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The Efficacy of Locally Delivered 25% Metronidazole Gel as an Adjunct to Scaling and Root Planning in the Treatment of Chronic Periodontitis: A Clinical Study

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ABSTRACT

Background: The main aim of periodontal therapy is to eradicate the plaque bacteria and ensuring the periodontal pockets are free of granulation tissue for proper healing to occur. Localized antimicrobial therapy, in particular, has evoked growing interest because of the site-specific nature of periodontal infections, the higher concentration of anti-microbial agent subgingivally and reduced side-effects of systemic antibiotic use. In the present clinical study, an attempt is made to evaluate the efficacy of metronidazole 25% dental gel with scaling and root planing as compared to that of scaling and root planing alone.

Material and Methods: A total number of 60 sites from 8 patients with probing pocket depth measuring 5mm and 8mm in different quadrants of the mouth were selected for the study. The selected sites were divided into two groups. Group A (control) comprised of 30 sites. Teeth in this group were treated by scaling and root planing at the baseline (0 day). Group B (test) comprised of 30 sites. Teeth in this group were treated by scaling and root planing followed by local application of Elyzol (metronidazole 25% gel). Prior to scaling and root planing at baseline, (day 0) the selected teeth with the sites were subjected to assessment of clinical parameters. The patients were recalled on the 30th, 60th and 90th day and all the clinical parameters i.e. plaque index, gingival index, gingival bleeding index and probing pocket depth were recorded. Student's independent t-test was used to calculate the p value.

Results: The percentage of reduction in plaque index score between 0-90th day in Group A was (45.28± 16.49) and in Group B was (61.83±13.49) which was statistically significant (P< 0.000l). The percentage of reduction in gingival index score between 0-90th day in Group A was (51.67 ±14.52), and in Group B was (66.00±14.65), which was statistically significant (P< 0.0001) On day 90 there was a 66.7% reduction in gingival bleeding sites in Group A and 93.3% in Group-B, which was statistically significant (P <0.02). The percentage of reduction in probing pocket depth from 0-90th day in group A was (22.94±8.39) and in group B was (26.13±8.45) which was not statistically significant (p=0.15).

Conclusion: The present study illustrates that the adjunctive use of 25% metronidazole gel along with scaling and root planing, was superior to the conventional treatment of subgingival scaling alone and these differences were maintained for three months. Furthermore, the differences were of sufficient magnitude which offers clinical relevance.

Keywords: Chronic periodontitis; Localized antimicrobial therapy; Metronidazole gel.

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INTRODUCTION

The traditional treatment modality of scaling and root planing remains the 'gold standard' for the non-surgical management of chronic periodontitis. Mechanical therapy may, however, fail to reduce or eliminate the anaerobic infection at the base of the pocket, within the gingival tissue or in furcations[1] and lead to frequent development of secondary effects as gingival recession, loss of tooth substance or dentin hypersensitivity.[2]

The main aim of periodontal therapy is to eradicate the plaque bacteria and ensuring the periodontal pockets are free of granulation tissue for proper healing to occur. Mechanical debridement along with some regenerative procedures/ recession management is done for deeper pockets in case of bone defects, but shallow pockets and horizontal bone loss have been managed conservatively by SRP and systemic microbial agents. The value of administering antimicrobial agents as an inexpensive and rapid means of augmenting mechanical periodontal debridement is worth consideration.[3] Localized antimicrobial therapy, in particular, has evoked growing interest because of the site-specific nature of periodontal infections, the higher concentration of anti-microbial agent subgingivally and reduced side-effects of systemic antibiotic use. [1]

Metronidazole is one of the most common broad spectrum antibiotics and is active against most of the periodontal pathogens. As anaerobic bacteria are believed to be the predominant causative factor in periodontitis and metronidazole, specifically targets anaerobic microorganisms that are used in the treatment of chronic periodontitis.[4] In the present clinical study, an attempt is made to evaluate the efficacy of metronidazole 25% dental gel with scaling and root planing as compared to that of scaling and root planing alone.

MATERIAL AND METHODS

The subjects for this study were selected from the Department of Periodontics, Meenakshi Ammal Dental College and Hospital. A total of eight patients, four males and four females in the age group of 28-45 years were included in this study. Patients who were diagnosed as having chronic periodontitis, patients with periodontal pockets measuring >5mm and <8mm in different quadrants of the mouth with radiographic evidence of bone loss, patients who have not undergone any form of periodontal surgical or non surgical periodontal therapy for the past six months, patients having pockets that readily bleed on probing and patients willing to take part in the study and maintain appointments regularly were included in the study. Patients who have taken antibiotics in the past six months, patients with a history of alcohol abuse, patients on drugs such as anticoagulants, patients known to be hypersensitive to metronidazole and pregnant women and nursing mothers were excluded from the study.

A total number of 60 sites from 8 patients with probing pocket depth measuring 5mm and 8mm in different quadrants of the mouth were selected for the study. Equal number of sites were taken as control and test in the same patient, which ranged from 3 to 5 sites. Of the selected sixty sites, thirty were test sites and the remaining thirty were the control sites on the contralateral side. Thus the selected sites were divided into two groups. Group A (control) comprised of 30 sites. Teeth in this group were treated by scaling and root planing at the baseline (0 day). Group B (test) comprised of 30 sites. Teeth in this group were treated by scaling and root planing followed by local application of Elyzol (metronidazole 25% gel). The second application was done on the 7th day. On the screening day, the patients were selected and the target sites were identified. Impressions were made for the fabrication of acrylic stents, which were used for measuring the probing depth in target sites. General, oral and periodontal examinations were carried out.

Prior to scaling and root planing at baseline, (day 0) the selected teeth with the sites were subjected to assessment of clinical parameters by using plaque index (Silness and Loe 1964), Gingival index (Loe and Silness 1963), Gingival Bleeding index (Ainamo and Bay 1975)[5] and probing pocket depth.

Thereafter, all patients underwent full mouth scaling and root planing, which was done using ultrasonic scalers and curettes. Following scaling and root planning, metronidazole 25% gel (Elyzol) was applied in the test sites (Group B). Patients were recalled to the dental clinic on the 7th day

again for the second application of metronidazole 25% gel (Elyzol) for the test sites (Group B). The patients were then appointed to attend the dental clinic on the 30th day. During this visit the clinical parameters i.e. plaque index, gingival index and gingival bleeding index were assessed in both control group A and test group B. The patients were recalled again on the 60th day and all the clinical parameters i.e. plaque index, gingival index, gingival bleeding index and probing pocket depth were recorded. All the clinical parameters were finally assessed in group A and group B on the 90th day. Student's independent t-test was used to calculate the p value.

RESULTS

Table 1: Comparison of mean plaque index score and percentage changes between group A and group B at different time points and its significance

Variable	Group A	Group B	p value
	Mean ±SD	Mean ±SD	
Day 0	1.16 ±0.15	1.16±0.12	1.00 Ns
Day 30	0.89±0.17	0.69±0.16	<0.0001(Sig)
Day 60	0.71±0.18	0.51±9.14	<0.0001(Sig)
Day 90	0.63±0.21	0.44±0.16	<0.0001(Sig)
Change From			
Day 30	0.27±0.06	0.47±0.14	<0.0001(Sig)
Day 60	0.45±0.15	0.65±0.16	<0.0001(Sig)
Day 90	0.53±0.20	0.72±0.17	<0.0001(Sig)
Percentage Change From			
Day 30	23.44±6.61	40.33±11.74	<0.0001(Sig)
Day 60	38.94±12.98	56.00±11.92	<0.0001(Sig)
Day 90	45.28±16.49	6183±13.49	<0.0001(Sig)

Table 2: Comparison of mean gingival index score and percentage changes between group A and group B at different time points.

Variable	Group A	Group B	p value
	Mean ±SD	Mean ±SD	
GINGIVAL INDEX DAY 0	1.10 ±0.13	1.06±.11	0.17 NS
DAY 30	0.89±0.14	0.68±0.15	<0.0001(SIG)
DAY 60	0.71±0.19	0.48±0.18	<0.0001(SIG)
DAY 90	0.53±0.17	0.36±0.16	<0.0001(SIG)
CHANGE FROM			
DAY 30	0.21±0.16	0.38±0.58	<0.0001(SIG)
DAY 60	0.39±0.22	0.58±0.18	<0.0001(SIG)
DAY 90	0.57±0.16	0.70±0.18	<0.0001(SIG)
PERCAENTAGE CHANGE FROM			
DAY 30	18.33±14.16	36.17±12.71	<0.0001(SIG)
DAY 60	35.00±18.38	55.17±16.17	<0.0001(SIG)
DAY 90	51.67±14.52	66.00±14.65	<0.0001(SIG)

Table 3: Distribution of gingival bleeding sites for group A and group B at different time points.

TIME POINTS	GBI	GROUP A		GROUP B		P-VALUE
		N	%	N	%	
DAY 0	+VE -VE	30 0	100% 0%	30 0	100% 0%	-
DAY 30	+VE -VE	27 3	90% 10%	18 12	60% 40%	0.02 (SIG)
DAY 60	+VE -VE	19 11	63.3% 36.7%	6 24	20% 80%0	0.002 (SIG)
DAY 90	+VE -VE	10 20	33.3% 66.7%	2 28	6.7% 93.3%	0.02 (SIG)

Table 4: Comparison of mean probing depth and percentage changes between group A and group B at different time points.

Variable	Group A	Group B	p value
	Mean ±SD	Mean ±SD	
PROBING POCKET DEPTH DAY 0	5.47 ±0.68	5.77±0.77	0.12 NS
DAY 0-60	4.33 ±0.72	3.97±0.67	<0.045(SIG)
DAY 90	4.20±0.61	4.23±0.57	0.83 (NON SIG)
CHANGE FROM			
DAY 0-60	1.14±0.50	1.80±0.61	<0.0001(SIG)
DAY 90	0.27±0.52	1.54±0.57	0.06 (NON SIG)
PERCAENTAGE CHANGE FROM			
DAY 0-60	20.21.94±8.95	30.91±9.34	<0.0001(SIG)
DAY 90	22.94±8.39	26.13±8.45	0.15 (NON SIG)

Mean plaque index score at day 0 in Group A (1.16 ±0.15) was higher than group B (1.16 ±0.12). However, there was no statistically significant difference. Mean plaque index score at day 30 in Group A (0.89±0.17) was higher than group B (0.69±0.16), which was statistically significant (P<0.0001), at day 60 in group A (0.71 ±0.18) was higher than group B (0.5±0.14) which was statistically significant (P<0.0001) and at day 90 in group A (0.63±0.21) was higher than group B (0.44±0.16), which was statistically significant (P<0.0001). The percentage of reduction in plaque index score between 0-30th day in Group A was (23.44± 6.61) and in Group B was (40.33±11.74) which was statistically significant (P<0.0001). The percentage of reduction in plaque index score between 0 and 60th day in Group A was (38.94± 12.98) and in Group B was (56.00±11.92) which was statistically significant (P<0.0001). The percentage of reduction in plaque index score between 0-90th day in Group A was (45.28± 16.49) and in Group B was (61.83±13.49) which was statistically significant (P< 0.000l) (table 1).

Mean gingival index score at day 0 in group A (1.10±0.13), was higher than Group B (1.06±0.11), however, statistically there was no statistically significant difference in mean gingival index score between group A and group B (p=0.17). At day 30, mean gingival index score in group A (0.89±0.14) was higher than group B (0.68±0.15), which was statistically significant (P< 0.0001). At day 60, mean gingival index score in Group A (0.71±0.19) was higher than Group B (0.48±0.18) which was statistically significant (P< 0.0001). Mean gingival index score at day 90 in Group A (0.53±0.17) was higher than Group B (0.36±0.16), which was statistically significant (p< 0.0001).

The percentage of reduction in gingival index score between 0-30th day in Group A was (18 33±14.16) and in Group B was (36.17±12.71) which was statistically significant (P< 0.0001). The percentage of reduction in gingival index score between 0- 60th day in Group A was (35.00 ± 18.38), and in Group B was (55.17±16.17), which was statistically significant (P< 0.0001). The percentage of reduction in gingival index score between 0-90th day in Group A was (51.67 ±14.52), and in Group B was (66.00±14.65), which was statistically significant (P< 0.0001) (table 2)

The positivity of gingival bleeding sites was 100% at day 0 in both Group A and Group B. On day 30 there was a 10% reduction in gingival bleeding sites in Group A and 40% in Group B, which was statistically significant (P< 0.02). On day 60 there was a 36.7% reduction in gingival bleeding sites in Group A and 80% in group B, which was statistically significant (P< 0.002). On day 90 there was a 66.7% reduction in gingival bleeding sites in Group A and 93.3% in Group-B, which was statistically significant (P <0.02) (table 3).

Mean probing pocket depth at day 0 in group A was (5.47±0.68 mm) and in group B was (5.77±0.77mm), which was statistically not significant. Mean probing pocket depth at day 60 in Group A was (4.33±0.72 mm) and in group B was (3.97±0.67 mm), which was statistically significant (P=0.045). Mean probing pocket depth at day 90 in Group A was (4.20±0.61 mm) and in Group B was (4.23±0.57 mm) which was not statistically significant (P=0.83). The percentage of reduction in probing pocket depth from 0-60th day in group-A was (20.71±8.95) and in group B was (30.91±9.34) which was statistically significant (P< 0.0001). The percentage of reduction in probing pocket depth from 0-90th day in group A was (22.94±8.39) and in group B was (26.13±8.45) which was not statistically significant (p=0.15) (table 4).

DISCUSSION

It is well recognized that periodontal diseases are bacterial in nature. An essential component of therapy is to eliminate or control these pathogens. This has been traditionally accomplished through mechanical means i.e. scaling and root planing, which is time-consuming, difficult, and sometimes ineffective. Over the past 20 years, locally delivered, anti-infective pharmacological agents, most recently employing sustained-release vehicles, have been introduced to achieve this goal.[6]

The present clinical study was undertaken to assess the efficacy of metronidazole 25% dental gel with scaling and root planing as compared to that of scaling and root planing alone. Here a split mouth design was used since split mouth clinical trials have been successfully used for the evaluation of topical subgingival antimicrobials in Periodontics.[7]

The clinical parameters used in this study were plaque index, gingival index, gingival bleeding index and probing pocket depth. These parameters were assessed at baseline 30th, 60th and the 90th day, but probing pocket depth was recorded only on the 60th and the 90th day. To standardize the direction of probing, grooved acrylic stents were prepared for each patient.[8]

The mean reduction in Plaque index scores on 0-30, 0-90th days were statistically significant in group A and B (P<0.000 1) and the percentage of reduction of group plaque index score in group A and group B was also significant for the same time periods. These findings are comparable to that of studies conducted by Hitzig C et al[9] and Awartani FA et al[10] who observed significant reductions in plaque scores from baseline to different time points.

In the present study, on comparison between group A and group B, group B showed a statistically significant (P<0.0001) reduction in plaque index score than Group A, on the 30th, 60th and the 90th day.

The mean reduction in gingival index score on 0-30, 0-60 and 0-90 days were statistically significant in group A and group B (P<0.0001) and the percentage of reduction of gingival index score in group A and group B were also significant for the same time periods. These findings are comparable to that of studies conducted by Radvar M et al.[8] Noyan U et al[11] and Awartani FA et al[10] who observed significant reductions in gingival index scores from baseline to different time points in test and control sites.

The mean reduction in the percentage of gingival bleeding sites between 0-30, 0-60, and 0-90th day were statistically significant in Group A and in

Group B. On comparison between Group A and Group B, Group B showed a statistically significant reduction in the percentage of bleeding sites, 40% on 30th day, 80% on 60th day and 93.3% on 90th day. These findings are comparable to the studies conducted by Awartani FA et al[10] and Griffith GS et al.[12]

The mean reduction in Probing Pocket depth on the 60th and the 90thday were statistically significant for both the groups (p<0.0001). In the present study, on comparison between Group A and Group B showed a statistically significant reduction in probing pocket depth on the 60th percentage of reduction was also statistically day and the significant (P<0.0001).

In this study, local subgingival dental gel application tends to be better in reducing probing pocket depth, since it gives a special firmness to the gingival tissues which provides an obvious resistance to probing forces even in deep periodontal pockets. This is consistent with the findings of Hirooka H.[13]

Bonito AJ et al[14] carried out a systematic review to study impact of local adjuncts to scaling and root planing in periodontal disease therapy and revealed that among the locally administered adjunctive antimicrobials, the most positive results occurred for tetracycline, minocycline, metronidazole, and chlorhexidine. Adjunctive local therapy generally reduced probing depth. Differences between treatment and SRP-only groups in the baseline-to-follow-up period typically favored treatment groups but usually only modestly (e.g., from about 0.1 mm to nearly 0.5 mm) even when the differences were statistically significant. Among the various locally delivered chemotherapeutic agents metronidazole, has a bactericidal action against anaerobes such as Prevotella intermedia, Porphyromonas gingivalis, Tannerella forsythia, Fusobacterium species and spirochetes such as Treponema denticola and Treponema vincentii, which are generally believed to be the main pathogens associated with periodontitis.[15] Griffiths GS et al[12] compared clinical outcomes following treatment of chronic adult periodontitis with subgingival scaling or subgingival scaling plus metronidazole gel and found that at the end of the study, the mean reductions for probing pocket depth were 1.0 mm (SRP) compared to 1.5 mm (SRP+gel), and for CAL they were 0.4 mm (SRP) compared to 0.8 mm (SRP+gel), with mean difference for clinical probing attachment levels between treatments of 0.4±0.6 mm (95% confidence intervals of 0.3–0.6 mm). Perinetti G et al[16] also reported that subgingival administration of metronidazole at 1% may have a role in the management of persistent pockets during chronic periodontitis.

Ainamo J et al[17] studied clinical responses to subgingival application of a metronidazole 25% gel compared to the effect of subgingival scaling in adult periodontitis and reported that probing pocket depth and bleeding on probing were significantly reduced in both groups and for both parameters ($p < 0.01$). Probing pocket depth was reduced by 1.3 mm after gel application and 1.5 mm after scaling; bleeding on probing was reduced by 32% and 39%, respectively and the difference between the treatments was statistically significant. Noyan U et al[11] conducted a clinical and microbiological evaluation of systemic and local metronidazole delivery in adult periodontitis patients and found that although both of the combined treatment groups responded to therapy with better resolution of infection than the pure mechanical and pure metronidazole treatments, local metronidazole in combination with scaling and root planing seems to be more effective in terms of producing both clinical and microbial improvements. Yilmaz S et al[18] suggested that microbial testing may be justified before prescribing the adjunctive antibiotic and selecting the mode of delivery for the successful clinical management of early onset periodontitis.

CONCLUSION

The present study illustrates that the adjunctive use of 25% metronidazole gel along with scaling and root planing, was superior to the conventional treatment of subgingival scaling alone and these differences were maintained for three months. Furthermore, the differences were of sufficient magnitude which offers clinical relevance.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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