Clinical Evaluation of Local Drug Delivery of Chlorhexidine and Ornidazole in the Treatment of Gingivitis as an Adjunct to Scaling and Root Planing

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Abstract

Background: Local drug delivery to gingival sulcus avoids adverse effects seen with systemic therapy and there is very little information to substantiate the additive effect of the drugs, the current study makes an attempt in same regard.

Aim: The objective of this study was to compare the local application of ornidazole and chlorhexidine gel (Clorni^{TM} gel) as an adjunct to scaling and polishing, with scaling and polishing alone.

Materials and methods: 33 patients meeting inclusion criteria were randomly allocated to treatment groups by computerized randomly selection method. Indices were recorded at baseline at their first visit. Supragingival and subgingival scaling and polishing was performed using hand and ultrasonic instruments. The patients were evaluated clinically by using the gingival index, plaque index and modified sulcus bleeding index. On test side, Clorni^{TM} gel was applied subgingivally after nonsurgical periodontal therapy. On the control side, no intervention was done following subgingival scaling and polishing. Patients were recalled at 7th day for subsequent administration of gel on the same site and followed up at 21st day and 3 months to compare the gingival condition by using the indices.

Results: All subjects showed significant improvement over 3 months recall period, irrespective of test or controls. Statistical significance ($p< 0.05$) was observed at 7 days and 21 days for test group for the gingival index and at 21 days for the plaque index and modified sulcus bleeding index.

Conclusion: The topical gel when used as an adjunct to scaling and polishing had significant results.

Keywords: *inflammation, gingivitis, chlorhexidine, ornidazole*

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Introduction

Gingivitis has a widespread prevalence, and is seen more in the younger and older age groups and lesser in the middle age groups; with an average of 50-100% in dentate individuals.[1]

As shown by Carranza et al, it is characterized by color change, edema, bleeding and in severe cases, if left unchecked, may lead to progression to periodontal involvement. As a result of this inflammation, the microorganisms that enter the sulcus release their destructive enzymes and cause the dissolution of the cellular and intercellular elements. This leads to widening of intercellular spaces of the junctional epithelium and as consequently allows the endotoxins to penetrate deeper, leading to further destruction if left untreated.[2]

Local drug delivery is the local application of the drug to gingival sulcus, avoiding adverse effects with systemic therapy and achieving a much higher concentration locally.[3] Many drugs have been tried for the application at the site of inflammation in order to alleviate the signs and symptoms of gingivitis. Use of metronidazole,[4,] minocycline,[5] tetracycline,[6] chlorhexidine,[7] doxycycline[8] are some of the examples of local drug delivery. Studies have shown that, tetracycline, minocycline, chlorhexidineand metronidazole when used as a monotherapy[9-11] have shown clinically significant results as an adjunct to scaling and root planing (SRP). However, there are lack of sufficient clinical trials to substantiate the additive effect of the drugs.

Metronidazole, an antimicrobial agent belonging to the 5-nitroimidazole group, has been used successfully in treating chronic periodontitis, alone or in combination with amoxicillin. Ornidazole is another antibiotic that belongs to the 5-nitroimidazole group with comparable or better antibacterial properties.[4] Better efficacy and antibacterial properties in comparison with metronidazole have been reported in literature.[12] Similar results were demonstrated while comparing ornidazole to metronidazole.[13] Ornidazole has a lower minimum inhibitory concentration compared to metronidazole and hence, safer for the patient in terms of the development of resistance to the drug. Ornidazole is shown to have higher water solubility and inturn, the mean half-life of elimination from human plasma is almost double than that of metronidazole.[14] This gives ornidazole an edge over metronidazole, in that, the dosage can be reduced with less frequent administration.[15] Ornidazole has previously been used systemically, as an adjunct to non-surgical periodontal therapy.[4] However, it may induce unnecessary side effects or systemic actions which are not desired.

A new commercially available gel (Clorni^{TM} gel, Group Pharmaceuticals, Ltd, Mumbai, India) containing a combination of ornidazole (1% w/w) and chlorhexidine (0.25% w/w) was used in this study. Since both the drugs have their individual advantages, so may be when used in combination may exhibit additive/synergistic effect for the treatment of gingival disease. The gel contains Pluronic F127 poloxmer as the base, which serves as a potent vehicle for the drugs and allows a controlled release of the drug at the site of application.[16]

To the best of author's knowledge, there is no such study comparing the local application of ornidazole in the treatment of gingivitis. Hence, the aim of the present study is to compare the local application of ornidazole and chlorhexidine gel (Clorni^{TM} gel) as an adjunct to scaling and polishing, with scaling and polishing alone as control.

Methods

The present study was designed as a randomized, double-blind, controlled, split-mouth and parallel arm trial. The study was conducted in the Department of Periodontology, Krishnadevaraya College of Dental Sciences, Bangalore and the study protocol was presented to institutional ethical review committee before obtaining the ethical approval to conduct the study. 42 systemically healthy patients (18 males, 12 females), with a chief complaint of bleeding, swollen and/or red gums, were recruited from the pool of the patients referred to the out-patient department of Periodontology.

After obtaining a detailed medical, dental, periodontal and personal history, the suitable patients fulfilling the inclusion criteria were included in the study. The decided inclusion criteria were; 1) Age between 20-40 years, 2) Bilaterally involved teeth, with moderate to severe gingivitis, 3) No previous history of periodontal treatment. The patients were excluded from the study if; 1) Pregnant or lactating 2) Smokers, 3) Patients with systemic diseases, 4) Patients taking systemic antibiotics over the last 2 months, 5) Use of non-steroidal anti-inflammatory drugs, 6) Any reported or suspected drug allergies, 7) subgingival scaling or surgical periodontal therapy in the previous year.

Finally, 33 patients meeting the inclusion criteria were included in the study. All patients were informed about the study protocol, advantages and possible adverse effects of the drug to be administered, and a written informed consent was obtained from all the patients. The participants were randomly allocated to one of the two treatment groups by computerized randomly selection method. To avoid inter-examiner variation; a single examiner scored all the parameters. The patients were evaluated clinically by using the gingival index,[17] plaque index[17] and modified sulcus bleeding index. [18] The examiner was calibrated on 5 patients prior to the scoring of the patients in the study, and the intra-examiner agreement was 95%.

All the indices were recorded at baseline at the first visit of the study subjects. Following this, a thorough full mouth supragingival and subgingival scaling and polishing was performed using hand and ultrasonic instruments. Test and control side were selected by computerized random selection method. On the test side, the ornidazole-chlorhexidine gel was applied subgingivally after nonsurgical periodontal therapy, until it completely filled the sulcus, using a 23 gauge needle (Figure 1). Patients were asked to remain on the dental chair for 10 minutes without moth rinsing to avoid flushing of the applied gel. On the control side, no intervention was done following subgingival scaling and polishing. Finally, patients were advised with uniform oral hygiene instructions for plaque control before leaving the clinics.

All patients were recalled at 7th day for subsequent administration of gel on the same site. The gingival index, plaque index, and modified sulcus bleeding index were used to evaluate and compare the change in the gingival condition on both test and control sides. The patients were then recalled after 21st day and 3 months, to evaluate and compare the gingival condition by using above indices. Three patients were excluded from the study, because they failed to show up at follow-up visits. Finally, data from 30 patients were analyzed to formulate the results.

Results

All the patients were evaluated at baseline, 7 days, 21 days and 3 months. Gingival index, Plaque index and modified sulcus bleeding index were used to assess the healing in the gingival tissues in both the test and control sites.

The number of tests and controls selected were similar, showing that the split mouth cases showed similar severity in all the cases selected. As shown in Figures 2,3 and 4, all the subjects showed significant improvement over the 3 months recall period, irrespective of test or controls. The number of healthy sites increased over the 3rd month recall visit when compared to the baseline in both the test and control sites, with better results in the test group.

Statistical analysis was done using Student's t-test for intergroup comparison. Statistically significant results ($P< 0.05$) were observed at 7 days and 21 days for the test group (Figure 2) for the Gingival index and at 21 days (Figure 3 and 4) for the Plaque index and modified sulcus bleeding index (Table).

None of the patients showed adverse drug reactions during the course of treatment.

Table: Gingival index, Plaque index, Modified sulcus bleeding index assessment at various patient visits for test and control sites

Variable	Baseline-7days	Baseline-21days	Baseline-3months
1.	Gingival index		
Control	0.64±0.22	0.97±0.25	0.99±0.31
Test	1.12±0.35	1.42±0.36	1.29±0.32
P Value	0.0019*	0.0415*	0.1785

2.	Plaque index		
Control	0.76±0.18	0.95±0.26	1.05±0.28
Test	0.98±0.24	1.3±0.34	1.19±0.30
P Value	0.0952	0.0067*	0.6589
3.	Modified Sulcus bleeding index		
Control	0.62±0.18	0.86±0.29	1.05±0.25
Test	0.83±0.21	1.13±0.30	1.16±0.27
P Value	0.0658	0.0256*	0.3674

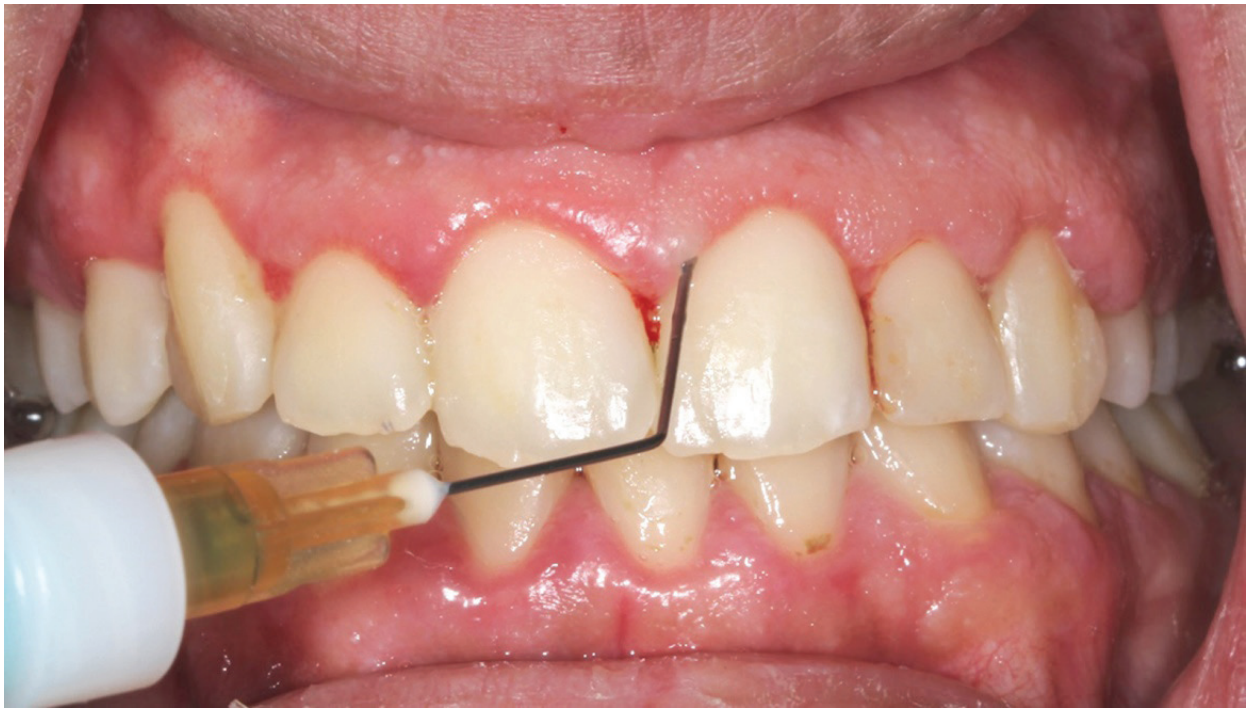
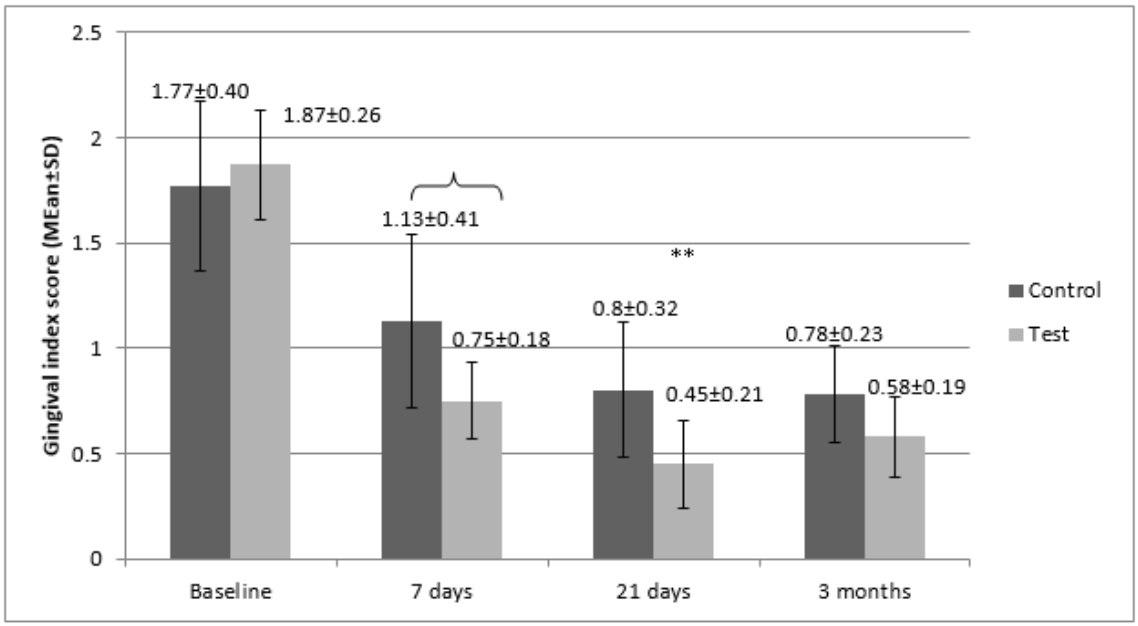


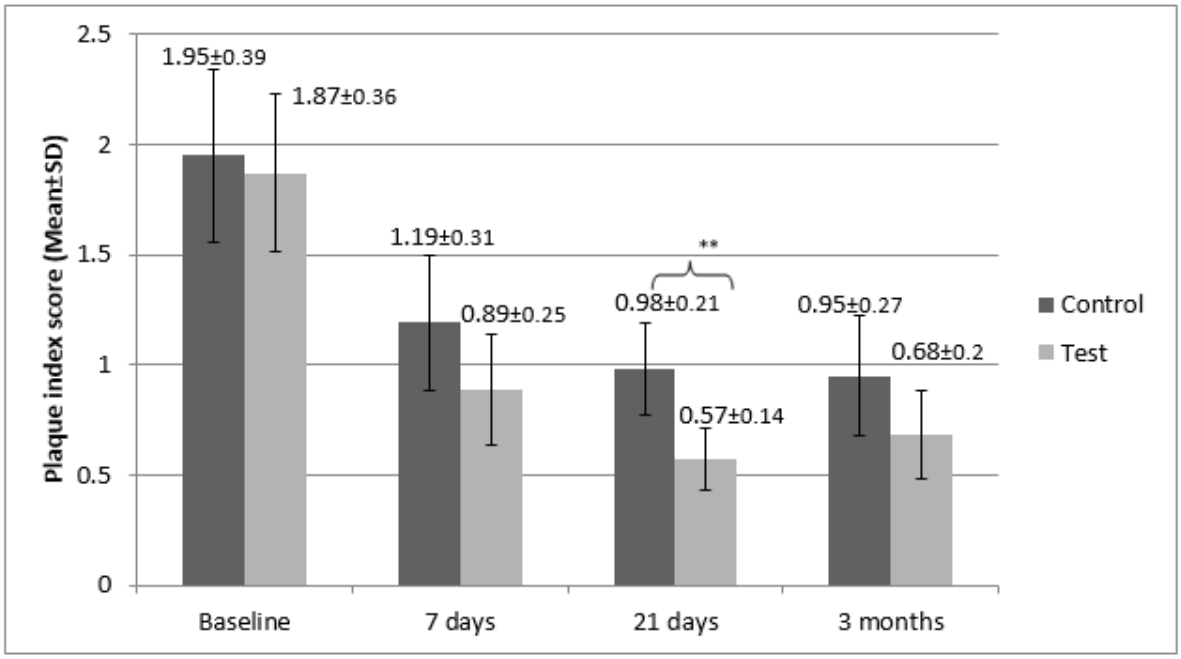
Figure 1: Placement of local drug delivery agent (Clorni gel)

****= Significance**



**= Significance

Figure 2: Gingival index assessed at various patient visits for test and control sites



**= Significance

Figure 3: Plaque index assessed at various patient visits for test and control sites

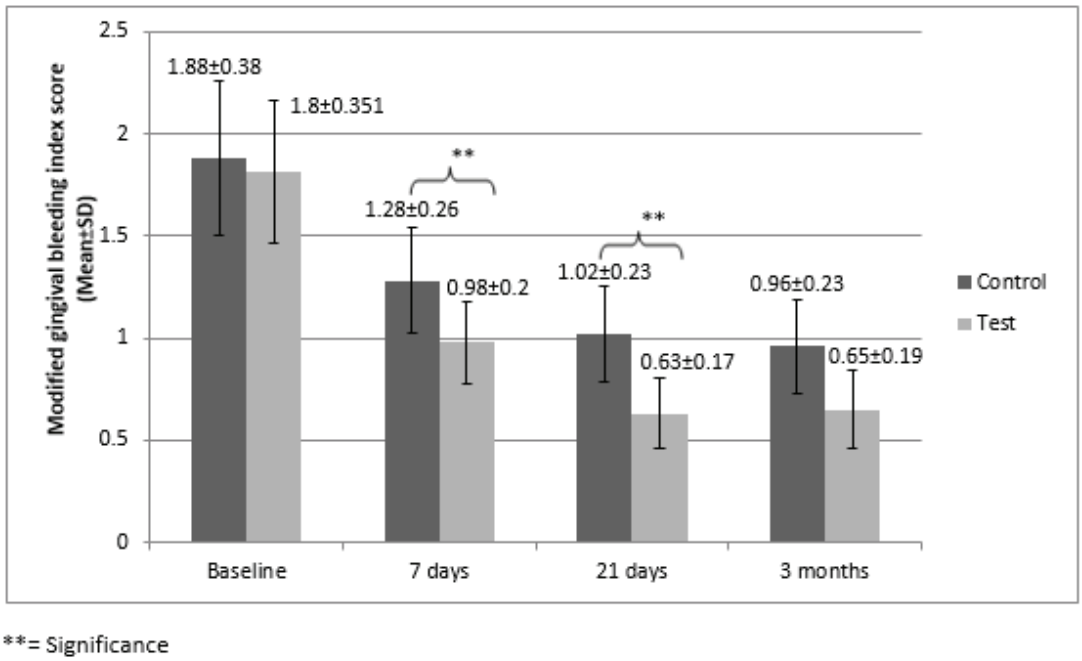


Figure 4: Modified sulcus bleeding index assessed at various patient visits for test and control sites

Discussion

This study shows the action of a newly commercially available Clorni^{TM} gel, containing a combination of Ornidazole and Chlorhexidine (CHX), when used as an adjunct to SRP to aid in faster healing of advanced gingivitis cases. This study, to the best of our knowledge is the first of its kind, using ornidazole as a local application formulation. Considering its systemic application and since ornidazole and metronidazole belong to the same group, the study was conducted on the basis of previous studies using local application of metronidazole, as shown by Slots and Rams.[4]

Chlorhexidine is an effective antimicrobial agent and shows action against a wide range of organisms.[19] Its mechanism of action relates to its inhibitory effect on the pellicle formation, alteration of bacterial adherence to teeth and due to its positive charge, it interacts with the negatively charged cell walls of the bacteriae and enters the cell, causing the lysis of the microbe. Chlorhexidine in a sustained release formulation, has been shown to be effective against subgingival plaque bacteria when used for 7-10 days. The antimicrobial effects were evident up to 6-9 months after treatment and clinical efficacy in terms of reduced bleeding on probing, reduced probing pocket depths and a gain in clinical attachment level were apparent.[20]

In our study the improvement in gingival status, plaque and bleeding were observed when gingival index, plaque index and modified sulcus bleeding index were used. An overall improvement was seen over 3 months in both test and control groups. However, significant improvement was seen in the test group at 7 and 21 days concerning gingival status and at 21 days when plaque index and modified sulcus bleeding index were considered.

The 20 ml/hour out flow of gingival crevicular fluid would be responsible for the 1 minute half-life of any gel within a periodontal pocket.[21] Furthermore, the lack of adherence of CHX to root surfaces[22] and its high affinity for blood and serum proteins[23]are also hypothesized to be among the reasons for its low subgingival substantivity.

Pluronic F127 is a member of the copolymer known as poloxomer, which is used as a vehicle for subgingival gel preparations. This component helps to provide a good bio-adhesive property to the preparation which helps in the permanence of the gel inside the sulcus, aiding in longer medicinal effects of the drug within the sulcus as suggested by Chávez et al, 2006.[16]

Also, the systemic administration of ornidazole has showed a significant reduction in the readings compared to the baseline readings as reported by studies by Kamma et al, 2000[24] and Pradeep et al, 2012.[15] When used in cases of chronic and aggressive periodontitis as an adjunct to scaling and root planning, Kamma et al (2000)[24] showed a probing depth reduction of 1.9 mm at the end of 6 months, when he used ornidazole with nonsurgical periodontal therapy to treat cases of aggressive periodontitis. Pradeep et al (2012) administered systemic ornidazole to 58 patients with chronic periodontitis, adjunctive to scaling and root planing and also showed significant results in treatment results.[15]

Systemic application has the possibility of systemic complications. As shown in our present study, no adverse drug reactions were noted with the local application of ornidazole. The mode of application and treatment method used in this study is simple, economical and effective.

However, further research needs to be done with larger sample size and longer follow up period, accompanied by microbiological tests, to validate the better results of Clorni^{TM} gel.

Conclusion

This study revealed that the topical gel as an adjunct to thorough scaling and polishing had significant results compared to baseline, and also statistically significant additional benefits when compared to scaling and polishing alone. Better clinical results have been seen when Clorni^{TM} gel has been used along with scaling and polishing. Therefore, this gel can be safely suggested as a good option in the treatment of severe gingivitis. Further studies are awaited, with a larger sample, to validate the treatment efficacy of this combination drug.

Conflicts of Interest: The authors declare no conflicts of interest.

Funding: No

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