Original Article

Efficacy of Xanthan-Based Chlorhexidine Gel on the Levels of Interleukin-1β in Chronic Periodontitis: An Interventional Study

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ABSTRACT

Aims and Objectives: Xanthan-based chlorhexidine gel (Chlosite®) is a local drug delivery system that exposes the sub-gingival bacteria to the effects of chlorhexidine (CHX) for a prolonged time. Hence, the study aimed at evaluating the clinical efficacy of the subgingival application of Chlosite gel as an adjunctive to mechanical scaling and root planing (SRP) and at evaluating the salivary interleukin (IL)-1β level to substantiate the clinical efficacy of xanthan-based CHX gel. **Materials and Methods:** A total number of 40 patients with chronic periodontitis in the age group of 30–50 years were enrolled in this interventional study. The patients were assigned to group A, in which only SRP was done, and group B, in which SRP along with the subgingival application of Chlosite gel was done. Periodontal parameters and salivary IL-1β level were evaluated, and the data obtained were statistically analyzed by using paired and unpaired "*t*" tests. **Results:** The results obtained showed a statistically significant reduction in the mean gingival index (GI), probing pocket depth (PPD), clinical attachment level (CAL), and salivary IL-1β values in both the groups from baseline to 30 days. There was a statistically significant reduction in GI, in group B when compared with group A, after the treatment. Salivary IL-1β value in group B was slightly lower when compared with group A after the treatment, but it was not statistically significant. **Conclusions:** The xanthan-based CHX gel is therapeutically effective when used as an adjunct to SRP. The study also indicated that salivary IL-1β can be used as a reliable biomarker.

Keywords: *Chlorhexidine, interleukin-1β, periodontitis, xanthan*

Introduction

In 1979, Goodson *et al.* introduced the concept of local drug delivery for periodontal therapy, which is based on the notion that locally delivered antimicrobial drugs can reach the base of the periodontal pocket and can be maintained for a prolonged period.[1] The common antimicrobials used for local drug delivery include tetracycline, doxycycline, minocycline, and CHX.[2] Various drug delivery vehicles include gels, films, chips, varnish, fibers, injectable systems, etc.[3]

CHX is considered as the gold standard antiplaque agent against which the efficacy of other antiplaque agents is measured because of its antimicrobial activity, substantivity, and nontoxic properties.[4,5] Xanthan-based chlorhexidine (Chlosite®) is an injectable gel formulation of CHX that is a distinctive combination of CHX digluconate (0.5%) and CHX dihydrochloride (1%) in a 1:2 ratio and 0.5% xanthan gel.[6] Xanthan gum, when in contact with water, forms a 3D pseudoreticulum; it has a prolonged adhesion time and

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is stable over a wide range of pH and temperature.[7] Hence, it is not easily washed away by the flushing action of gingival crevicular fluid or saliva.[8] It dissolves in 10–30 days on application into the periodontal pocket, which helps in maintaining the therapeutic concentration for at least 15 days.[9]

IL-1, also called osteoclast activating factor, is a potent pro-inflammatory cytokine that is synthesized by various cell types, including fibroblasts, macrophages, and monocytes.[10] Various studies concluded that the mean levels of salivary IL-1β were higher in patients with periodontitis when compared with healthy individuals.[1,11,12] Hence, salivary IL-1β can be used as a reliable candidate biomarker for periodontitis.

Numerous studies have been conducted to evaluate the efficacy of CHX, but there is scanty literature that shows the efficacy of CHX on the levels of IL-1β. Therefore, the present study was designed to evaluate the efficacy of the subgingival application of xanthan-based chlorhexidine (Chlosite®) as an adjunct to SRP in the management of chronic periodontitis. The levels of IL-1β were also compared along with the periodontal status of the individuals.

Subjects and Methods

A total of 40 subjects were selected for the study. Written informed consent was obtained from all the participants before the start of the study. The study was approved by the Central Ethics Committee of the Institution.

Study sample

- The study design comprised 40 subjects, divided into two equal groups.
- Group A: Patients with chronic periodontitis treated by SRP alone.
- Group B: Patients with chronic periodontitis treated by xanthan-based chlorhexidine gel (Chlosite®) subgingivally adjunctive to SRP.

Criteria for selection

Inclusion criteria were patients with:

- Moderate to severe periodontitis with clinical attachment loss of ≥3 mm.

(1999 International Workshop for a classification of Periodontal Diseases and Conditions),

- A minimum of three teeth with PPD ≥4 mm and that bled easily on initial visit in patients suffering from chronic periodontitis.
- Age group between 30 and 50 years,
- Systemically healthy,
- A minimum of 20 complements of teeth,
- Not allergic to CHX (group B),
- A GI score of 1.1 to 3.0

Exclusion criteria were patients with:

- A history of anti-inflammatory or antimicrobial therapy for the past three months,
- History of any systemic disease or conditions,
- Pregnant or lactating women,
- Chronic smokers,
- Aggressive periodontitis,
- History of periodontal treatment in the past six months.

Screening and clinical procedure

A case proforma consisting of patients' names, age, gender, dental history, and periodontal parameters, such as GI, PPD, CAL, was used to record the findings at baseline and after one month.

Acrylic stents with the cold cure acrylic material were prepared over the occlusal one-third on the dental stone cast models made by the upper and lower arches' alginate impression. The GI, PPD, and CAL were measured at baseline and after one month of the treatment [Figure 1].

Saliva samples were collected from group A and group B. Scaling was performed by using ultrasonic scalers (Woodpecker, China) to remove the supragingival plaque. Root planing was carried out in all sites having periodontal pockets by using Gracey curettes in both groups. A patch test was done in group B patients to rule out any allergic reactions to CHX. In group B patients, after SRP, xanthan-based chlorhexidine gel (Chlosite®) was placed subgingivally to the base of the pockets by using the blunt syringe provided along with the gel [Figure 2]. The patients were asked not to rinse their

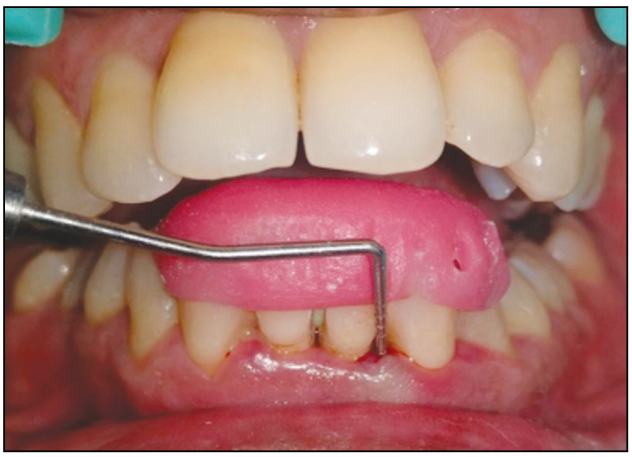

Figure 1: PPD measurement using Williams graduated periodontal probe

mouths for 30 min after the placement of Chlosite®. They were advised to report back immediately if they felt any discomfort after the subgingival placement of the medicament. Patients in both groups were instructed to refrain from the usage of any sort of chemical plaque control measures except for regular toothbrushing and rinsing. Oral hygiene instructions were given to all patients. The patients were recalled after one month for follow-up. All the parameters were rechecked, and the saliva samples were collected for reevaluation.

Method of collection of salivary samples

Whole saliva was collected by the unstimulated passive drool method. Participants were instructed not to eat, drink, and chew gum for at least 30 min before sampling. The sample collection was done between 9 am and 11 am. They were asked to rinse the mouth before the start of the saliva collection and were advised to tilt their head forward and drool down their saliva to the saliva collection aid.[13] The process was repeated as necessary until a sufficient quantity of samples was collected. The collected saliva samples were immediately sent to the Central Research Laboratory, where they were stored at −20°C. The samples were later on centrifuged at 3000 rpm for 20 min, and the supernatant saliva was collected to measure salivary IL-1β levels.

Assessment of salivary IL-1β

Diaclone human IL-1β ELISA KIT was used to estimate the level of salivary IL-1β. The salivary IL-1β kit is a competitive immunoassay that is specifically designed and validated for the quantitative measurement of salivary IL-1β.[14]

Statistical analysis

Descriptive statistics (mean and standard deviation) were calculated for continuous variables. The paired *t*-test was used to compare the mean values at baseline and after treatment within the groups. The unpaired *t*-test was used to calculate mean values between group A and group B; $P < 0.05$ was considered statistically significant. IBM SPSS (Version 22.0) software was used for statistical analysis.

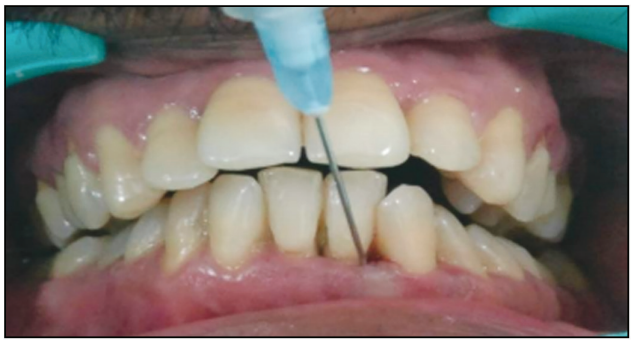

Figure 2: Placement of xanthan-based chlorhexidine gel

Results

In group A, the mean GI was 2.17 ± 0.48 at baseline compared with 1.24 ± 0.28 after treatment. The mean PPD was 4.82 ± 0.66 at baseline compared with 3.40 ± 0.66 one month after treatment. The mean CAL was 5.74 ± 0.77 at baseline compared with 4.91 ± 0.78 after treatment. All the periodontal parameters differed significantly with *P*-value <0.001 [Table 1].

In group B, the mean GI was 2.03 ± 0.46 at baseline compared with 1.00 ± 0.33 after treatment. The mean PPD was 5.06 ± 0.64 at baseline when compared with 3.07 ± 0.61 after treatment. The mean CAL was 6.18 ± 0.67 at baseline when compared with 4.86 ± 0.69 after treatment. All the periodontal parameters differed significantly with *P*-value <0.001 [Table 2].

In group A, the mean salivary IL-1β was 129.08 ± 45.25 at baseline when compared with 90.27 ± 32.43 after the treatment and it differed significantly ($P < 0.001$) [Table 3]. In group B, the mean salivary IL-1β was 131.74 ± 45.08 at baseline when compared with 84.21 ± 37.30 after the treatment and it differed significantly ($P < 0.001$) [Table 4].

The mean GI after treatment differed significantly between group A and group B ($P = 0.015$) when compared with baseline. The mean PPD and mean CAL after the treatment did not differ significantly ($P > 0.05$) between group A and group B when compared with baseline [Tables 5 and 6].

In group A, the mean salivary IL-1β was 90.27 ± 32.43 after the treatment, whereas in group B, it was 84.21 ± 37.30; however, it was not statistically significant ($P = 0.587$) [Tables 7 and 8].

Discussion

The present study results showed a statistically significant reduction in the mean GI, PPD, CAL, and salivary interleukin-1β values in both the groups from baseline to 30 days. There was a statistically significant reduction in GI in group B when compared with group A, after the treatment. Salivary IL-1β value in group B was slightly lower when compared with group A after the treatment, but it was not statistically significant.

In the present study, there was a significant reduction in the mean GI in both the groups after the treatment, when compared with the baseline values. This reduction in the GI might be due to the meticulous oral hygiene practice of the patient and the effects of extensive SRP. A similar result was reported by Stabholz *et al.*, Gupta *et al.*, and Verma *et al.* in their study.[15-17] Also, when the intergroup comparison was done, a statistically

Table 1: Comparison of GI, PPD, and CAL before and after treatment in group A

	N	Mean	Std. deviation	95% Confidence interval of the difference		*t*	*P*
				Lower	Upper		
GI before SRP	20	2.17	0.48	0.68	1.17	7.946	*<0.001
GI after SRP	20	1.24	0.28				
PPD before SRP (mm)	20	4.82	0.66	1.21	1.63	14.348	*<0.001
PPD after SRP (mm)	20	3.40	0.66				
CAL before SRP (mm)	20	5.74	0.77	0.73	0.93	17.541	*<0.001
CAL after SRP (mm)	20	4.91	0.78				

P value = probability value (<0.001); CAL = clinical attachment level; SRP = Scaling and Root Planing; N = sample size; PPD = probing pocket depth; Std. deviation = standard deviation

Table 2: Comparison of GI, PPD, and CAL before and after treatment in group B

	N	Mean	Std. deviation	95% Confidence interval of the difference		*t*	*P*
				Lower	Upper		
GI before SRP	20	2.03	0.46	0.87	1.19	13.364	<0.001*
GI after SRP	20	1.00	0.33				
PPD before SRP (mm)	20	5.06	0.64	1.83	2.16	25.447	<0.001*
PPD after SRP (mm)	20	3.07	0.61				
CAL before SRP (mm)	20	6.18	0.67	1.09	1.55	12.011	<0.001*
CAL after SRP (mm)	20	4.86	0.69				

P value = probability value (<0.001); CAL = clinical attachment level; SRP = Scaling and Root Planing; N = sample size; PPD = probing pocket depth; Std. deviation = standard deviation

*Statistically significant

Table 3: Comparison of salivary IL-1β (pg/mL) before and after treatment in group A

	N	Mean	Std. deviation	95% Confidence interval of the difference		*t*	*P*
				Lower	Upper		
Salivary IL-1β baseline	20	129.08	45.25	30.38	47.25	9.632	<0.001*
Salivary IL-1β after treatment	20	90.27	32.43				

P value = probability value (<0.001); *N* = sample size; IL-1β = interleukin-1β; Std. deviation = standard deviation; pg/mL = picograms per milliliter

*Statistically significant

Table 4: Comparison of salivary IL-1β (pg/mL) before and after treatment in group B

	N	Mean	Std. deviation	95% Confidence interval of the difference		*t*	*P*
				Lower	Upper		
Salivary IL-1β baseline	20	131.74	45.08	34.51	60.55	7.638	<0.001*
Salivary IL-1β after the treatment	20	84.21	37.30				

P value = probability value (<0.001); *N* = sample size; IL-1β: Interleukin-1β; Std. deviation = standard deviation; pg/mL = picograms per milliliter

*Statistically significant

significant reduction in the mean GI was found in group B than in group A. This statistical significance of GI in group B might be due to the antiplaque effects of CHX that might have leaked into the oral cavity from the treated subgingival sites. In their study, Soskolne *et al.*[18] also observed a significant decrease in GI score in SRP with CHX-treated sites when compared with the SRP sites alone. Similarly, in their study, He *et al.*[19] found a significant reduction of GI in the SRP combined with the CHX chip compared with the SRP alone.

The PPD measurement is an important diagnostic tool that is used to evaluate the periodontal status of an individual. The present study showed a statistically significant reduction in PPD from baseline to after the

Table 5: Comparison of GI, PPD, and CAL at baseline between group A and group B

Group		*N*	Mean	Std. Deviation	95% Confidence interval of the difference		*t*	*P*
					Lower	Upper		
GI Baseline	Group A	20	2.17	0.48	-0.16	0.44	.954	0.346
	Group B	20	2.03	0.46				
PPD (mm)	Group A	20	4.82	0.66	-0.66	0.17	-1.198	0.238
Baseline	Group B	20	5.06	0.64				
CAL (mm)	Group A	20	5.74	0.77	-0.90	0.02	-1.928	0.061
Baseline	Group B	20	6.18	0.67				

P value = probability value (<0.001); CAL = clinical attachment level; SRP = Scaling and Root Planing; N = sample size; PPD = probing pocket depth; Std. deviation = standard deviation

Table 6: Comparison of GI, PPD, and CAL after treatment between group A and group B

Group		*N*	Mean	Std. deviation	95% Confidence interval of the difference		*t*	*P*
					Lower	Upper		
GI after treatment	Group A	20	1.24	0.28	0.05	0.44	2.557	0.015*
	Group B	20	1.00	0.33				
PPD after treatment (mm)	Group A	20	3.40	0.66	-0.08	0.73	1.623	0.113
	Group B	20	3.07	0.61				
CAL after treatment (mm)	Group A	20	4.91	0.78	-0.42	0.52	.198	0.844
	Group B	20	4.86	0.69				

P value = probability value (<0.001); CAL = clinical attachment level; SRP = Scaling and Root Planing; N = sample size; PPD = probing pocket depth; Std. deviation = standard deviation

*Statistically significant

Table 7: Comparison of salivary IL-1β (pg/mL) at baseline between group A and group B

Group		N	Mean	Std. Deviation	95% Confidence Interval of the Difference		t	P
					Lower	Upper		
Salivary IL-1β baseline	Group A	20	129.08	45.25	-31.57	26.26	-.186	0.853
	Group B	20	131.74	45.08				

P value = probability value (<0.001); N = sample size; IL-1β = interleukin-1β; Std. deviation = standard deviation; pg/mL = picograms per milliliter

Table 8: Comparison of salivary IL-1β (pg/mL) after treatment between group A and group B

Group		*N*	Mean	Std. deviation	95% Confidence interval of the difference		*t*	*P*
					Lower	Upper		
Salivary IL-1β after treatment	Group A	20	90.27	32.43	-16.31	28.43	.548	0.587
	Group B	20	84.21	37.30				

P value = probability value (<0.001); N = sample size; IL-1β = interleukin-1β; Std. deviation = standard deviation; pg/mL = picograms per milliliter

treatment in both groups. This is in accordance with the study conducted by Rusu *et al.*[7] and Gupta *et al.*[16] When compared between group A and group B, PPD values showed no statistical significance. This finding was similar to the study conducted by Oosterwaal *et al.*,[20] which measured the effects of 2% CHX gel along with SRP and concluded that when compared with SRP alone the PPD values showed no significant difference when 2% CHX gel was used. Even though the study showed a statistically significant reduction in PPD from baseline to after treatment within the group, the intergroup comparison showed a nonsignificant result. The reason for this lack of significance might be due to the smaller sample size and shorter follow-up interval in this study, which might have yielded only a slightly higher reduction in PPD values in group B. The earlier results contradict the findings of a multicenter study by Paolantonio *et al.*[21] on xanthan-based chlorhexidine gel (Chlosite®), using a larger sample size, which reported a significant reduction in

PPD after using xanthan-based chlorhexidine along with SRP when compared with SRP alone. A weighted mean difference (WMD) of 0.56 mm in PPD reduction and 0.53 mm CAL gain was seen in a review on the use of xanthan-based chlorhexidine gel (Chlosite®) as an adjunctive agent for nonsurgical treatment of periodontitis.[22] A recent systematic review by Zhao *et al.* concluded that adjunctive placement of xanthan-based chlorhexidine gel (Chlosite®) at individual sites provided slight benefit in PPD reduction when compared with nonsurgical periodontal therapy (NSPT) alone.[23]

The CAL is considered the most reliable measurement in evaluating periodontitis. The CAL in both groups showed a statistically significant reduction from baseline to after treatment. A similar reduction in both the groups that were treated by SRP alone and SRP with the CHX chip was observed by Mızrak *et al.*[24] When CAL was compared between group A and group B, it showed no significant difference after the treatment from baseline. Similarly, Unsal *et al.*[25] found that, when compared with the periodontal sites treated with SRP alone, CAL gain was less in sites treated with SRP and 1% CHX sub-gingival gel administration.

Katrin *et al.* stated that saliva is an effective local source for examining cytokines; it influences periodontal health and has numerous benefits over the gingival crevicular fluid.[26] In the present study, the mean salivary IL-1β was higher at baseline compared with after treatment in both the groups and it reduced significantly. This result was similar to the study done by Konopka *et al.*[27] The mean salivary IL-1β after treatment in group B was slightly lesser than the values in group A, but it was not statistically significant. It could be inferred that a slight reduction in IL-1β level could be obtained by the use of xanthan-based chlorhexidine gel (Chlosite®) along with SRP when compared with SRP alone. IL-1β is considered a major proinflammatory cytokine that mainly targets the adaptive host immune response, stimulates bone resorption, and results in tooth loss.[28] A study that evaluated the inflammatory response to chlorhexidine remarked that locally applied antimicrobials can reduce interleukin responses and have a marked anti-inflammatory effect on periodontal disease activity.[29]

The smaller sample size and short duration of the study limit the generalizability of the study. The study would have yielded better significant results if conducted in a larger sample size with long-term follow-up periods. There were variable factors that would have impacted the results, such as the non-standardization of the PPD and age of the patients. The microbiological response of the subgingival flora should have been done simultaneously to validate the efficacy of Chlosite.

Conclusion

Within the limitations of the study, the clinical improvements showed that subgingival xanthan-based chlorhexidine gel (Chlosite®) is therapeutically effective when used as an adjunct to SRP. The observations were supported by the clinical parameters and the biochemical outcomes obtained after the treatment.

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Nil.

Conflicts of interest

There are no conflicts of interest.

Authors' contributions

All authors had contributed to study conception, design, data acquisition, analysis, and article writing. All authors have read and approved the article.

Ethical policy and institutional review board statement

The study was conducted on the patients reporting to the outpatient department of A.B. Shetty Institute of Dental Sciences, Nitte (Deemed to be University) hence ethical clearance was obtained from the institution ethical board.

Patient declaration of consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Data availability statement

Data will be available on request from authors.

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