

# Comparative Effect of 1.2% Atorvastatin Gel and 1.2% Rosuvastatin as a Local Drug Delivery in treatment of intra-bony defects in Chronic Periodontitis

## Abstract

**Background:** The present study was aimed to evaluate the efficacy of 1.2% Atorvastatin (ATV) with 1.2% Rosuvastatin (RSV) as local drug delivery for treatment of Chronic Periodontitis (CP). **Method and Material:** Forty patients were equally divided into two groups. Group A underwent scaling and root debridement and 1.2% ATV gel (1.2 mg/0.1 mL) was placed, whereas group B received scaling and root debridement and RSV (1.2 mg/0.1 ml) was placed. **Results:** The results showed that both the groups had improvement in all the recorded parameters, and the results obtained were statistically significant. When comparison was made between the groups, no significant difference was obtained between atorvastatin and rosvustatin at baseline in all recorded parameters. However, after 6 months significant improvement was recorded in CAL (Clinical attachment level) and PD (Probing depth). The plaque index (PI) and gingival index (GI) score however showed improvement, but it did not attain the level of significance. **Conclusion:** The present study showed improvement in clinical parameters with the use of ATV and RSV gel when used in combination with scaling and root planning (SRP) in CP patients. Patients with RSV gel showed up significantly better than the ones in which ATV gel was placed.

**Keywords:** Atorvastatin gel, chronic periodontitis, rosuvastatin

## Introduction

Periodontitis is a multifactorial disease, which is a result of the host immune inflammatory response to microbial complexes.<sup>[1]</sup> The endotoxins produced by these pathogens activate the defence cells, thus leading to the production of various cytokines like IL-1 beta, TNF- alpha, IL-6 and MMPs. These chemical mediators lead to the increased osteoclastic activity, thus affecting the supporting tissue of the periodontium—cementum, periodontal ligament and alveolar bone.<sup>[2-4]</sup>

The rationale of periodontal therapy is to prevent the progression of the disease and regenerate the lost tissue structures. Various treatment modalities such as scaling and root planning (SRP) in conjunction with local or systemic anti-inflammatory and antimicrobial agents can be used for tissue regeneration. Other treatment options that are known to decrease the intra-bony defects (IBDs) include using various regenerative materials such as bone

grafts, growth factors, bisphosphonates, statins, platelet analogues like platelet rich fibrin (PRF) and metformin.<sup>[4,5]</sup>

Statins are competitive inhibitors that belong to a group of HMG CoA (3-hydroxyl -3- methyl glutaryl coenzyme A) and are most commonly employed to prevent the risk of major coronary events by reducing the levels of low-density lipoprotein cholesterol. Other than that, it also has antioxidant, immunomodulatory, endothelium stabilisation and antithrombotic actions. Statins have also been found to increase the expression of Bone Morphogenetic Protein-2 mRNA in osteogenic cells, thus triggering the bone formation.<sup>[5,6]</sup>

These bone stimulating and anti-inflammatory actions of statins can be used to treat the periodontal defects, especially hard tissue regeneration. The present study was aimed to evaluate the efficacy of 1.2% ATV with that of 1.2% RSV as local drug delivery in the treatment of Chronic Periodontitis (CP).

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## Materials and Method

The study was conducted in the Department of Periodontics, and was approved by Institutional Ethical Review Board. Forty patients based on inclusion and exclusion criteria formed the part of the study.

### Inclusion criteria

- Healthy patients with no systemic disease
- Patients with probing depth (PD)  $\geq 4$  mm
- Subjects with  $\geq 20$  teeth with no history of antibiotic and periodontal therapy six months prior to the initiation of the study.

### Exclusion criteria

- Patients on statin therapy
- Immuno-compromised patients
- Patients using any form of tobacco
- Pregnant and lactating females.

Patients were randomly and equally divided into two groups. Group A underwent scaling and root debridement and 1.2% RSV gel (1.2 mg/0.1 mL) was placed, whereas group B received scaling and root debridement and ATV gel (1.2 mg/0.1 mL) was placed.

### LDD gel formulation

For preparation of RSV and ATV gels, a biocompatible solvent was mixed with pre-measured quantity of methylcellulose, which was then heated to 50–60°C in a vial. Mechanical shaker was used for constantly agitating the solution so that clear solution could be obtained. After the solution became clear, pre-weighed quantity of RSV or ATV was added.

### Collection of data

Clinical parameters like Plaque Index (PI), Gingival index (GI), Clinical attachment level (CAL) and pocket PD were measured at different time intervals (at baseline, 1 month of gel placement and after 6 months). 21 gauge needle with blunt cannula was used for placing the gel in the oral cavity. About 0.25 ml of gel was placed into the periodontal pocket followed by Coe pack dressing. Radiographic assessment was done at baseline and after 6 months.

## Results

Table 1 showed that there were 11 males and nine females in group 1 and eight males and 12 females in group 2.

Table 2 showed mean and standard deviation of the clinical parameters at baseline and at sixth month for patients treated with RSV (group A). The mean PI at baseline and after 6 months was 1.70 and 1.18, respectively, GI was 1.63 and 1.13, respectively, clinical attachment loss was 6.1 and 5.1, respectively and PD was 5.3 and 4.15, respectively. There was significant difference between baseline and after 6 months ( $P < 0.05$ ).

Table 3 showed mean and standard deviation of the clinical parameters at baseline and at sixth month for patients treated with ATV (group B). The mean PI at baseline and after 6 months was 1.54 and 1.27, respectively, GI was 1.59 and 1.2, respectively, clinical attachment loss was 5.9 and 5.3, respectively and PD was 5.1 and 4.6, respectively. There was significant difference between baseline and after 6 months ( $P < 0.05$ ).

Table 4 showed intergroup comparison between different parameters at different time intervals. The results showed that both the groups showed improvement in all the recorded parameters, and the results obtained were statistically significant ( $P < 0.05$ ) [Tables 1 and 2]. When comparison was made between the groups no significant difference was

**Table 1: Distribution of patients**

Groups	Group I	Group II
Method	SRP + 1.2% RSV gel	SRP + ATV gel
Male:Female	11:9	8:12

**Table 2: Clinical parameters at baseline and at sixth month for patients treated with RSV (group A)**

Parameters	Baseline		6 months		<i>t</i>	<i>P</i> *
	Mean	SD	Mean	SD		
PLAQUE INDEX	1.70	0.37	1.18	0.35	4.5	0.000
GINGIVAL INDEX	1.63	0.45	1.13	0.30	4.1	0.000
CAL	6.1	0.55	5.1	0.71	4.9	0.000
PD	5.3	0.63	4.15	0.74	2.3	0.01

\*Significant at 5% level of significance ( $P < 0.005$ ). SD: Standard deviation

**Table 3: Clinical parameters at baseline and at sixth month for patients treated with ATV (group B)**

Parameters	Baseline		6 months		<i>t</i>	<i>P</i> *
	Mean	SD	Mean	SD		
PLAQUE INDEX	1.54	0.42	1.27	0.38	2.13	0.01
GINGIVAL INDEX	1.59	0.50	1.2	0.37	2.4	0.009
CAL	5.9	0.44	5.3	0.59	3.07	0.001
PD	5.1	0.83	4.65	0.81	1.7	0.04

\*Significant at 5% level of significance ( $P < 0.005$ ). SD: Standard deviation

**Table 4: Intergroup comparison among different parameters at different time intervals**

		Group I	Group II	<i>F</i>	<i>P</i> *
PLAQUE INDEX	BASELINE	1.7 $\pm$ 0.37	1.54 $\pm$ 0.42	1.46	0.23
	6 MONTHs	1.18 $\pm$ 0.35	1.27 $\pm$ 0.38	0.62	0.43
GINGIVAL INDEX	BASELINE	1.63 $\pm$ 0.45	1.59 $\pm$ 0.50	0.09	0.76
	6 MONTHs	1.13 $\pm$ 0.30	1.2 $\pm$ 0.37	1.19	0.25
CAL	BASELINE	6.1 $\pm$ 0.55	5.9 $\pm$ 0.44	1.58	0.21
	6 MONTHs	4.65 $\pm$ 0.74	5.3 $\pm$ 0.59	12.09	0.001
PD	BASELINE	5.3 $\pm$ 0.63	5.1 $\pm$ 0.83	0.71	0.40
	6 MONTHs	4.15 $\pm$ 0.74	4.65 $\pm$ 0.815	4.1	0.04

\*Significant at 5% level of significance ( $P < 0.005$ )

obtained between ATV and roxustatin at baseline in all recorded parameters. However, after 6 months significant improvement was recorded in CAL and PD. The PI and GI score however showed improvement, but it did not attain the level of significance.

## Discussion

Periodontal therapy aims to restore the periodontal tissue that has been lost due to periodontal diseases. Periodontitis is a condition in which there is a collection of inflammatory cells, which produce cytokines that lead to activation of osteoclasts thereby resulting in resorption of alveolar bone and attachment loss.<sup>[4,6]</sup> Statins have been suggested to have osteoblastic properties and have shown to stimulate the bone formation, thus being useful for patients with periodontal infection.<sup>[7,8]</sup> The present study was aimed to evaluate the efficacy of 1.2% ATV with that of 1.2% RSV as local drug delivery in the treatment of CP.

The present study showed that significant improvement was seen on PI, GI, PD and CAL after 6 months of treatment in both the groups. The results of the present study are in accordance with the study conducted by Sinjab *et al.*<sup>[9]</sup> who in their meta-analysis found that use of statin as a locally delivered drug in combination with mechanical SRP was useful in periodontal regeneration. There was improvement in the inflammatory condition seen. The PD got reduced and there was gain in clinical attachment loss. In a study by Chatterjee *et al.*,<sup>[10]</sup> it was showed that 1.2% RSV gel when delivered locally into IBD improved periodontal clinical parameters such as PD and CAL and showed significant bone fill.

On comparing RSV with ATV, it was seen that there was no significant difference observed in the PI and GI between both groups; however, the PD and CALs showed significant difference after 6 months.

The mean reduction in the value of PD in group A in the present study after 6 months was  $0.45 \pm 0.02$ , whereas for group B it was  $0.5 \pm 0.1$ . The results were in accordance to the study conducted by Pradeep *et al.*<sup>[11]</sup> who also showed that RSV group showed significant improvement in all clinical parameters when compared to ATV group in treatment of mandibular class II furcation defects as an adjunct to SRP.<sup>[4]</sup> Similar results were obtained by Garg *et al.*<sup>[12]</sup> who showed that RSV is a better choice of statin and showed significant improvement than ATV. Similarly, Singh *et al.*<sup>[13]</sup> found the antimicrobial effects of ATV giving significant reduction in PI, GI, PPD and gain in CAL along with significant decrease in the microbial load.

Kanoriya *et al.*<sup>[14]</sup> assessed the effectiveness of 1.2% RSV gel in addition to SRP in smokers with CP in 60 patients, which were divided into two treatment groups, that is SRP with placebo gel (Group 1) and SRP with 1.2% RSV gel (Group 2). Clinical parameters were determined at regular intervals (baseline, 3, 6 and 9 months). The authors

found significant greater mean PD reduction and greater mean gain in CAL in the RSV group at different time periods as compared to placebo. A greater mean defect depth reduction was obtained in the RSV group ( $23.91 \pm 1.03$ ,  $29.24 \pm 0.834$ ) after 6 and 9 months, respectively. Similar results were also found among different studies conducted by Pradeep *et al.*<sup>[15]</sup> and Ramesh *et al.*<sup>[16]</sup>

Cao *et al.*<sup>[17]</sup> assessed IBD, PD and CAL. It was observed that there was greater filling of IBD, reduction in PD and gain in CAL for SRP treated in combination with statins when compared to SRP alone for treating CP without systemic diseases. In CP patients with type 2 diabetic (T2DM) or in smokers, additional benefits were observed from locally delivered statins.

Kumari *et al.*<sup>[18]</sup> determined utility of 1.2% ATV gel in the treatment of IBDs in 75 CP patients with T2DM who were categorized into two groups: 1) SRP plus 1.2% ATV and 2) SRP plus placebo. Results showed greater mean PD reduction and mean RAL gain in the ATV group than the placebo group at 3, 6 and 9 months. Furthermore, ATV group sites presented with a significantly greater percentage of radiographic defect depth reduction at 6 and 9 months. Similar results were also found among different studies conducted by Singh *et al.*<sup>[19]</sup> and Cao *et al.*<sup>[17]</sup>

## Conclusions

The present study shows improvement in clinical parameters with the use of ATV and RSV gel when used in combination with SRP in CP patients. Patients with RSV gel showed significantly better than the ones in which ATV gel was placed. There is scope for these two gels to be used for future studies, which can involve larger population to show better results. Other studies evaluating the use of host modulators (modulators of inflammation, pre-biotics, probiotics, antioxidant micronutrients) administered either topically or systemically in combination with non-surgical periodontal therapy may be used to evaluate their effect other than statins.

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## Conflicts of interest

There are no conflicts of interest.

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