Clinical and microbiological efficacy of 3% satranidazole gel as a local drug delivery system in the treatment of chronic periodontitis: A randomized, controlled clinical trial

N Priyanka, Nitish Kalra, Shahab Saquib[1], Nitin Kudyar[2], Nikhil Malgaonkar[3], Hunny Jain[4], A. R. Pradeep

Abstract

Aim: The present clinical trial was designed to investigate the effectiveness of subgingivally delivered satranidazole (SZ) gel as an adjunct to scaling and root planing (SRP) in the treatment of chronic periodontitis. **Materials and Methods:** Seventy subjects with probing depth (PD) ≥5 mm were selected. Thirty-five subjects each were randomly assigned to SRP + placebo (Group 1) and SRP + SZ (Group 2). The clinical outcomes evaluated were plaque index, gingival index, clinical attachment level (CAL), and PD at baseline; 1 month, 3 months, and 6 months interval. Furthermore, microbial analysis using polymerase chain reaction was done to estimate the number of sites harboring periodontopathogens. **Results:** Sixty four subjects were evaluated up to 6 months. At 6 months, the Group 2 resulted in greater mean reduction (4.10 mm) in PD as compared to Group 1 (1.49 mm), and also a greater mean CAL gain (4.20 mm) in Group 2 as compared to Group 1 (1.13 mm). These subjects also showed a significant reduction in the number of sites harboring periodontopathogens. **Conclusion:** The use of 3% SZ gel, when used as an adjunct to nonsurgical periodontal therapy in subjects with periodontitis, achieved better results than initial periodontal treatment alone.

Keywords: Chronic periodontitis, local drug delivery, satranidazole, scaling and root planing

Introduction

Chronic periodontitis (CP) is an inflammatory disease of the supporting tissues of the tooth caused by specific microorganisms in a susceptible host. Gram-negative anaerobic bacteria are most commonly associated with the initiation of periodontitis. The bacteria and their products evoke an immunoinflammatory reaction in the host tissue.[1]

Specific microorganisms or groups of species, including *Aggregatibacter actinomycetemcomitans*, *Porphyromonas gingivalis*, and *Tannerella forsythia* occur more frequently and/or in higher levels and proportions in periodontitis sites and subjects, whereas others such as members of the *Actinomyces* genus, are primarily associated with periodontal health.[2-4]

Previous studies[5-7] have reported that substantial improvements of periodontal condition measured by reduction in the probing depth (PD), and gains in the clinical attachment level (CAL) are a common outcome of scaling and root planing (SRP). However, traditional SRP may fail to eliminate the subgingival periodontopathogenic bacteria located in areas such as multi-rooted teeth, furcation sites, concavities, interproximal areas, and deep pockets inaccessible to periodontal instruments.[6,7] In addition, conventional SRP does not completely eliminate periodontal pathogens, as bacteria can persist in root cementum and dentinal tubules, or migrate from reservoirs within the mouth to periodontal areas.[8] Therefore for periodontal therapy, anti-infective agents such as topical antiseptics or local or systemic antibiotics may be used as adjunctive measures.[9]

The local delivery of an antibiotic offers the potential to achieve and maintain a therapeutic concentration at the site of infection; since the drug is applied directly to the site it delivers a significantly higher drug concentration than can be achieved with systemic dosages. Local drug delivery (LDD) can provide 100-fold higher therapeutic doses of the agent in subgingival areas than systemic therapy.[10] Several antimicrobial agents (e.g., tetracycline,[11] metronidazole (MTZ),[11] clarithromycin,[12] azithromycin[13]) have been tested for LDD use in periodontal therapy.[4]

Departments of Periodontics, Government Dental College and Research Institute, Bengaluru, and [1]Yogita Dental College and Hospital, Khed, Ratnagiri, Maharashtra, [2]Himachal Dental College, Sundernagar, Himachal Pradesh, India, [3]Department of Oral Pathology, Al-Farabi College of Dentistry and Nursing, Riyadh, Saudi Arabia, [4]Department of Oral Surgery, Yogita Dental College and Hospital, Khed, Ratnagiri, Maharashtra, India

Correspondence: Dr. N. Priyanka,
Department of Periodontics, Government Dental College and Research Institute, Bengaluru - 560 002, Karnataka, India.
E-mail: priyanka.n7@gmail.com

Access this article online	
Quick Response Code:	Website: www.contempclindent.org
	DOI: 10.4103/0976-237X.161891

MTZ[11] and related nitroimidazole derivatives including ornidazole[14] and tinidazole[15] have a spectrum of activity against strictly anaerobic microorganisms and have been used successfully in the treatment of periodontal diseases. Satranidazole (SZ) is another antibiotic that belongs to the 5-nitroimidazole group. SZ, (1-methylsulphonyl-3-[1-methyl-5-nitro-2-imidazolyl]-2-imidazolidinone) is a novel nitroimidazole which differs from other 5-nitroimidazoles such as MTZ, ornidazole, and tinidazole, in that the 2°C of the imidazole ring is connected through nitrogen to a substituted imidazolidinone moiety.[16] It possesses similar activity as MTZ against cecal amebiasis in the mouse model[17] and in the hamster model.[18] SZ has been shown to damage DNA as a consequence of the reduction of the nitro group.[19] Pharmacokinetic studies of SZ in humans have demonstrated a longer half-life (SZ 14 h; MTZ 8 h) and higher blood levels than MTZ. This necessitates lesser frequent dosing of SZ as compared to MTZ. These factors combined with its greater potency are believed to contribute to its therapeutic efficacy.[16]

A previous study[20] has concluded improved clinical outcomes with LDD of SZ in CP. We hypothesized similar benefits with LDD of SZ in the treatment of CP. To the best of our knowledge, there is no published literature on evaluation of the microbiological efficacy of *in situ* gel using SZ. Keeping the above facts in mind, the aim of this double blinded, placebo-controlled randomized clinical trial was to evaluate the clinical and microbiological efficacy of subgingivally delivered SZ in CP.

Materials and Methods

Source of data

The subjects for this study were selected from the outpatient section of the Department of Periodontics, Government Dental College and Research Institute, from October 2011 to April 2012. Seventy patients, aged 30–50 years (37 males and 33 females) and who were diagnosed with CP were enrolled in this study. It was made clear to the potential subjects that participation was voluntary. Written informed consent was obtained from subjects and ethical clearance for the study was received from the Institutional Ethical Committee and Review Board, Government Dental College and Research Institute.

Selection criteria

Systemically healthy subjects with PD ≥5 mm and/or CAL ≥4 mm and vertical bone loss ≥3 mm on intraoral periapical radiographs and no history of antibiotic or periodontal therapy in the preceding 6 months were included. Patients with known or suspected allergy to the SZ group, those on systemic antimicrobial therapy, patients with aggressive periodontitis, smokers, and alcoholics; patients with diabetes, immunocompromised patients, and pregnant or lactating females were excluded.

Seventy-eight subjects were initially analyzed for the study. Eight subjects were excluded because they did not meet the inclusion criteria. After subject selection (by ARP), 35 subjects were randomly (by computer generated system) assigned to each treatment group, and one site per subject was treated with SRP plus placebo gel (Group 1) or SRP plus SZ gel (3%/0.1 ml) *in situ* gel (Group 2). A full mouth SRP was performed at baseline until the root surface was considered smooth and cleans by the operator (PN). No antibiotics or antiplaque and anti-inflammatory agents were prescribed after treatment.

Clinical parameters including a gingival index (GI),[21] plaque index (PI),[22] PD, and CAL were recorded at baseline (before SRP) and at 3 and 6 months. A custom-made acrylic stent and a University of North Carolina no. 15 color-coded periodontal probe (UNC 15 Periodontal Probe, Hu-Friedy, IL, USA) were used to standardize the measurement of PD and CAL. CAL was calculated by measuring the distance from the stent (apical extent) to the base of the pocket minus the distance from the stent to the cementoenamel junction.

A single clinician (PN) provided treatment to both groups, and all pre- and post-treatment clinical parameters were recorded by another examiner (ARP) who was masked to the type of treatment received by the subjects.

Intra-examiner calibration

Intra-examiner calibration was achieved by examination of 20 patients twice, 24 h apart before beginning the study. Calibration was accepted if measurements at baseline and 24 h were similar to 1 mm at the 95% level.

Primary and secondary outcome measures

The primary outcome of the study was CAL. The secondary outcomes included PI, GI, PD, and reduction in the number of sites harboring periodontopathogens.

Formulation of 3% satranidazole *in situ* gel

After intensive *in vitro* investigations for optimization and stability at the collaborative center (Department of Pharmaceutics, Al–Ameen College of Pharmacy, Bengaluru, India), the following formulation was developed.

The SZ gel (3%) was prepared as described in a previous study. Twenty weighed carbopol 934P was dissolved in 50 ml of McIlvaine buffer pH 6.6. The SZ drug was also dissolved in about 25 ml of McIlvaine buffer pH 6.6. This solution of SZ was slowly added in the solution of CB 934P with stirring. Then, the gelling agent sodium carboxymethyl cellulose (SCMC) was added slowly under continuous magnetic stirring at 100 rpm. The volume was made up to 100 ml with McIlvaine buffer pH 6.6. The prepared gel was kept for 24 h at room temperature for complete polymer dissolution. Thus, the SZ *in situ* gel was prepared with a concentration of 3%.

Local drug delivery

For standardization, 0.1 ml prepared SZ gel (3%/0.1 ml) was injected into the periodontal pockets using a syringe with a blunt cannula. No periodontal dressing was applied after delivery of the drug because the prepared formulation decreases in viscosity, which causes swelling and occlusion of the periodontal pocket.

After placement of the *in situ* gel, subjects were instructed to refrain from chewing hard or sticky foods, brushing near the treated areas, or using any interdental aids for 1 week. Adverse effects were noted at recall visits, and any supragingival deposits were removed.

Microbiological analysis

Sample collection

After the removal of supragingival plaque, teeth were isolated using cotton rolls. The subgingival plaque samples were obtained using sterile paper points inserted into an assigned periodontal site in each subject. Samples were collected from the same sites at baseline and at 3 and 6 months. The paper point was allowed to remain in position for 30 s and was transferred to an Eppendorf tube. The samples were stored at −200°C until analyzed by polymerase chain reaction (PCR).

Primers

Species-specific PCRs were performed to detect *T. forsythia*, *P. gingivalis*, and *A. actinomycetemcomitans*. Primers used for *T. forsythia*: 23 5'GCG TAT GTA ACC TGC CCG CA 3'5'TGC TTC AGT GTC AGT TAT ACC T 3'; *P. gingivalis*: 24 5'AAT CGT AAC GGG CGA CAC AC 3'5'GGG TTG CTC CTT CAT CAC AC 3'; and *A. actinomycetemcomitans*: 25 5'AAA CCC ATCTCT GAG TTC TTC TTC 3'5'ATG CCA ACT TGA CGT TAA AT 3.'

Polymerase chain reaction detection

Samples collected at baseline, 3 and 6 months were analyzed by PCR. Species-specific PCRs were performed to detect *T. forsythia*, *P. gingivalis*, and *A. actinomycetemcomitans*.

For *T. forsythia*:[23] A denaturation step at 950°C for 2 min followed by 36 cycles of denaturation at 950°C for 30 s, annealing at 600°C for 1 min, an extension at 720°C for 1 min, and a final elongation step at 720°C for 2 min.

For *P. gingivalis*:[24] A denaturation step at 940°C for 5 min followed by 30 cycles of denaturation at 940°C for 1 min, annealing at 700°C for 1 min, an extension at 720°C for 1 min, and a final elongation step at 720°C for 2 min.

For *A. actinomycetemcomitans*:[25] A denaturation step at 950°C for 2 min followed by 36 cycles of denaturation at 940°C for 30 s, annealing at 550°C for 1 min, an extension at 720°C for 2 min, and a final elongation step at 720°C for 10 min.

Collection of gingival crevicular fluid samples

Gingival crevicular fluid (GCF) was collected from drug-delivery sites in six randomly selected patients from Group 2 (SRP + SZ) using 1–5 µl calibrated volumetric microcapillary pipettes (Sigma-Aldrich, St. Louis, MO, USA) at baseline; at 2, 4, 6, 24, and 48 h; and weeks 1, 2, 3, and 4. Collected samples were stored at 40–80°C until the estimation was done.

Estimation of quantity of satranidazole

The drug estimation was done using gradient reverse phase high-performance liquid ([HPLC], [1200 Series, Agilent Technologies, Palo Alto, CA, USA]) with pumps, a variable wavelength programmable ultraviolet/visible spectroscopy detector, and a system controller; an operating software data station (Agilent Dissolution Testing UV-visible ChemStation software [G1118AA], Agilent Technologies) were used.

Chromatographic conditions

A column (Agilent HPLC columns-Zorbax Column Compartment SL Support, Agilent Technologies) 150 mm (length), 4.6 mm (internal diameter), and particle size of 5 mm was used as the stationary phase. The mobile phase consisted of 35% volume of buffer (0.1% phosphoric acid) and 65% volume of acetonitrile (volume/volume). The mobile phase was filtered through a 0.45 mm membrane filter (Sartorius, Goettingen, Germany) and sonicated to remove air bubbles. The flow rate was 1.0 ml/min, and the column effluent was monitored at 238 nm.

Calibration curve in gingival crevicular fluid

A standard stock solution of SZ (1 mg/ml) was prepared in acetonitrile in a 100 ml volumetric flask, adding 30–40 ml diluent prepared by mixing 40% volume of 1.4 g/l solution of dihydrogen phosphate, pH 4 with phosphoric acid, and 60% volume of acetonitrile. The flask was sonicated to dissolve the solvents. The standard stock solutions were diluted 100 times to get a concentration of 10.4 mg/ml by using the GCF stock solution. GCF stock solution was prepared by spiking the GCF samples from 10 capillary tubes obtained at baseline from patients in Groups 1 and 2 for standardization, to the 1 ml solution that contained acetonitrile. An aliquot of 80 ml working stock solution (10.4 mg/ml) was added to 20 ml 1% phosphoric acid buffer (in the pH range of 4) in microcentrifuge tubes and vortexed for 1 min. Acetonitrile was used as an extracting solvent, and 1 ml was taken for the extraction of SZ. The microcentrifuge tubes were vortexed for 2 min and then centrifuged at 10,000 rpm in a cold centrifuge for 10 min. After centrifugation, an aliquot of 20 µl supernatant solution was injected via HPLC. The amount of SZ present in a capillary tube was determined by comparing the peak responses of the standard and the sample of SZ solution.

Sample preparation

GCF was transferred to a 1–5 µl centrifuge tube containing 80 µl acetonitrile. Eighty microliters of GCF (after transfer) and 20 µl buffer (1% phosphoric acid) were combined in a

microcentrifuge tube and vortexed for 1 min. One milliliter of acetonitrile was added to the above mixture, and it was vortexed for 1 min. Then the solution was centrifuged at 10,000 rpm in a cold centrifuge for 10 min. After centrifugation, an aliquot of 20 μl supernatant solutions was injected via HPLC, and the chromatogram was recorded. The amount of SZ present in the GCF was determined by comparing the peak responses of the standard and the sample of SZ solution.

Statistical analysis

Power analysis calculations were performed before the study was initiated. To achieve 90% power and detect mean differences of the clinical parameters between groups, 30 sites in each group were required. Continuous variables (PI, GI, PD, CAL) were expressed as the mean ± standard deviation (SD). The normality assumption was tested using Shapiro–Wilk's W-test. Between the treatment groups, the comparison was carried out using Mann–Whitney test. Wilcoxon signed ranks test was used for comparison within SZ and control group, respectively. Statistical significance was defined as $P < 0.05$. Statistical analysis was performed with statistical software (SPSS version 10.5, SPSS, Chicago, IL, USA).

Results

Consort flowchart exhibiting the number of subjects finally analyzed and those dropping out has been described [Figure 1]. Sixty-four of 70 subjects completed the study. Four subjects did not follow-up after the baseline examination, and two subjects refused to participate because of reasons unrelated to the study. Sixty-four treatment sites (one site/subject) were evaluated for clinical parameters at baseline, 3 and 6 months. SZ concentrations (mean ± SD) in GCF by HPLC are tabulated in Table 1.

Clinical evaluation

No adverse reaction was observed in any subject from the test group, and no patient reported any discomfort. Healing was uneventful. All subjects tolerated the drug, without any postapplication complications.

Plaque index and gingival index

There was a reduction, but no significant difference was found between the two groups in PI and GI at any point [Table 2].

PD

The decrease in PD was statistically significant within both groups compared to baseline at all time intervals [Tables 3 and 4]. At the end of 6 months mean PD for the SZ group was 3.11 ± 1.37 as against 5.92 ± 1.08 for the placebo group. When the groups were compared to each other, the decrease in PD at each time period was statistically significant.

Clinical attachment level

At the end of 6 months mean PD for the SZ group was 3.72 ± 1.26 as against 6.99 ± 1.22 for the placebo group. The difference from baseline was statistically significant in both groups, CAL gain was greater in Group 2 compared to Group 1 at all periods, and the difference reached the level of significance [Tables 3 and 4].

Microbial analysis

The PCR analysis showed a significant difference in the number of sites harboring *P. gingivalis*, *T. forsythia* and *A. actinomycetemcomitans* at 3 and 6 months ($P < 0.05$). At baseline, the intergroup difference was not significant ($P > 0.05$). At 6 months, there was a slight increase in the number of sites harboring these organisms in Group 1. A significant reduction ($P < 0.05$) in the number of sites harboring *P. gingivalis*, *T. forsythia*, *A. actinomycetemcomitans* was greater in Group 2 compared to Group 1 at all periods except baseline [Table 5].

Analysis of statins like simvastatin concentration in gingival crevicular fluid

SZ in GCF peaked at 2 h after application (14.67 ± 0.03 μg/ml; Table 1). The mean concentrations on weeks 1, 2, 3, and 4 indicate that SZ was retained in this target compartment for a long period suggesting a controlled release of the drug until the 4th week.

Discussion

This study was designed with the aim of assessing the efficacy of LDD of 3% SZ gel as an adjunct to nonsurgical periodontal therapy in the treatment of CP subjects as compared to a placebo group. The results of this study indicate that Group 2 (SRP + LDD of 3% SZ) resulted in significant improvements. Using a subject based analysis, patients in Group 2 showed enhanced clinical outcome ($P < 0.05$) over a period of 6 months as compared to Group 1. The number of sites harboring *T. forsythia*, *P. gingivalis*, and *A. actinomycetemcomitans* were significantly reduced in Group 2 compared to Group 1. Furthermore, SZ was detected in GCF till the period of 7 weeks after the LDD, thus satisfying the criteria for controlled drug release for this formulation.

The repeated, long-term use of systemic antibiotics is fraught with potential dangers including resistant strains and superimposed infections[26] and problems like lack of patient compliance. Therefore, the local administration of antimicrobials provides a useful solution to these complications. It offers the advantages of high concentrations at the target site with reduced dosage, fewer applications, and high patient acceptability.[27] In a previous study, 20 LDD of SZ resulted in a reduction of GI, PD, and gain in CAL in the treatment of CP. Hence, this study aimed to evaluate whether the use of adjunctive local antimicrobial therapy would better reduce the number of sites harboring specific subgingival periodontopathogens in the treatment of CP.

SZ is a 5-nitroimidazole substituted at the 2-position and has been found to be more active against aerobic,

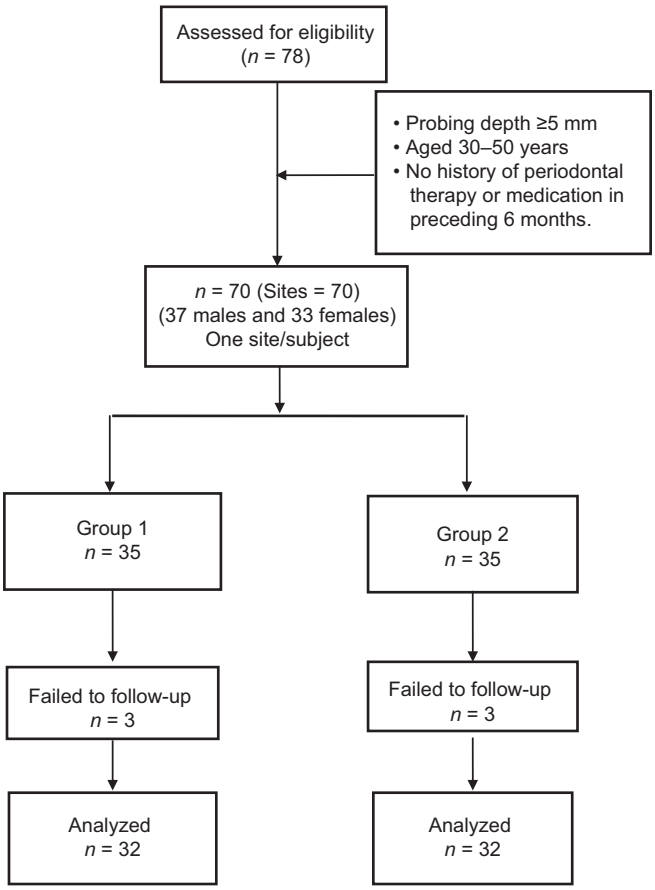

Figure 1: Study flow chart

Table 1: SZ concentration (mean±SD) in GCF after treatment

Time	Concentration of SZ (μg/mL)
Baseline	0.00±0.00
2 h	14.67±0.03
4 h	13.21±0.41
6 h	12.45±0.11
24 h	11.62±0.25
48 h	11.01±0.19
1-week	07.75±0.14
2 weeks	03.13±0.22
3 weeks	01.44±0.19
4 weeks	0.81±0.14

SD: Standard deviation; SZ: Satranidazole; GCF: Gingival crevicular fluid

microaerophilic, and anaerobic bacteria. The MIC90 of SZ was found to be 4-fold lower than MTZ against 50 clinical isolates of anaerobes.[28] The finding that SRP combined with administration of SZ gel was more effective than mechanical therapy alone in terms of eliminating deep pockets and promoting CAL gain at such sites is in agreement with results reported in the previous study.[20] The effect of SRP combined with SZ also led to a significant reduction in the number of sites harboring subgingival periodontopathogens: *P. gingivalis*, *T. forsythia*, *A. actinomycetemcomitans*, at all time periods compared to baseline. Hence, SZ was found to be highly effective against the tested anaerobes.

The present study showed a greater reduction in the frequency of *P. gingivalis* at 3 months following initial and supportive therapy in CP subjects when locally delivered SZ was associated with SRP. *P. gingivalis* is one of the pathogens belonging to the red complex defined by Socransky *et al*.;[29] it is associated with periodontal disease progression, and its reduction is associated with periodontal health.[30,31] Therefore, the reduction in sites harboring this species could be important for the reestablishment of periodontal health.

Bacteria are difficult to eliminate in deep pockets following SRP;[30] thus, the adjunctive use of SZ in deep pockets might have inhibited the recolonization of bacteria in these sites. It could be suggested that the use of the local antimicrobial SZ, in deep sites, could have provided the additional benefits to clinical parameter improvements by the reduction of important subgingival microorganisms. This is in agreement with Haffajee *et al*.,[30] who reported that sites presenting gains of ≥2 mm following SRP showed a significant reduction of certain periodontopathogens: *P. gingivalis*, *T. forsythia*, *A. actinomycetemcomitans*.

The reevaluation period of subgingival bacteria in the present study was 3 months, which is longer than the expected period of 42 days for recolonization.[32] Therefore, the use of the locally delivered SZ could maintain significantly low levels of *P. gingivalis*, *T. forsythia*, and *A. actinomycetemcomitans* subgingivally even after this period while the control group could not.

Few randomized controlled clinical trials have reported success with the use of local delivery of antimicrobials as an adjunct to SRP in the treatment of CP patients.[13,33] Our previous study has concluded significant improved clinical and microbiological outcomes with systemic use of SZ in CP patients as an adjunct to mechanical periodontal therapy.[34] Similar to findings in these studies, the results of this study indicate that both therapies (SRP + LDD of placebo in Group 1 and SRP + LDD of 3% SZ in Group 2) resulted in improvement but patients in Group 2 showed enhanced clinical and microbiological outcome ($P < 0.05$) over a period of 6 months as compared to Group 1.

The mean concentration of SZ at all observed periods (from baseline to 8 weeks), as estimated by reverse-phase HPLC provided sufficient anti-inflammatory activity and fulfilled the conditions for a controlled-release device. A decrease in PD and gain in CAL are the major clinical outcomes measured to determine the success of any periodontal treatment. A significant decrease in PD and gain in CAL were found within both groups compared to baseline at all time intervals. When

Table 2: Mean±SD and *P* values of PI and GI of the two groups at various intervals

Parameter	Visits	Group 1	Group 2	*P*
PI	Baseline	2.81±0.19	2.80±0.18	NS
	1-month	2.55±0.18	2.51±0.13	NS
	3 months	2.63±0.18	2.62±0.17	NS
	6 months	2.76±0.21	2.72±0.18	NS
GI	Baseline	2.59±0.20	2.61±0.25	NS
	1-month	2.30±0.29	2.21±0.26	NS
	3 months	1.89±0.38	1.72±0.36	NS
	6 months	1.73±0.37	1.22±0.28	NS

NS: Not significant; PI: Plaque index; GI: Gingival index; SD: Standard deviation

Table 3: PD, CAL for Groups 1 and 2 (mean±SD) at different time intervals

Parameter	Visits	Group 1	Group 2
PD	Baseline	7.41±1.27	7.21±1.49
	1-month	6.85±1.15	5.92±1.29
	3 months	6.23±1.12	5.11±1.34
	6 months	5.92±1.08	3.11±1.37
CAL	Baseline	8.12±1.02	7.92±1.24
	1-month	7.72±1.23	6.21±1.15
	3 months	7.55±1.30	5.77±1.51
	6 months	6.99±1.12	3.72±1.26

SD: Standard deviation; CAL: Clinical attachment level

Table 4: Decrease in PD and CAL gain from baseline (mean±SD) at different time intervals for Groups 1 and 2

Parameter	Visits	Group 1	Group 2	*P*
PD	1-month	0.61±1.11	1.31±1.01	0.001*
	3 months	1.23±0.53	2.15±1.24	0.001*
	6 months	1.49±1.01	4.10±1.11	0.001*
CAL	1-month	0.41±1.22	1.74±1.41	0.001*
	3 months	0.63±1.15	2.27±1.62	0.001*
	6 months	1.13±0.49	4.20±1.12	0.001*

*Statistically significant at 5% level of significance ($P<0.05$). SD: Standard deviation; CAL: Clinical attachment level

Table 5: Number of sites positive by PCR for each species

	Time interval	Group 1	Group 2	*P*
Porphyromonas gingivalis	Baseline	30	31	NS
	3 months	22	13	0.001*
	6 months	28	06	0.001*
Tannerella forsythia	Baseline	29	27	NS
	3 months	23	17	0.001*
	6 months	26	14	0.001*
Aggregatibacter actinomycetemcomitans	Baseline	26	26	NS
	3 months	22	18	0.001*
	6 months	25	12	0.001*

*Statistically significant at 5% level of significance ($P<0.05$).
NS: Not significant; PCR: Polymerase chain reaction

the two groups were compared, the decrease in PD and CAL gain were statistically significant at each period, even after 6 months ($P < 0.05$).

With regard to the dose of SZ used, 3%/0.1 ml per site was injected in the present study. In a study[20] various gelling agents have been used for LDD of SZ in patients with periodontitis. Among them, SCMC gelling agent in a concentration of 3% w/v has been reported to show the desired balance of mechanical properties (mucoadhesiveness, hardness, adhesiveness, compressibility, and cohesiveness). Furthermore, the *in vitro* release of SZ gel containing SCMC gelling agent showed long-term controlled release. Hence, in the present study of 3% SZ gel with SCMC as a gelling agent appeared to be more suitable for obtaining a long-term release of the drug, assuring a constant and prolonged concentration at the application site.

Conclusion

This study has shown that the use of SZ gel, when used in conjunction with an initial periodontal treatment consisting of SRP in adult subjects with periodontitis, achieves significantly better clinical and microbiological results than initial periodontal treatment alone. Further long-term, multicenter longitudinal trials may are required to assess and establish the efficacy of SZ gel in the management of CP to affirm the observations of our study, and also to compare this treatment protocol with other established drugs of this group.

Acknowledgments

The authors express their gratitude to Alkem Laboratories Ltd., Mumbai, India for providing gift sample of SZ. The authors also express their thanks to Mr. Manjunath Sharma, Bangalore for carrying out the required statistics. The authors also express their gratitude to Dr. B. G. Shivananda (Principal) and Mr. M. Nagraju Patro (Ph.D student), Department of Pharmaceutics, Al-Ameen College of Pharmacy, Bengaluru, India, for helping us in preparation of SZ and placebo gel.

References

1. Gokhale SR, Sumanth S, Padhye AM. Evaluation of blood parameters in patients with chronic periodontitis for signs of anemia. J Periodontol 2010;81:1202-6.
2. Haffajee AD, Cugini MA, Tanner A, Pollack RP, Smith C, Kent RL Jr, *et al.* Subgingival microbiota in healthy, well-maintained elder and periodontitis subjects. J Clin Periodontol 1998;25:346-53.

3. Haffajee AD, Socransky SS. Microbial etiological agents of destructive periodontal diseases. Periodontol 2000 1994;5:78-111.
4. Ximénez-Fyvie LA, Haffajee AD, Socransky SS. Comparison of the microbiota of supra- and subgingival plaque in health and periodontitis. J Clin Periodontol 2000;27:648-57.
5. Walmsley AD, Lea SC, Landini G, Moses AJ. Advances in power driven pocket/root instrumentation. J Clin Periodontol 2008;35:22-8.
6. Oda S, Nitta H, Setoguchi T, Izumi Y, Ishikawa I. Current concepts and advances in manual and power-driven instrumentation. Periodontol 2000 2004;36:45-58.
7. Obeid PR, D'Hoore W, Bercy P. Comparative clinical responses related to the use of various periodontal instrumentation. J Clin Periodontol 2004;31:193-9.
8. Umeda M, Takeuchi Y, Noguchi K, Huang Y, Koshy G, Ishikawa I. Effects of nonsurgical periodontal therapy on the microbiota. Periodontol 2000 2004;36:98-120.
9. Drisko CH. Non-surgical pocket therapy: Pharmacotherapeutics. Ann Periodontol 1996;1:491-566.
10. Jorgensen MG, Slots J. Responsible use of antimicrobials in periodontics. J Calif Dent Assoc 2000;28:185-93.
11. Kinane DF, Radvar M. A six-month comparison of three periodontal local antimicrobial therapies in persistent periodontal pockets. J Periodontol 1999;70:1-7.
12. Agarwal E, Pradeep AR, Bajaj P, Naik SB. Efficacy of local drug delivery of 0.5% clarithromycin gel as an adjunct to non-surgical periodontal therapy in the treatment of current smokers with chronic periodontitis: A randomized controlled clinical trial. J Periodontol 2012;83:1155-63.
13. Pradeep AR, Sagar SV, Daisy H. Clinical and microbiologic effects of subgingivally delivered 0.5% azithromycin in the treatment of chronic periodontitis. J Periodontol 2008;79:2125-35.
14. Pradeep AR, Kalra N, Priyanka N, Khaneja E, Naik SB, Singh SP. Systemic ornidazole as an adjunct to non-surgical periodontal therapy in the treatment of chronic periodontitis: A randomized, double-masked, placebo-controlled clinical trial. J Periodontol 2012;83:1149-54.
15. Pritchard JR, Higgins TJ. Tinidazole in clinical periodontics. The effects upon the subgingival microflora. J Dent Res 1987;66:821.
16. Nair MD, Nagarajan K. Nitroimidazoles as chemotherapeutic agents. Prog Drug Res 1983;27:163-252.
17. Ray DK, Tendulkar JS, Shrivastava VB, Nagarajan K. Comparative efficacy of metronidazole and another 5-nitroimidazole, CG-10213-Go, in caecal amoebiasis in albino mice (Mus musculus). J Antimicrob Chemother 1982;10:355-7.
18. Ray DK, Shrivastava VB, Tendulkar JS, Dutta AK, Bhopale KK, Chatterjee DK, *et al*. Comparative studies on the amebicidal activity of known 5-nitroimidazole derivatives and CG-10213-go in golden hamsters, *Mesocricetus auratus*, infected in the liver or caecum or both with trophozoites of *Entamoeba histolytica*. Ann Trop Med Parasitol 1983;77:287-91.
19. Zahoor A, Knight RC, Whitty P, Edwards DI. Satranidazole: Mechanism of action on DNA and structure-activity correlations. J Antimicrob Chemother 1986;18:17-25.
20. Bansal K, Rawat MK, Jain A, Rajput A, Chaturvedi TP, Singh S. Development of satranidazole mucoadhesive gel for the treatment of periodontitis. AAPS PharmSciTech 2009;10:716-23.
21. Glavind L, Löe H. Errors in the clinical assessment of periodontal destruction. J Periodontal Res 1967;2:180-4.
22. Löe H. The gingival index, the plaque index and the retention index systems. J Periodontol. 1967;38 Suppl: 610-6.
23. Slots J, Ashimoto A, Flynn MJ, Li G, Chen C. Detection of putative periodontal pathogens in subgingival specimens by 16S ribosomal DNA amplification with the polymerase chain reaction. Clin Infect Dis 1995;20 Suppl 2:S304-7.
24. Benkirane RM, Guillot E, Mouton C. Immunomagnetic PCR and DNA probe for detection and identification of *Porphyromonas gingivalis*. J Clin Microbiol 1995;33:2908-12.
25. Ashimoto A, Chen C, Bakker I, Slots J. Polymerase chain reaction detection of 8 putative periodontal pathogens in subgingival plaque of gingivitis and advanced periodontitis lesions. Oral Microbiol Immunol 1996;11:266-73.
26. Steinberg D, Friedman M, Soskolne A, Sela MN. A new degradable controlled release device for treatment of periodontal disease: *In vitro* release study. J Periodontol 1990;61:393-8.
27. Slots J, Research, Science and Therapy Committee. Systemic antibiotics in periodontics. J Periodontol 2004;75:1553-65.
28. Gowrishankar R, Phadke RP, Oza SD, Talwalker S. Satranidazole: Experimental evaluation of activity against anaerobic bacteria *in vitro* and in animal models of anaerobic infection. J Antimicrob Chemother 1985;15:463-70.
29. Socransky SS, Haffajee AD, Cugini MA, Smith C, Kent RL Jr. Microbial complexes in subgingival plaque. J Clin Periodontol 1998;25:134-44.
30. Haffajee AD, Cugini MA, Dibart S, Smith C, Kent RL Jr, Socransky SS. The effect of SRP on the clinical and microbiological parameters of periodontal diseases. J Clin Periodontol 1997;24:324-34.
31. Socransky SS, Haffajee AD. The bacterial etiology of destructive periodontal disease: Current concepts. J Periodontol 1992;63:322-31.
32. Magnusson I, Lindhe J, Yoneyama T, Liljenberg B. Recolonization of a subgingival microbiota following scaling in deep pockets. J Clin Periodontol 1984;11:193-207.
33. Pradeep AR, Kalra N, Priyanka N, Khaneja E, Naik SB, Singh SP. Systemic ornidazole as an adjunct to non-surgical periodontal therapy in the treatment of chronic periodontitis: A randomized, double-masked, placebo-controlled clinical trial. J Periodontol 2012;83:1149-54.
34. Pradeep AR, Priyanka N, Kalra N, Naik SB. A randomized controlled clinical trial on the clinical and microbiological efficacy of systemic satranidazole in the treatment of chronic periodontitis. J Int Acad Periodontol 2013;15:43-50.

How to cite this article: Priyanka N, Kalra N, Saquib S, Kudyar N, Malgaonkar N, Jain H, *et al*. Clinical and microbiological efficacy of 3% satranidazole gel as a local drug delivery system in the treatment of chronic periodontitis: A randomized, controlled clinical trial. Contemp Clin Dent 2015;6:364-70.

Source of Support: Nil. **Conflict of Interest:** None declared.