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Original Article

Effect of topical simvastatin (1.2 mg) on gingival crevicular fluid interleukin-6, interleukin-8 and interleukin-10 levels in chronic periodontitis – A clinicobiochemical study

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ABSTRACT

Objectives: The impact of simvastatin (SMV), a cholesterol lowering drug, on bone metabolism appears to involve complex interaction with cholesterol metabolites, hormones, inflammatory mediators and growth factors, thus having direct influence on extent and severity of periodontitis. The present study aims to evaluate the in vivo effect of subgingivally delivered SMV gel (1.2 mg) as a local drug-delivery agent on clinical parameters and on interleukin-6 (IL-6), interleukin-8 (IL-8) and interleukin-10 (IL-10) levels in gingival crevicular fluid (GCF) of chronic periodontitis patients.

Materials and methods: 50 patients were selected and categorized into two treatment groups: control (scaling and root planing) and test group (scaling and root planing with SMV gel). At initial appointment, clinical parameters were measured. Biochemical analysis of GCF samples was done to evaluate the amount of IL-6, IL-8 and IL-10. GCF sampling and clinical parameters were repeated at one and three months for both the groups.

Results: SMV has an inhibitory effect on pro-inflammatory cytokines (IL-6, IL-8) and stimulatory effect on anti-inflammatory cytokines (IL-10) in GCF of periodontitis patients and has significantly positive effect on all clinical parameters except relative attachment level (RAL). The addition of SMV, thereby, further alters the levels of cytokine that reflect enhanced antibacterial host defence activity at that site.

Conclusion: Topical SMV has a beneficial effect on periodontal health. Removal of the bacterial plaque and subgingival delivery of SMV significantly modulates the chemokines present in GCF. To summarize, SMV shows promising role in the management of periodontitis.

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1. Introduction

An imbalance between the destruction and repair of periodontal tissue triggered by periopathogenic bacteria of dental plaque results in chronic inflammatory disease called periodontitis.¹ Resident cells in periodontal ligament (PDL) have the ability to recognize these bacterial pathogens thus inducing the production of pro-inflammatory cytokines, systemic inflammatory reactants, tissue degradative enzymes and chemokines.² Cytokines play a major role in the pathogenesis of periodontal disease. These are detected in GCF and are beneficial for diagnosing periodontal disease activity and addressing effect of periodontal treatment.³ The primary cytokines identified in chronic periodontal disease includes (interleukin – IL) IL-1, IL-1 β , IL-6, IL-8, IL-10 and INF, which further influences the activity of immune cells.^{4,5}

Simvastatin (SMV), a synthetic statin, has a beneficial impact from a periodontal therapeutic standpoint on bone metabolism through osteoclast inactivation by affecting the generation of isoprenoids.⁶ It has an anabolic effect and is a local stimulant for bone-growth regulatory factor. SMV also influences production of inflammatory cytokines via C-reactive protein.⁷ We restricted the present study to three cytokines, which are strongly associated with periodontal inflammation namely IL-6, IL-8 and IL-10.

IL-6: Associated with terminal differentiation of B-lymphocytes (plasma cell) and activation of complement cascade. It is a predominant cytokine associated with bone destruction in advanced periodontal disease.² IL-8: It is a α chemokine. It is a relevant mediator of granulocyte accumulation by attracting PMNs in inflammatory region. It represents host defence against periodontal bacteria.^{8,9} IL-10: Inhibits cytokine production by activated T helper (Th1) clones due to inhibitory effect on monocyte and macrophages. It specifically modulates the expression of cytokine of myeloid origin, thus affecting activation and maintenance of immune response in periodontitis.¹⁰

The action of statin on cytokines of gingival tissue is poorly understood and data available till date are in vitro. Therefore, in the present study, we examine the in vivo effects of subgingivally delivered SMV gel 1.2 mg on clinical parameter (PI, mSBI, PD, RAL) and total amount of IL-6, IL-8 and IL-10, and levels in GCF among chronic periodontitis patients before and after SRP at baseline, one month and three months.

2. Material and method

2.1. Source of data

Patients in the age range of 25–45 years of both the sexes were selected from the Out-Patient Department of Periodontology, after the approval of the ethical committee of the Sri Gobind Tricentenary Dental College, Hospital and Research Institute, Gurgaon, Haryana.

A written informed consent was obtained from all the patients prior to commencement of the study. Systemically healthy patients with Pocket Probing depth of 5–8 mm in posterior and with no history of periodontal surgery or

antibiotic therapy in the preceding three months were included in the study. Patients with aggressive periodontitis, smokers, alcoholics, systemic disease and pregnant or lactating mothers, dental infections, known or suspected allergy to the SMV group and patients on systemic statin therapy were excluded from the group.^{2,4,11}

2.2. Study design

Fifty selected patients were divided into two groups (coin and toss method).

Group I (n = 25): Patients treated by SRP.

Group II (n = 25): Patients treated by SRP with subgingival 1.2 mg SMV gel.

At each patient's initial appointment, baseline data were obtained on modified Sulcus bleeding index (mSBI)² by the method of Mombelli A and on plaque index (PI)¹² by the method of Loe on four posterior teeth in each quadrant (1st premolar, 2nd premolar, 1st molar and 2nd molar).⁴ Probing depth (PD) and relative attachment level (RAL) (custom-made occlusal stent) were measured with a UNC-15 periodontal probe for the same teeth. GCF samples were taken at 16 sites for each patient. These sites were the mesio-buccal surfaces of the above stated 4 posterior teeth in each upper quadrant and at the mesio-lingual surfaces of the same in each lower quadrant. SRP is performed until the root surface is considered smooth and clean by the operator. Scaling and root planing were performed in both the groups. No antibiotics or anti-plaque and anti-inflammatory agents were prescribed after treatment.

2.3. Collection of GCF

Each GCF sample was collected by calibrated volumetric microcapillary pipettes^{13,14} (Sigma Aldrich, USA), which were inserted in the gingival sulcus immediately after the area has been isolated with cotton rolls, dried, and supragingival plaque has been removed with a sterile Gracey curette (Hu Friedy®, USA). The calibrated microcapillary pipettes were placed in a polypropylene tube and immediately transferred to coated plastic vial and then stored at –70 °C till the time of cytokine assay. Microcapillary pipettes contaminated with blood and saliva were excluded from the sampled group.

2.4. GCF analysis

Biochemical analysis of GCF samples was done to estimate the level of IL-6, IL-8 and IL-10 using ELISA kit (Avibion, human ELISA, Finland). Samples were kept at room temperature (18–25 °C) before use.

Standardization of sample diluent:

- Dilution of test standard: Dissolve lyophilized IL-6, IL-8 and IL-10 standard with sample diluent volume. The solution obtained is unstable and was used immediately.
- 150 μ l of IL-6 standard (1000 pg/ml of IL-6) was added to 150 μ l sample diluent in first tube to obtain 500 pg/ml concentration.
- 150 μ l of sample diluents was added to the other 6 tubes.
- 150 μ l from first tube (500 pg/ml) was taken and two-fold serial dilution was started.

- Sample diluents served as the zero standard (0 pg/ml) in the tube.

150 μ l standard (1000 pg/ml) + 150 μ l sample diluents.

2.5. Quantification of cytokines

GCF samples were assayed by an ELISA to determine the levels of IL-6, IL-8 and IL-10 using matched antibody pairs. Samples were kept at room temperature before use.

- Prepared all reagents, sample and standard to dilution of sample at initial screening.
- Added 50 μ l of standard starting from 500 pg/ml, test sample as a blank into the appropriate wells of the strips.
- 50 μ l ready-to-use green coloured biotin antibody was added to each well. Covered and incubated for 1 h 30 min at room temperature. After that washed 5 times with wash buffer.
- 100 μ l ready-for-use HRP-streptavidin solution (peroxidase) was added to each well. Covered and incubated for 30 min at room temperature. After that washed 5 times with wash buffer.
- 50 μ l TMB (tetramethylbenzidine) one-step substrate reagents were added to each well. Covered and incubated for 20 min at room temperature.
- Added 25 μ l stop solution (H_2SO_4) to each well.
- Took reading immediately by ELISA reader.
- The amount of each cytokine is determined in picograms.

2.6. Formulation of SMV gel

SMV gel was prepared in the Department of Pharmacology, Ram Gopal College of Pharmacy, Farukhnagar. 105 mg of Methylcellulose was added into 5 ml of distilled water and continuous stirring was done at 50–60 °C to make a gel form (Solution A). Then, 84 mg of SMV was added into 2 ml distilled water and stirred (Solution B). Then, Solution B was added to Solution A while stirring, so as to make a homogenous gel. Thus, 0.1 ml of SMV gel contains 1.2 mg of SMV drug.²

2.7. Local drug delivery

For standardization, 0.1 ml prepared SMV gel (1.2 mg/0.1 ml) was injected into the periodontal pockets using a syringe with a blunt cannula in Group II (Fig. 1). No periodontal dressing was applied after delivery of the drug because the prepared formulation decreases in viscosity, which causes swelling

Fig. 1 – Placement of simvastatin gel.

and occlusion of the periodontal pocket.² After placement of the gel in situ, patients were instructed to refrain from chewing hard or sticky foods, brushing near the treated areas or using any interdental aids for 1 week.

One and three months later, all clinical measurements and GCF samplings were repeated for both the groups from the same sites. A single clinician provided treatment to both groups, and all pre- and post-treatment clinical parameters were recorded by the same examiner.

2.8. Statistical analysis

Data analysis is performed using the statistical package SPSS version 18.0 (Inc Chicago, Illinois, USA) for all time intervals. The total cytokines and clinical values from the test and control groups were used for the purpose of analysis. Negative sample was not used for consideration. The level of significance set as:

- $p > 0.05$ Not significant
- $p < 0.05$ Significant
- $p < 0.01$ Highly significant
- $p < 0.001$ Very highly significant

3. Results

The study included a total of 50 healthy patients; 25 patients were assigned to each treatment group. In test group, 14 males and 11 females and in control group 11 males and 14 females were included with an average age of 25–45 years. With the exception of periodontitis, all subjects were medically healthy. During the study period, all patients remained stable and there were no changes in lifestyle issues and habits including exercise, diet, smoking and medications.

3.1. Clinical parameters

Periodontal treatment led to improvement in all clinical parameters in test and control groups. **Intragroup (with in one group)** The PI, mSBI, PD and RAL score showed significant decrease from baseline to one month and baseline to three months over the period of study for both test and control groups ($p < 0.001$) (Fig. 2).

Intergroup: (between test and control groups) There was statistically significant difference found between test and control groups for PI and mSBI. Test group (SMV) showed better reduction in PI and mSBI at three-month interval when compared to control. No significant difference was found between test and control groups for PD and RAL.

Table 1 clearly depicts that there was highly significant difference in mean score for PI and mSBI and PD between test and control groups. No significant mean difference was found for RAL between test and control groups.

3.2. Cytokines

3.2.1. Interleukin-6 (IL-6)

3.2.1.1. **Intragroup.** Mean IL-6 score at baseline, 1 month and 3 months for test and control groups, is as shown in Table 2. On

Fig. 2 – Comparison of mean of all clinical parameters: mean values for PI, mSBI, PD and RAL showed decline from baseline to three months in both the groups.

intragroup comparison, IL-6 levels increase at 1 month for both test and control groups. At 3 months, IL-6 levels fall for both groups settling below the baseline values. The decrease of IL-6 levels from 1 month to 3 months was statistically significant in test group.

3.2.1.2. *Intergroup.* Comparison IL-6 levels showed better reduction in test group at three-month interval when compared to control group ($p < 0.05$) (Table 3).

3.2.2. Interleukin-8 (IL-8)

3.2.2.1. *Intragroup.* Mean IL-8 score at baseline, 1 month and 3 months for test and control groups, is as shown in Table 4. IL-8 follows exactly the same pattern as IL-6, both being

pro-inflammatory cytokines suggesting a strong positive correlation.

3.2.2.2. *Intergroup comparison.* On intergroup comparison, no statistically significant difference was seen in both the groups at any time of study (Table 5).

3.2.3. Interleukin-10 (IL-10)

3.2.3.1. *Intragroup.* Mean IL-10 score at baseline, 1 month and 3 months for test and control groups, is as shown in Table 6. The increase in IL-10 level was significant at all time intervals of study, for both the groups.

3.2.3.2. *Intergroup.* Although the increase in IL-10 levels was more with test group (SMV), there was no statistically significant difference found between test and control groups at 1 month and 3 months (Table 7).

3.3. Interleukin-10

Periodontal treatment resulted in increased IL-6 and IL-8 concentrations in both test and control groups at 4 weeks, but at 12 weeks, the levels fall both for test and control groups settling below the baseline values at three months. The decrease of IL-6 levels is from baseline to three months for control group but is highly significant for the test group. IL-8 follows the similar pattern as IL-6, as both being pro-inflammatory cytokines; a total of two patients in test group and 5 patients of control group showed increased level of IL-8 at 3 months. A strong correlation was found between IL-6 and IL-8 concentrations. The levels of IL-10 increase for both the test and

Table 1 – Comparison of mean of all clinical parameters: mean values for PI, mSBI, PD, and RAL showed decline from baseline to three months in both the groups.

Group statistics					
	Group	N	Mean	Std. deviation	p-Value
PI	Test	25	37.42	11.47	0
	Control	25	23.92	9.63	
mSBI	Test	25	37.45	11.33	0
	Control	25	22.26	12.08	
PD	Test	25	22.66	9.05	0.008
	Control	25	14.14	12.61	
RAL	Test	25	25.56	10.44	0.437
	Control	25	23.40	8.94	

Table 2 – Comparison of IL-6 for test and control groups (intragroup) at 0, 1 and 3 months: the decrease of IL-6 levels from 1 month to 3 months was statistically significant and in control group, the decline was significant.

		N	Var 1		Var 2		p-Value
			Mean	Std. deviation	Mean	Std. deviation	
Test group							
Pair 1	IL6-0-IL6-1	25	13.15	12.35	15.12	13.26	0.210
Pair 2	IL6-0-IL6-3	25	13.15	12.35	7.056	4.778	0.006
Pair 3	IL6-1-IL6-3	25	15.12	18.53	7.056	4.778	0.001
Control group							
Pair 1	IL6-0-IL6-1	25	12.92	10.34	13.35	9.80	0.30
Pair 2	IL6-0-IL6-3	25	12.92	10.34	11.84	9.62	0.07
Pair 3	IL6-1-IL6-3	25	13.35	9.80	11.84	9.62	0.05

Table 3 – Comparison of IL-6 for test and control groups at 0, 1 and 3 months: intergroup comparison IL-6 levels showed better reduction in test group at three-month interval when compared to control group.

Group statistics					
	Group	N	Mean	Std. deviation	p-Value
IL6-0	Test	25	13.16	12.35	0.941
	Control	25	12.92	10.34	
IL6-1	Test	25	15.13	13.26	0.592
	Control	25	13.35	9.80	
IL6-3	Test	25	7.06	4.78	0.031
	Control	25	11.84	9.62	

Table 4 – Comparison of IL-8 for test and control groups (intragroup) at 0, 1 and 3 months: IL-8 levels increase at 1 month for both test and control groups but was not significant. At 3 months, IL-8 levels fall both for control and test groups settling below the baseline values.

		N	Var 1		Var 2		p-Value
			Mean	Std. deviation	Mean	Std. deviation	
Test group							
Pair 1	IL8-0–IL8-1	25	287.890	171.808	294.20	174.15	0.767
Pair 2	IL8-0–IL8-3	25	287.890	171.808	274.060	188.294	0.625
Pair 3	IL8-1–IL8-3	25	294.20	174.15	274.060	188.294	0.308
Control group							
Pair 1	IL8-0–IL8-1	25	277.39	209.22	313.91	217.35	0.071
Pair 2	IL8-0–IL8-3	25	277.39	209.22	266.17	209.39	0.524
Pair 3	IL8-1–IL8-3	25	313.91	217.35	266.17	209.39	0.005

control groups over the period of study. The increase in levels of IL-10 was more with SMV group but not statistically significant.

The comparison between IL-6, IL-8 and IL-10 levels and clinical parameters revealed positive correlation of IL-6 and IL-8 with RAL (Table 8). IL-6 and IL-8 do not show any correlation with PI, mSBI and PD. IL-10 does not show any correlation with clinical parameters.

4. Discussion

Periodontitis is an inflammatory disease of supporting tissues of the teeth. It ranges in severity from mild and reversible inflammation of the gingiva to chronic destruction of periodontal tissues (gingiva, PDL and alveolar bone) with

Table 5 – Comparison of IL-8 for test and control groups at 0, 1 and 3 months: on intergroup comparison no statistically significant difference in both the groups at any time of study.

Group statistics					
	Group	N	Mean	Std. deviation	p-Value
IL8-0	Test	25	287.890	171.808	0.847
	Control	25	277.390	209.219	
IL8-1	Test	25	294.20	174.15	0.725
	Control	25	313.91	217.34	
IL8-3	Test	25	274.060	188.294	0.889
	Control	25	266.170	209.389	

Table 6 – Comparison of IL-10 for test and control groups (intragroup) at 0, 1 and 3 months: the increase in IL-10 level was significant at all time intervals of study.

		N	Var 1		Var 2		p-Value
			Mean	Std. deviation	Mean	Std. deviation	
Test group							
Pair 1	IL10-0–IL10-1	25	4.802	3.048	5.848	2.449	0.002
Pair 2	IL10-0–IL10-3	25	4.802	3.048	6.914	3.097	<0.001
Pair 3	IL10-1–IL10-3	25	5.848	2.449	6.914	3.097	0.033
Control group							
Pair 1	IL10-0–IL10-1	25	4.26	2.07	4.93	2.53	0.059
Pair 2	IL10-0–IL10-3	25	4.26	2.07	5.54	3.42	0.02
Pair 3	IL10-1–IL10-3	25	4.93	2.53	5.54	3.42	0.167

Table 7 – Comparison of IL-10 for test and control groups at 0, 1 and 3 months: although the increase in IL-10 levels was more with test group (SMV) but there was no statistically significant difference found between test and control groups at 1 month and 3 months.

Group statistics					
	Group	N	Mean	Std. deviation	p-Value
IL10-0	Test	25	4.802	3.048	0.465
	Control	25	4.260	2.068	
IL10-1	Test	25	5.848	2.449	0.198
	Control	25	4.929	2.532	
IL10-3	Test	25	6.914	3.097	0.142
	Control	25	5.539	3.418	

Table 8 – Correlation of relative attachment level with IL-6, -8 and -10 at 0, 1 and 3 months: the comparison between IL-6, -8 and -10 levels and clinical parameters revealed positive correlation of IL-6 and IL-8 with RAL.

		RAL-0	RAL-1	RAL-3
IL6-0	Pearson correlation	0.48	0.33	0.23
	Sig. (2-tailed)	0.01	0.1	0.26
IL6-1	Pearson correlation	0.54	0.47	0.36
	Sig. (2-tailed)	0.005	0.01	0.07
IL6-3	Pearson correlation	0.23	0.17	0.05
	Sig. (2-tailed)	0.25	0.39	0.78
IL8-0	Pearson correlation	0.34	0.40	0.48
	Sig. (2-tailed)	0.08	0.04	0.01
IL8-1	Pearson correlation	0.52	0.57	0.68
	Sig. (2-tailed)	0.008	0.003	0
IL8-3	Pearson correlation	0.43	0.43	0.63
	Sig. (2-tailed)	0.03	0.03	0.001
IL10-0	Pearson correlation	0.14	0.11	0.01
	Sig. (2-tailed)	0.49	0.58	0.93
IL10-1	Pearson correlation	0.17	0.16	0.08
	Sig. (2-tailed)	0.39	0.44	0.69
IL10-3	Pearson correlation	0.18	0.20	0.06
	Sig. (2-tailed)	0.37	0.32	0.75

eventual exfoliation of teeth. The destruction process of the periodontal tissues begins with the accumulation of biofilms on the tooth surface that contains bacterial masses at or below the gingival margin.

SMV has been reported to promote osteoblastic activity and inhibit osteoclastic activity. The successful use of SMV to promote bone formation in vivo depends on the local concentration. Thylin et al.¹⁵ compared increase in bone thickness using 2.2 mg dose of topical SMV gel (membrane) to multiple injection protocol. The increase of total bone area and compact bone area for membrane was higher than increase in bone area with injection protocol. A negative side effect of high dose of SMV was inflammation and scabbing of the overlying skin. Stein et al.¹⁶ stated that by reducing simvastatin dose from 2.2 mg/30 μ l to 0.5 mg/80 μ l, there was a decrease in the inflammation reaction without sacrificing bone-growth potential. Seto et al.¹⁷ stated that topical application of simvastatin 0.2 mg/50 μ l is effective for reducing periodontal tissue involving alveolar bone destruction.

In the present study, 1.2 mg SMV concentration was used to prepare a flowable gel, as it was difficult to achieve proper viscosity with lower concentration, and this flowable gel can easily pass through syringe.

PI: The PI score for control and test groups showed significant improvement over the period of study at all time intervals

($p < 0.001$). The change may be due to removal of bacterial deposits; moreover, improved plaque control by the patients may have led to favourable subgingival microbial changes as explained by Bollen et al.¹⁸ Similar observations were made by Hunter et al.¹⁹ Eaton et al.²⁰ PI score was significantly lower at three months ($p < 0.013$) for test group, which is in favour of the study done by Lindy et al.²¹ mSBI: The score of mSBI for control group showed statistically significant improvement over the study period. The reduction in bleeding is due to resolution of gingival inflammation after removal of bacterial deposits by scaling and root planing.¹⁸ The decrease in mSBI score was greater in test group. This may be due to anti-inflammatory effect of SMV.¹⁵ The present study is in agreement with the study done by Pradeep et al.² and Lindy et al.²¹ also found that patients on statin medication have fewer signs of periodontal inflammation than subjects without statin regimen.

PD and RAL: On intragroup comparison, the score of PD and RAL for test and control groups showed significant improvement in both the groups, $p < 0.001$. It is suspected that either a continued reorganization of the connective tissue permitting less probe penetration or coronally creeping attachment is responsible for this occurrence.²² Similar observation were made by Cobb,²³ Kaldahl et al.,²² Lindy et al.²¹ and Nordland et al.²⁴

There was better reduction of PD with SMV group. This was in agreement with the study done by Pradeep et al.² Yazawa

et al.⁶ stated the effect of SMV on human periodontal (PDL) cells in vitro and showed that, at a low concentration, SMV exhibits a positive effect on the proliferation and osteoblastic differentiation of human PDL cells, and these effects may be caused by inhibition of mevalonate pathway, indicating the role of SMV in bone regeneration.

IL-6 and IL-8: In the present study, IL-6 and IL-8 levels are found to be higher in periodontitis patients, which is in accordance with studies done by Bartold et al.²⁵ and Takahashi et al.²⁶ This could be explained as *Aggregatibacter actinomycetemcomitans* and *Campylobacter rectus* have been shown to stimulate IL-6 and IL-8 production by human gingival fibroblasts. Reddi et al.²⁷ stated that surface-associated material (SAM) from a number of oral pathogens including *A. actinomycetemcomitans*, *Eikenella corrodens*, *Porphyromonas gingivalis*, *C. rectus* and *Prevotella intermedia* induced IL-6 and IL-8 production. Gingival fibroblasts thus contribute to periodontal tissue inflammation. In this study, mean IL-6 and IL-8 levels increase after phase 1 therapy at one month and then falls for both test and control groups, settling below the baseline values at three months. Our results are in agreement with the study done by Goutoudi et al.,²⁸ which states that periodontal treatment results in significantly increased level of IL-6 concentration at diseased sites. Mean IL-6 concentration starts declining at 6 weeks and at 32 weeks they again increase to pretreatment levels. Tsai et al.²⁹ stated higher concentration of IL-6 and IL-8 in GCF of periodontitis patients and decreased after 2 months of periodontal treatment.

The decrease of IL-6 levels from baseline to three months was significant for control group (0.05) and highly significant for test group (0.001). This is in accordance with Ikeda et al.³⁰ who stated that addition of statins significantly decreased IL-6 production by these cells and suggested that the statin-mediated decrease in CRP concentrations could be due to an inhibition of IL-6 in the vascular tissues. Our study is also in agreement with Sakoda et al.³¹ that SMV has inhibiting effect on cytokine production. Total of 2 patients in test group and 5 patients in control group showed increased level in IL-8 at 3 months. This is in agreement with the study done by Chung et al.,³² which stated that root planing led to decreased and in some others increased levels of IL-8 and β -glucuronidase, which correlate them with individuals at risk for progression of periodontitis.

IL-10: In the present study, there is significant increased level in IL-10 levels at 1 month followed by increase in the levels at 3-month values for both test and control groups. On intergroup comparison, there was increase in IL-10 levels in both the groups but there was no statistically significant difference found between test and control groups at any point of study. Till date, no published data are available for effect of the SMV on IL-10 levels in GCF at different time intervals. In this study, an attempt was made to compare them, which was found to be statistically significant.

5. Conclusion

Removal of the bacterial plaque modulates the chemokines present in GCF. The dynamic interaction between cytokines, their production rates and the quantity represent factor

controlling induction, perpetuation and closure of cytokine network in periodontal disease. To summarize, intergroup comparison of control and test groups (SRP with SMV) shows better clinical results on clinical parameters as well as interleukin levels, being efficient in management of periodontal pockets. No adverse reaction was observed in any subject from the test group, and no patient reported any discomfort. All subjects well tolerated the drug, without any postapplication complications. Within the limits of our study, it can be concluded that local delivery of SMV is a safe, easy and efficacious method along with SRP in the management of periodontal disease.

However, further studies are advised with larger sample size, longer follow-up duration and confirmation with microbiological analysis to overcome the drawbacks of the present study.

Ethical approval

The guidelines for this study were approved by Ethical Committee of SGT University Gurgaon.

Conflicts of interest

The authors have none to declare.

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