



Effect of 1% Metronidazole Gel as an Adjunct to Subgingival Scaling in the Treatment of Periodontitis

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ABSTRACT:

Background: Periodontitis is a chronic inflammatory condition confined to periodontium. Antibiotics have been suggested in conjunction with scaling and root planning for the treatment of periodontitis. Systemic antibiotics are biologically active substances that can lead to side effects of various intensities. The undesirable side effects can be minimized by locally administering drugs at the site of infection.

Objectives: The aim of this study was to compare clinical effects of topical application of metronidazole gel (1%) in periodontal pockets as an adjunct to scaling and root planning in chronic periodontitis.

Materials and Methods: This randomized split mouth study was conducted in the Department of Periodontology at Fatima Jinnah Dental College, Karachi after its approval from the ethical committee. Hundred (100) voluntary patients with diagnosed cases of chronic periodontitis aged 25-50 years (66 males and 34 females) were included in the study. Written informed consent was obtained from enrolled patients. Patients' quadrants were divided into two treatment groups. Group 1 received SRP alone and Group 2 received 1% metronidazole gel after SRP. The data was analyzed by SPSS 20. Descriptive and Wilcoxon signed rank non parametric test was used to draw statistical values.

Results: The mean reduction of probing pocket depth at day 180 was 1.16 mm and 1.98 mm in scaling alone and scaling + metronidazole gel respectively. Similarly the mean gain of clinical attachment at day 180 was 1.49 mm and 2.7 mm in scaling and scaling + metronidazole gel groups respectively. The mean depth at which bleeding on probing could be elicited was reduced to 0.12 mm in scaling alone group and 0.52 mm in scaling + metronidazole gel group. The oral hygiene index was significantly improved in scaling alone (1.7) group and scaling + metronidazole gel group.

Conclusion: Local metronidazole gel application is clinically effective as an adjunct to scaling and root planning (SRP) in the treatment of chronic periodontitis.

KEYWORDS: Periodontitis, metronidazole gel, probing pocket depth, scaling and root planning (SRP).

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INTRODUCTION

Plaque associated periodontal disease involves inflammatory reaction that results in destruction of periodontal structures. The increased pocket depth,

loss of clinical attachment, destruction of alveolar bone and ultimately tooth loss are common sequelae of periodontitis¹. The overgrowth of anaerobic Gram negative bacteria is usually responsible for periodontal infections. The two important Gram negative anaerobic pathogens responsible for periodontal disease are *Actinobacillus actinomycetemcomitans* (*A. actinomycetemcomitans*) and *Porphyromonas gingivalis* (*P. gingivalis*). *A. actinomycetemcomitans* secretes leukotoxin that kills human leukocytes, neutrophils and monocytes while *P. gingivalis* produces lipopolysaccharides, capsular material and proteases^{2,3}.

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Several studies have shown that periodontal pathogens are associated with substandard periodontal therapy. The absolute removal of plaque and calculus from deep pockets is difficult due to limited access compared to shallow pockets; as a result, pathogens are re-established after treatment. The optimal treatment of plaque associated periodontal disease includes marked reduction in pathogens by several methods including scaling and root planning, mechanical and chemical debridement^{4,5,6,7}. Another approach is the use of local and systemic antibiotics. Antibiotics can inhibit or kill pathogens that are found in deep pockets and furcation areas that are difficult to access by mechanical debridement^{8,9}. Prolong use of systemic antibiotics increases the risk of nausea, diarrhea, antibiotic resistance and pseudomembranous colitis¹⁰. Local antimicrobial drugs can attain high concentrations in gingival fluid and significantly suppress subgingival microbiota. In addition, it reduces the potential side effects caused by use of systemic antibiotics. Therefore, local application of antibiotics in periodontal pockets is becoming more frequent. Local administration of antibiotics in periodontal pockets through fibers, films and micro-particles is considered as an effective method in periodontal therapy^{7,9}.

Among local antibiotics metronidazole is used as an appropriate antibiotic for the treatment of periodontitis, because of its limited action against anaerobes and restricted unwanted effects compared to tetracycline. Metronidazole selectively inhibits DNA synthesis in gram negative anaerobic bacteria found in oral cavity¹¹. Few clinical trial studies have established a significant effect on the adjunctive use of local antimicrobials compared to scaling and root planning (SRP) alone¹². Therefore, we designed this study to assess clinical effects of metronidazole gel in the treatment of periodontitis. We hypothesized that the combined therapy of scaling and use of 1% metronidazole gel has an increased reduction in periodontal pocket depth, compared to scaling only. The aim of the current study was to assess the clinical effects of topically applied metronidazole (1%) gel in periodontal pockets deeper than 4 mm as an adjunct to subgingival scaling and treatment of periodontitis.

MATERIALS AND METHODS

This study was conducted at the Department of Periodontology, Fatima Jinnah Dental College and Hospital, Karachi from December 2012 to December 2013, after its approval from Fatima Jinnah Dental College Institutional Ethical and Scientific Review Board BEH No.DEC-2012-PRO-01. Sample size calculation was performed using open epi website, by using the data collected from a study

conducted by Stelzel.¹³ Total hundred (100) systemically healthy patients with diagnosed cases of chronic periodontitis, aged 25-50 years (66 males and 34 females), having at least one tooth in each quadrant with probing pocket depth (PPD) ≥ 4 mm, were recruited in this single blind, split mouth randomized study. Smoking, non-plaque associated periodontal diseases, patients allergic to drugs, patients receiving periodontal therapy and antibiotic therapy or drugs for medical and dental conditions, pregnant or lactating females, and systemic conditions such as diabetes mellitus, tumor, radiation, or immuno-suppressive therapy were excluded from the study. After explaining objectives of study, written informed consent was obtained from selected patients. Detailed history was taken and general clinical examination was done. The clinical parameters including oral hygiene index (OHI), periodontal pocket depth (PPD), clinical attachment loss (CAL) and bleeding on probing (BOP) were recorded by CPITN* at baseline before giving treatment. The quadrants of patients were randomly assigned by computer generated table to receive 1% w/w metronidazole gel** after scaling and root planning by ultrasonic scaler*** as an adjunctive treatment. The patients' quadrants were divided into two groups. Group 1 received scaling and root planning (SRP) alone in one quadrant and group 2 received 1% w/w metronidazole gel after scaling and root planning (SRP) in contralateral quadrant. Oral hygiene instructions and demonstration on application of gel through applicator after morning and evening tooth brushing were reinforced. The patients were recalled for evaluation of clinical parameters (OHI, PPD, BOP and CAL) at day 30, 90 and 180 and oral hygiene instructions were reinforced during follow ups. These parameters were compared before and after application of metronidazole gel from baseline to day 180. The data was analyzed using SPSS version 20. Non parametric Wilcoxon Signed Rank test was used to analyze results.

RESULTS

Among hundred (100) patients 66 were males and 34 were females. The age range was 25 to 50 years. The clinical parameters showed statistically significant difference ($p < 0.05$) in both treatment groups. The mean reduction of probing pocket depth at day 180 was 1.16 mm and 1.98 mm in scaling alone and scaling + metronidazole gel respectively (Table 1). Similarly the mean gain of clinical attachment at day 180 was 1.49 mm and 2.7 mm in scaling and scaling + metronidazole gel groups (Table 2). The mean depth at which bleeding on probing could be elicited was reduced to 0.12 mm in scaling alone group and 0.52 mm in scaling + metronidazole gel group (Table 3). The oral hygiene index

Table 1. Comparison of probing pocket depth (PPD) at baseline and day 180.

Group		Mean	N	Std. Deviation	Std. Error Mean	P value
Group 1	Probing pocket depth before scaling alone (Baseline)	6.2000	100	0.78246	.11066	<0.0001
	Probing pocket depth after scaling alone (Day 180)	5.0400	100	.81541	.11532	
Group 2	Probing pocket depth before scaling and application of Metronidazole gel (Baseline)	6.4000	100	.72731	.10286	
	Probing pocket depth after scaling and application of Metronidazole gel (Day 180)	4.4200	100	.78246	.11066	

Table 2. Comparison of clinical attachment loss (CAL) at baseline and Day 180

Clinical Attachment Loss (CAL)	N	Mean	Std. Deviation	P value
Group 1				<0.0001
CAL before scaling alone (Baseline)	100	6.96	.880	
CAL after scaling alone (Day 180)	100	5.47	.739	
Group 2				
CAL before scaling and application of metronidazole gel (Baseline)	100	6.67	.880	<0.0001
CAL after scaling and application of metronidazole gel (Day 180)	100	3.97	.723	

Table 3. Comparison of bleeding on probing (BOP) at baseline and Day 180.

Group	N	Mean	Std. Deviation	P value
Group 1				<0.0001
BOP before scaling alone (Baseline)	100	.72	.454	
BOP after scaling alone (Day 180)	100	.60	.431	
Group 2				
BOP before scaling and metronidazole gel (Baseline)	100	.64	.454	<0.0001
BOP after scaling and application of metronidazole gel (Day 180)	100	.12	.404	

Table 4. Comparison of oral hygiene index (OHI) at baseline and day 180

Oral Hygiene Index (OHI)	N	Mean	Std. Deviation	P value
Group 1				<0.0001
OHI before scaling alone (Baseline)	100	5.26	.888	
OHI after scaling alone (Day 180)	100	3.56	.611	
Group 2				
OHI before application of metronidazole gel (Baseline)	100	5.32	.891	<0.0001
OHI after application of metronidazole gel (Day 180)	100	2.68	.438	

was significantly improved in scaling alone (1.7) group and scaling + metronidazole gel group (2.64) (Table 4).

DISCUSSION

The efficacy of scaling and root planning (SRP) by retarding the bacterial plaque for the management of periodontal conditions is well-accepted. The SRP reduces bleeding and probing depths and facilitates the clinical attachment¹⁴. The microflora in diseased sites at one week following SRP is similar to healthy sites¹⁵. Pathogenic bacteria can recolonize within a few days of SRP, requiring regular visits. Since the periodontal disease is an infection, the use of antibacterial agents as an adjunct to mechanical debridement is persuasive, therefore, it would seem logical to use antibiotics to eliminate the problem. In our population, no data has been reported with locally formulated 1% metronidazole gel as an adjunct to SRP compared to international studies¹⁶. Therefore, the aim of this study was to see the effects of clinical parameters of periodontitis by using 1% w/w metronidazole gel as an adjunct to SRP. In this study, Group 1 and Group 2 showed statistically significant improvement in probing pocket depth (PPD), clinical attachment loss (CAL), bleeding on probing (BOP) and oral hygiene index (OHI) ($p < 0.0001$) at day 180 (after 6 months) when compared to baseline (day 0). These findings are in consistence with other studies^{17,18,19}. However, Group 2 had statistically significant greater improvement in PPD, CAL, BOP and OHI than Group 1 at day 180 compared to baseline (day 0). These findings are in accordance with other studies^{20,21,22}. Griffith also reported that the metronidazole gel as an adjunct to SRP was superior to SRP alone regarding PPD, BOP and CAL and these differences were consistent for 9 months²³. Arthur *et al.*²⁴ in a systematic review of 11 studies of SRP in conjunction with metronidazole gel reported four studies that showed statistically significant reduction in periodontal pocket depth. Three studies reported a net periodontal depth reduction favoring treatment group. Another study reported significant difference between treatment and control groups at 12 weeks. Two studies reported gain of clinical attachment loss (CAL); 0.66mm and 0.4mm at 6 and 39 weeks respectively ($p < 0.001$)²⁴. Several studies reported that local application of metronidazole in conjunction with SRP is more effective in improving clinical and microbial outcomes^{25,26}. Since anaerobic bacteria play important role in periodontitis, metronidazole is particularly suitable for the treatment of periodontitis, due to its action against anaerobes and its restricted unwanted effects compared to tetracycline. Also, metronidazole requires a lesser concentration to achieve complete reduction of the subgingival flora. In order

to minimize adverse effects of systemic antibiotics other topical gel applications such as chlorhexidine and minocycline with controlled releasing properties are capable of being used as a therapeutic component for the treatment of periodontitis²⁷⁻³². Local delivery of antibiotics to pockets not only results in minimum side effects but it also reduces the chance of producing resistant bacteria compared to systemic antibiotics. Also, the concentration of the antibiotic at the diseased site can be 100 times greater than oral medication^{5,7}. However, it is important to note that local application of locally prepared metronidazole gel can be administered instead of systemic antibiotics in conjunction to SRP in our population. There were some limitations in our study like it was a single centre study, there was no control group in the other quadrant, minimum inhibitory concentration (MIC) of the drug was not evaluated, and molecular analysis of microbial culture was not performed. Moreover, reliable microbiological and clinical findings can be obtained by extending study period in future clinical trials.

CONCLUSION

Local metronidazole gel application is clinically effective as an adjunct to scaling and root planning in the treatment of chronic periodontitis.

* Community Periodontal Index Treatment Need (CPITN)

**1% w/w Revomet Gel 60 grams (Platinum Pharmaceuticals)

*** VRN Ultrasonic Scaler, Gullin Veirun Medical Technology Co. Ltd

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CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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