction

INTRODUCTION

Periodontal disease occurs as a consequence of the host inflammatory response to oral pathogens. Periodontal pathogens produce harmful by products and enzymes that break down extracellular matrices and collagen, as well as host cell membranes and lead to bone resorption, creating

bony defects that may cause tooth loss.[1] Various treatment modalities such as mechanical debridement and use of antimicrobials have been followed in the treatment of such conditions. Introduction of local drug delivery (LDD) system in the periodontal pocket is a promising therapeutic modality for achieving better clinical outcomes when used as an adjunct to conventional non-surgical periodontal therapy.[2]

The local delivery of antimicrobial therapy to periodontal pockets has the benefit of administering more drugs at the target site while minimizing the exposure of total body to the drug and the sustained release of antimicrobial in the periodontal pockets. Sustained local delivery systems might also be recommended for sites considered as difficult to instrument because of depth or anatomical complexity, for example, in the case of furcation defects.[3] Current techniques to treat bone defects associated with periodontitis or dental implants consist of surgically placing bone particles or substitutes into the defects to stimulate host bone formation. The use of inexpensive pharmacologic compounds to stimulate the host to produce autogenous bone growth factors, such as bone morphogenetic protein 2 (BMP-2), could be a cost-effective alternative in the management of osseous defects.[1]

Statins are 3-hydroxy-3-methylglutarylcoenzyme a reductase inhibitors, which are lipid lowering drugs. Statins have additionally, also shown to stimulate the expression of vascular endothelial growth factor, BMP-2, and to promote osteoblast differentiation. Moreover, statins alter the inflammatory cascades, by inducing heme oxygenase, altering leukocyte-endothelial cell interaction, and reducing expression of major histocompatibility complex-II,[4] atorvastatin (ATV) therapy has been found to decrease tumor necrosis factor-α (TNF-α) production in LPS activated monocytes, lower levels of nuclear NFκB, and reduce activation of the guanosine triphosphate which is involved to increasing oxidative stress.

Local application of statins has shown that it has both bone regenerative and anti-inflammatory effect. Recent studies have shown that ATV has beneficial effects on alveolar bone loss and tooth mobility and local delivery of simvastatin and ATV into periodontal pocket stimulated a significant improved bone fill as compared to placebo gel, as an adjunct to scaling and root planning (SRP) in the treatment of chronic periodontitis.[5]

The anti-inflammatory and antibacterial effects of statins should be evaluated by detecting the number of periodontal pathogens. Plaque and saliva samples have been studied using culture, immunoassays, deoxyribonucleic acid (DNA) probes, and polymerase chain reaction (PCR) techniques.[6] The traditional culture methods have inherent advantages, but have shortcomings, including the need to preserve bacterial vitality, the inability to detect the lower numbers of microorganisms with a detection limit averaging 103–104 bacterial cells, labor intensiveness, need for experienced personnel, strict sampling, transport conditions, and a prolonged period of time before results. Other microbial tests such as dark field microscopy are not able to detect the non-motile periodontal pathogen, and immunodiagnostic methods such as flow cytometry, immunofluorescence assay and enzymatic assays can lead to false positive results and cross reactions. DNA strands to produce double stranded nucleic acid and ecologic studies require sophisticated laboratory equipment and expertise. The development of PCR has generated vast benefits in genetic analysis for the study of gene expression and diagnosis of genetic diseases. Genetic analysis using PCR for the identification of susceptibility of an individual to periodontitis will help in the determination of the type and frequency of treatment. Studies based on PCR for the determination of mRNA expression of various immune and inflammatory markers are useful in understanding the pathogenesis of periodontitis.[6]

Thus, the present study evaluated the anti-inflammatory effects of statins as LDD agents in treating chronic periodontitis and their antimicrobial effects using PCR.

MATERIALS AND METHODS

The present study was carried out on a sample size of 40 patients with equal male and female ratio between the age group of 40 and 60 years reporting to the outpatient Department of Periodontology, New Horizon Dental College And Research Institute, Sakri, Bilaspur.

Inclusion criteria

The following criteria were included in the study:

- Subjects with clinical attachment loss (CAL) of 3–5 mm in more than 30% of sites
- Vertical bone loss ≥3 mm on intraoral periapical radiographs
- No history of periodontal therapy
- No history of use of antibiotics in the preceding 6 months
- Subjects with minimum number of 20 teeth.

Exclusion criteria

The following criteria were excluded from the study:

- Known systemic disease
- Known or suspected allergy to ATV
- On ATV therapy
- Having aggressive periodontitis
- Use of tobacco of any form
- Diabetes mellitus
- Immunocompromised
- Pregnant or lactating.

Study design 40 patients from the outpatient Department of Periodontology, New Horizon Dental College and Research

Institute having chronic periodontitis with a minimum of 20 teeth were selected for the study. Bilateral quadrants were selected and a split mouth study was conducted.

Why split mouth? Ramfjord *et al*.[7] introduced the "split-mouth" clinical trial in 1968 when they compared the efficacy of two types of periodontal therapy by randomizing the treatment methods to half of each subject's dentition divided by the mid-sagittal plane between the central incisor teeth. Lesaffre *et al*. stated that the attractiveness of the design is that it removes a lot of interindividual variability from the estimates of the treatment effect.[8]

Drug formulation

Methylcellulose gel was prepared at Chouksey Pharmacy College, Bilaspur, Chhattisgarh by adding the required amount of polymer in hot distilled water and cooling to gel at room temperature.[9] *In situ,* ATV gel was prepared by a weighed amount of ATV to the above solution and dissolved completely to obtain a homogeneous phase of polymer, solvent, and drug. Thus, the ATV *in situ* gel was prepared with a concentration 1.2%.[10]

Supragingival scaling was carried out in each patient in one long appointment. The patient was then recalled after 1 week for subgingival SRP. Root planning was carried out in two consecutive visits. Left side of the mouth on the 1st day followed by the right side of the mouth on the next day. On the 2nd day, after completion of the root planning, followed by placement of 1.2% ATV gel and finally the Coe Pak was placed in one quadrant which was called the test site. In the other quadrant which was called control site placebo gel was placed and the treated site was covered by the Coe Pak.

Patients were advised to follow modified bass brushing technique in all areas except for the test site and control site. They were also given CHX mouthwash from the department and advised to rinse twice a day with 10 ml of the solution and recalled after 7 days for the removal of the Coe Pak. The recording of clinical parameters plaque index (PI)[11] gingival index (GI)[11] probing pocket depth (PPD), CAL[12] (PI, GI, PPD, and CAL, respectively) was done at baseline, 1 month and 3 months.

Statistical analysis

The data obtained were subjected to statistical analysis. The mean, standard error, and standard deviation were tabulated. One-way ANOVA, Tukey's HSD test, and student *t*-test were used for intergroup and intragroup comparison.

RESULTS

In our study, when intergroup comparison of PI was done at baseline, 1 month and at 3 months, the mean values of PI for control group were 2.357 ± 0.652, 0.608 ± 0.490, and 0.237 ± 0.380 and for test group it was 2.382 ± 0.631, 0.419 ± 0.514, and 0.231 ± 0.298, respectively, which was not clinically significant ($P < 0.05$) [Table 1].

When intergroup comparison of GI was done at baseline, 1 month and at 3 months, the mean values for GI in control group were 2.295 ± 0.770, 0.503 ± 0.432, and 0.3350 ± 0.48756 and for test group it was 2.387 ± 0.486, 0.503 ± 0.432, and 0.1600 ± 0.26679, respectively. The difference in mean values was clinically insignificant ($P = 0.524$) at baseline whereas the difference in mean values was found clinically significant at 1 month and 3 months ($P < 0.05$) [Table 2].

When intergroup comparison of PPD was done at baseline, 1 month at 3 months, the mean values of PPD for control group were 5.650 ± 1.166, 4.427 ± 1.395, and 2.645 ± 0.906 and for test group it was 5.950 ± 1.153, 3.450 ± 1.852, and 1.512 ± 0.472, respectively. The difference in mean values was clinically insignificant at baseline ($P = 0.251$), whereas the difference in mean values was found clinically significant at 1 month and 3 months ($P < 0.05$) [Table 3].

When intergroup comparison of clinical attachment level was done at baseline, 1 month at 3 months, the mean values for clinical attachment level for control group were 6.050 ± 1.299, 4.927 ± 1.118, and 4.405 ± 1.193 and for test group it was 6.225 ± 0.891, 4.260 ± 1.593, and 3.497 ± 0.888,

Table 1: Intergroup comparison for PI at baseline, 1 month and 3 months.

Time period	Groups	Mean	SD	*P*-value
Baseline	Control	2.3575	0.65269	0.360
	Test	2.3825	0.63119	
1 month	Control	0.6088	0.49057	0.096
	Test	0.4195	0.51463	
3 months	Control	0.2375	0.38075	0.932
	Test	0.2310	0.29804	

Mean values, SD, and *P*-values between the control and test groups for PI at baseline, 1 month, 3 months. SD: Standard deviation, PI: Plaque index

Table 2: Intergroup comparison for GI at baseline, 1 month and 3 months.

Time period	Groups	Mean	SD	*P*-value
Baseline	Control	2.2955	0.77095	0.524
	Test	2.3878	0.48625	
1 month	Control	1.8683	0.50659	0.000
	Test	0.5030	0.43204	
3 months	Control	0.3350	0.48756	0.050
	Test	0.1600	0.26679	

Mean values, SD, and *P*-values between the control and test groups for GI at baseline, 1 month, 3 months. SD: Standard deviation, GI: Gingival index

respectively. The difference in mean values was clinically insignificant at baseline ($P = 0.481$), whereas the difference in mean values was found clinically significant at 1 month and 3 months ($P < 0.05$) [Table 4].

When intergroup comparison of microbial count was done at baseline, the mean values for microbial count for control group were 1.058 ± 0.494 and for test group it was 1.006 ± 0.485. The difference in mean values was clinically insignificant ($P = 0.640$). When intergroup comparison of microbial count was done at 3 months, the mean values for microbial count for control group were 0.843 ± 0.398 and for test group it was 0.287 ± 0.271. The difference in mean values was clinically significant ($P = 0.000$) [Table 5].

Table 3: Intergroup comparison for PPD at baseline, 1 month and 3 months.

Time period	Groups	Mean	SD	*P*-value
Baseline	Control	5.6500	1.16685	0.251
	Test	5.9500	1.15359	
1 month	Control	4.4275	1.39504	0.009
	Test	3.4500	1.85293	
3 months	Control	2.6450	0.90609	0.000
	Test	1.5125	0.47241	

Mean values, SD, and *P*-values between the control and test groups for PPD at baseline, 1 month, 3 months. SD: Standard deviation, PPD: Probing pocket depth

Table 4: Intergroup comparison for CAL at baseline, 1 month and 3 months.

Time period	Groups	Mean	SD	*P*-value
Baseline	Control	6.0500	1.29990	0.485
	Test	6.2250	0.89120	
1 month	Control	4.9275	1.11838	0.033
	Test	4.2600	1.59387	
3 months	Control	4.4050	1.19378	0.000
	Test	3.4970	0.88836	

Mean values, SD, and *P*-values between the control and test groups for CAL at baseline, 1 month, 3 months. SD: Standard deviation, CAL: Clinical attachment loss

Table 5: Intergroup comparison for microbial count at baseline and 3 months.

Time period	Groups	Mean	SD	*P*-value
Baseline	Control	1.0583*	0.49417	0.640
	Test	1.0067*	0.48561	
3 months	Control	0.8433*	0.39880	0.000
	Test	0.2873*	0.27174	

Mean values, SD, and *P*-values between the control and test groups for microbial count at baseline and 3 months. *Microbes are measured in cfu and are in multiples of 10^3. SD: Standard deviation

DISCUSSION

The primary objective of periodontal therapy is to reduce the microbial load, thereby tending to an improvement in the clinical parameters using nonsurgical and surgical therapies. The most widely used non-surgical approach has been SRP that effectively decreases the microbial load, but recolonization of the same can occur as early as 60 days after SRP. Furthermore, it fails to eliminate the pathogenic bacteria completely especially at the base of the periodontal pocket and the areas inaccessible to periodontal instruments. Consequently, this has led to the adjunctive use of antimicrobials, assuming that chemicals would compensate for technical limitations, prevent early microbial recolonization, and provide a chance for clinical improvements. Surgical procedures have inherent disadvantages such as greater patient morbidity, marginal bone resorption, and compromised postsurgical esthetics in the form of gingival recession and interproximal soft-tissue cratering. Earlier, a greater emphasis was laid on the microbiologic etiology of periodontal disease. The microbial ecology of human periodontitis suggests therapies with antimicrobial agents in addition to mechanical therapy. Goodson in 1979 first proposed the concept of controlled delivery in the treatment of periodontitis. It has been observed that the local route of drug delivery can attain 100-fold higher concentrations of an antimicrobial agent in subgingival sites than a systemic drug regimen.[12]

Statin use is associated with increased bone mineral density by stimulating osteoblast-derived BMP-2 expression. ATV has been found to enhance osteoblastic differentiation and the production of osteoprotegerin, which could contribute to the bone-sparing effects of statins.[13] ATV therapy has been found to decrease TNF-α production in lipopolysaccharides-activated monocytes and matrix metalloproteinases.[14,15] ATV has been shown to have beneficial effects on alveolar bone loss and tooth mobility in humans and also in ligature-induced periodontitis in Wistar rats.[16]

In our study, when intergroup comparison of PI was done at baseline, 1 month and at 3 months, the mean values of PI for control group were 2.357 ± 0.652, 0.608 ± 0.490, and 0.237 ± 0.380 and for test group it was 2.382 ± 0.631, 0.419 ± 0.514, and 0.231 ± 0.298, respectively, which was not clinically significant ($P < 0.05$) [Table 1].

When intragroup comparison was done for PI within control group at different time intervals, there was clinically significant difference ($P = 0.000$) seen between baseline and 1 month, baseline and 3 months. However, when seen between 1 month and 3 months there was clinically insignificant difference ($P = 0.769$) [Table 6]. When intragroup comparison was done for PI within test group at different time intervals, there was clinically significant difference ($P = 0.000$) seen

between baseline and 1 month, baseline and 3 months, and 1 month and 3 months [Table 7] which is in accordance with the studies of Pradeep *et al.* (2016),[17] Priyanka *et al.* (2017),[18] and Gayathri *et al.* (2017).[19]

When intergroup comparison of GI was done at baseline, the mean values for GI in control group were 2.295 ± 0.770 and for test group it was 2.387 ± 0.486. The difference in mean values was clinically insignificant (P = 0.524). When intergroup comparison of GI was done at 1 month, the mean values for GI for control group were 1.868 ± 0.506 and for test group was 0.503 ± 0.432. The difference in mean values was clinically significant (P = 0.000) [Table 2].

When intergroup comparison of GI was done at 3 months, the mean values for GI in control group were 0.3350 ± 0.48756 and for test group it was 0.1600 ± 0.26679. The difference in mean values was clinically significant (P = 0.050) [Table 2] when intragroup comparison was done for GI within control group at different time intervals, there was clinically significant difference ($P \leq 0.05$) between baseline and 1 month, baseline and 3 months, and 3 months and 1 month [Table 6].

When intragroup comparison was done for GI within the test group at different time intervals, there was clinically significant difference ($P \leq 0.05$) seen between baseline and 1 month [Table 7]. However, when seen between baseline and 3 months, 3 months and 1 month there was no statistically significant difference [Table 7] which is in accordance with the studies of Rosenberg *et al.* (2015)[20] and Pradeep *et al.* (2015).[21]

When intergroup comparison of PPD was done at baseline, the mean values of PPD for control group were 5.650 ± 1.166 and for test group it was 5.950 ± 1.153. The difference in mean values was clinically insignificant (P = 0.251) [Table 3].

When intergroup comparison of PPD was done at 1 month, the mean values for PPD in control group were 4.427 ± 1.395 and for test it group was 3.450 ± 1.852. The difference in mean values was clinically nonsignificant (P = 0.009) [Table 3].

When intergroup comparison of PPD was done at 3 months, the mean values for PPD in control group were 2.645 ± 0.906 and for test group it was 1.512 ± 0.472. The difference in mean values was clinically significant (P = 0.000) [Table 3].

When intragroup comparison was done for PPD within the control group at different time intervals, there was clinically significant difference (P = 0.000) between baseline and 1 month, baseline and 3 months, and 3 months and 1 month, [Table 6].

When intragroup comparison was done for PPD within the test group at different time intervals, there was clinically significant difference (P = 0.000) between baseline and 1 month, baseline and 3 months, and 3 months and 1 month [Table 7] which is in accordance with the studies conducted by Pradeep *et al.* (2010),[10] Pradeep *et al.* (2013),[1] Rao *et al.* (2013),[22] Rosenberg *et al.* (2015),[20] and Pradeep *et al.* (2015).[21]

When intergroup comparison of clinical attachment level was done at baseline, the mean values for clinical attachment level for control group were 6.050 ± 1.299 and for test group

Table 6: Intragroup comparison of PI, GI, PPD, CAL between baseline, 1 month and 3 months in control groups.

Time period	Groups	PI Mean	*P*-value	GI Mean	*P*-value	PPD Mean	*P*-value	CAL Mean	*P*-value
Baseline	1 month	2.3787	0.000	0.4272	0.005	1.22250	0.000	1.1225	0.000
	3 months	2.7500	0.000	1.9605	0.000	3.00500	0.000	1.6450	0.000
1 month	Baseline	2.3787	0.000	−0.4272	0.005	−1.2225	0.000	−1.122	0.000
	3 months	0.3712	0.769	1.5332	0.000	1.7825	0.000	0.5225	0.133
3 months	Baseline	2.7500	0.000	−1.9605	0.000	−3.0050	0.000	−1.645	0.000
	1 month	−0.3712	0.769	−1.5332	0.000	1.7825	0.000	−0.522	0.133

PI: Plaque index, GI: Gingival index, PPD: Probing pocket depth, CAL: Clinical attachment loss

Table 7: Intragroup comparison of PI, GI, PPD, CAL between baseline, 1 month and 3 months in test groups.

Time period	Groups	PI Mean	*P*-value	GI Mean	*P*-value	PPD Mean	*P*-value	CAL Mean	*P*-value
Baseline	1 month	1.7487	0.000	0.427	0.005	1.222	0.000	1.1225	0.000
	3 months	2.2120	0.000	1.960	0.000	3.00	0.000	1.6450	0.000
1 month	Baseline	−1.7487	0.000	−0.42	0.005	−1.22	0.000	−1.122	0.000
	3 months	0.3712	0.005	1.533	0.000	1.78	0.000	0.5225	0.133
3 month	Baseline	−2.1200	0.000	−1.96	0.000	−3.005	0.000	−1.645	0.000
	1 month	−0.3712	0.005	−1.53	0.000	−1.782	0.000	−0.522	0.133

PI: Plaque index, GI: Gingival index, PPD: Probing pocket depth, CAL: Clinical attachment loss

it was 6.225 ± 0.891. The difference in mean values was clinically insignificant ($P = 0.481$) [Table 4].

When intergroup comparison of clinical attachment level was done at 1 month, the mean values for clinical attachment level for control group were 4.927 ± 1.118 and for test group it was 4.260 ± 1.593. The difference in mean values was clinically significant ($P = 0.033$) [Table 4].

When intergroup comparison of clinical attachment level was done at 3 months, the mean values for clinical attachment level for control group were 4.405 ± 1.193 and for test group was 3.497 ± 0.888. The difference in mean values was clinically significant ($P = 0.000$) [Table 4].

When intragroup comparison was done for clinical attachment level within control group at different time intervals, there was clinically significant difference ($P = 0.000$) between baseline and 1 month, baseline and 3 months. However, when the comparison between 1 month and 3 months was done it was found to be clinically insignificant ($P = 0.133$) [Table 6].

When intragroup comparison was done for clinical attachment level within the test group at different time intervals, there was clinically significant difference ($P = 0.000$) between baseline and 1 month, baseline and 3 months which is in accordance with the studies conducted by Pradeep *et al*. (2010),[10] Rao *et al*. (2013),[22] Pradeep *et al*. (2013),[1] Rosenberg *et al*. (2015).[20] However, when the comparison between 1 month and 3 months was done it was found to be clinically insignificant ($P = 0.133$) [Table 7], which was similar to the findings of the study conducted by Gayathri *et al*. (2017).[19]

When intergroup comparison of microbial count was done at baseline, the mean values for microbial count for control group were 1.058 ± 0.494 and for test group it was when intergroup comparison of microbial count was done at 3 months, the mean values for microbial count for control group were 0.843 ± 0.398 and for test group it was 0.287 ± 0.271. The difference in mean values was clinically significant ($P = 0.000$) [Table 5].

When intragroup comparison was done for microbial count within control group between baseline and test group, the difference in mean values was statistically significant ($P = 0.000$) [Table 8].

When intragroup comparison was done for microbial count within test group between baseline and test group, the difference in mean values was clinically significant ($P = 0.000$) [Table 9].

ATV apart from being a lipid lowering agent has various other properties such as anti-inflammatory, osteogenic, and antimicrobial properties. Hence, we conducted a split mouth study where we used ATV as an adjunct to SRP in the treatment of periodontal diseases. The results of the study showed that there was a marked reduction in the periodontal parameters in the test group at the end of the study as compared to the control group. As microbes are an important etiologic factor in the progression of periodontal disease, we also assessed the microbial count through PCR. At the end of the study, the microbial count was found to be significantly less in the test group as seen in Graph 6. Hence, ATV can be used an adjunct to SRP in the treatment of periodontal diseases.

Table 8: Intragroup comparison of microbial count at baseline and 3 months in control group.

	Mean	Std. Deviation	Std Error	*P* value
Baseline	1.0583	0.49417	0.07814	0.000
3 months	0.8433	0.39880	0.06306	

Mean values, standard deviation, and *P*-values for microbial count between baseline and 3 months within the control group

Table 9: Intragroup comparison of microbial count at baseline and 3 months in test group.

	Mean	Std. Deviation	Std Error	*P*-value
Baseline	1.0067	0.48561	0.07678	0.000
3 months	0.2873	0.27174	0.04297	

Mean values, standard deviation, and *P*-values for microbial count between baseline and 3 months within the test group

The study has certain drawbacks; hence, more studies with greater sample size, longitudinal study design, and use of more controls should be conducted.

CONCLUSION

Thus to summarize, our study evaluated the anti-inflammatory, osteoconductive, and antimicrobial properties of statins when used as a LDD agent in 40 patients with chronic periodontitis. Clinical parameters such as PI, GI, PPD, and CAL and also, microbial evaluations for periodontal pathogenic bacteria *Porphyromonas* gingivalis were recorded using real-time PCR.

Hence, we came to the following conclusions:

1. There was a significant reduction in gingival inflammation in the test group as compared to the control group
2. There was a significant reduction in the periodontal probing depth and gain in clinical attachment level when ATV gel was used in comparison to the placebo gel as an adjunct to SRP
3. A significant reduction in the number of *Porphyromonas* gingivalis was seen in the test group.

ATV is seen to amplify the regenerative potential of bone, yet long-term, multicenter, randomized, and controlled clinical trials using different vehicles and larger sample size

will be required to understand its clinical, histological, and radiographical effects in bone regeneration.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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