

Subgingival application of 25% metronidazole gel, 1% chlorhexidine gel as adjunctive therapy to scaling and root planing in treatment of chronic periodontitis



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Abstract

Objectives: The aim of this study was to compare the clinical effect of subgingival application of 25% metronidazole gel or 1% chlorhexidine gel as an adjunctive to scaling and root planing over a root planing alone.

Materials and Methods: Ten adults (6 females and 4 males) with an age range of (30-60) years, each with at least three non-adjacent periodontally involved teeth with a probing pocket depth of ≥ 5 mm and bleeding on probing participated in this randomized, split mouth, clinical study. A total of (394) sites were included in the study, the selected sites in each patient were divided into: Group 1 (root planing plus 25% metronidazole gel), Group 2 (root planing plus 1% chlorhexidine gel) and Group 3 (root planing alone). Clinical evaluation included: plaque index PLI (Silness and Loe, 1964), gingival index GI (Loe and Silness, 1963), bleeding on probing (BOP), probing pocket depth (PPD) and clinical attachment level (CAL).

Results: All groups showed a fluctuated mean PLI scores between visits and a gradual reduction of GI, BOP, PPD and CAL scores for all groups during subsequent visits. Intergroup comparisons for PLI, BOP, PPD and CAL parameters showed no significance difference between the 3 groups, whereas GI showed a significant difference between groups except at week 2 only; this significance observed when group 1 compared with group 3.

Conclusions: The 3 treatment modalities similarly showed improvement in almost all clinical parameters applied in this study. Also, there was no significance difference between the application of metronidazole gel and chlorhexidine gel on improvement of clinical periodontal parameters.

Keywords: Salivary glands, neoplasm, parotidectomy, submandible gland, parotid gland.

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Introduction:

Periodontal disease is characterized by tissue inflammation and destruction of the tooth-supporting structures that eventually leads to the loss of affected teeth⁽¹⁾. The beneficial effect of traditional therapy by mechanical debridement, which is the combination of scaling and root planing plus patients daily meticulous oral hygiene in the treatment of periodontal disease have been validated⁽²⁾.

Although mechanical and surgical interventions are the most widely used methods of controlling disease progression, they may fail to remove complete infection due to failure of instruments to reach the bases of deep pockets, diffusion of periodontal pathogens into soft tissue and dentinal tubules, migration of periodontal pathogens from other sites, and complexity of teeth anatomy which makes it difficult for instrumentation⁽³⁾. Thus, during the past two decades, dentist and microbiologist have adopted arrange of adjunctive antimicrobial regimens based on

the bacterial specification in periodontitis designed to aid the mechanical methods⁽⁴⁾.

Currently, three delivery systems for periodontal chemotherapeutic agents have been studied: systemic, topical and controlled release. For systemic antibiotic therapy, they need large doses to be administered, because they are not able to achieve high gingival crevicular fluid (GCF) concentration or to gain sufficient concentration of the drug at the site of disease⁽⁵⁾, with other disadvantages like: increased of antibiotic resistant, drug interaction, and inconsistent patient compliance⁽⁶⁾.

Topical rinses or irrigates, remain for a short time within the periodontal pocket, and therefore do not provide a significant concentration for a sufficient time at the site of the disease, thus make them poorly effective in the treatment of periodontitis⁽⁷⁾. The controlled release of local delivery system is designed

to release a drug slowly for more prolonged availability and sustained action⁽⁸⁾. Different devices have been used for sustained release of antimicrobial agents such as hollow fibers⁽⁹⁾, acrylic strips⁽¹⁰⁾ and monolithic fibers⁽¹¹⁾. Unfortunately, problems were encountered with these non-degradable delivery devices in that they were dislodged from the sulcus, their application are difficult, time-consuming and have to be removed again which may cause irritation to gingival tissue⁽¹²⁾. Therefore, biodegradable devices have been developed that can be left in-situ and eliminate the risk of disturbing a healing site after therapy⁽¹³⁾. Different devices have been used such as collagen film preparation⁽¹⁴⁾, and dental gel.

Unlike other formulations, the gel provides the ability to syringe the drug into the periodontal pocket, thus providing ease of use and patient comfort⁽¹⁵⁾. The local antimicrobial agents have the ability to be retained within the periodontal pocket and slowly release from the adsorbed tissue⁽¹⁶⁾.

Among those that have these characteristics are: metronidazole that is a chemotherapeutic agent with a range of activity use in the treatment of periodontal disease mostly against anaerobic bacteria⁽¹⁷⁾. Also chlorhexidine remains to be one of the most effective agents used in the treatment of periodontitis because it exhibiting an action against Gram-negative and Gram-positive, and fungi^(18,19), therefore, the present study was carried out to compare the clinical effect of subgingival application of 25% metronidazole gel or 1% chlorhexidine gel as an adjunctive to scaling and root planing over a root planing alone, and to determine the most appropriate adjunctive treatment in relation to conventional periodontal therapy on improvement of the clinical periodontal parameters.

Materials and Methods:

Subjects & Materials

25% metronidazole gel (Elyzol[®] dental gel, Colgate-Palmolive GmbH) is supplied as 1g metronidazole gel cartridge that containing 40.2% metronidazole benzoate, corresponding to (250mg metronidazole) and chlorhexidine gluconate 1% dental gel (Corsodyl[®] dental gel, Smith Kline Lmt. U.K) (equivalent to 5% w/v solution) used in this study. (10) Patients (4 males and 6 females) with an age range of (30-60) years (mean 41 years) were participated in this study. Subject recruited for the study were patients attending the periodontics department at School of Dentistry, University of Sulaimani.

All patients had no history of systemic diseases and fitted the following inclusion criteria:

- (1) Patient had not taken any systemic antibiotic or received periodontal treatment (except supragingival scaling) for the past 3 months.
- (2) Patient had at least one pocket per quadrant of the mouth with a clinical probing depth of ≥ 5 mm.

Exclusion criteria:

- (1) Pregnant or lactating patients.
- (2) Patients with known or suspected hypersensitivity to metronidazole or chlorhexidine (CHX).

A total of (124) teeth with (394) sites were included in the study.

Study design:

The initial examination consists of evaluating the periodontal condition of the teeth, all patients received a supragingival prophylaxis consisting of scaling and polishing, the subjects were instructed for oral hygiene regime including daily correct use of toothbrush (modified Bass technique) and dental floss. Oral hygiene compliance was checked at each visit weekly, and further instruction were given when necessary until their mean of PLI equal to (0.5), this considered to be the baseline data. An alginate impression was taken and an occlusal stent was constructed for each patient by using of Biostar machine.

Periodontal examination carried out utilizing the following parameters:

1- Plaque index (PLI): Plaque index system in score from (0-3) by Silness & Loe, 1964 ⁽²⁰⁾.

2- Gingival index (GI): Gingival index system in score from (0-3) by Loe & Silness 1963 ⁽²¹⁾.

3- Bleeding on probing (BOP): The site is gently probe to the base of the pocket, if bleeding occurs within 30 seconds after probing, the site is given score 1, it does not occur score 0 is given ⁽²²⁾.

4-Clinical probing pocket depth (PPD): Each tooth was probed at 6 sites (mesio- buccal, mid-buccal, distobuccal, mesiolingual, mid-lingual and distolingual). Only sites showed probing pocket depths of ≥ 5 mm were recorded.

5- Clinical attachment level (CAL): The occlusal stent was made and adjusted to fit the teeth, and then vertical grooves corresponding to the probed sites were made using a rotary fissure bur, these grooves provided reference mark for periodontal probe insertion and angulation. CAL was considered as the distance from the base of the pocket to the lower periphery of the stent. The measurements were taken and nearest to mm ⁽²³⁾.

These periodontal parameters were registered using William's periodontal probe were recorded in about 2 months at 2 weeks intervals (at day 0 which is the baseline record, week 2, week 4, week 6 and week 8). A total of five records for each person were undertaken.

Treatments:

A split-mouth, randomized study design carried out. Following registration of all parameters, the selected teeth were randomly divided into 3 groups, each group

designed to receive different treatment modality as follows:

Group 1: Included 130 sites that received mechanical debridement plus 25% metronidazole gel on day 0 and 7. On day 0 subgingival root planing (RP) was performed using (Gracey curette), irrigation of the pockets with 0.9% normal saline, after that the sites were isolated with cotton pellets and dried then immediately 25% metronidazole gel subgingivally was applied. On day 7 the same sites received a second application of 25% metronidazole gel.

Group 2: Included 131 sites that received mechanical debridement plus 1% chlorhexidine gel on day 0 and 7. On day 0 subgingival root planing (RP) was performed using (Gracey curette), irrigation of pocket with 0.9% normal saline, after that the sites were isolated with cotton pellets and dried then immediately 1% chlorhexidine gel subgingivally was applied with a 5ml disposable syringe with 23 gauge hypodermic needle. On day 7 the same sites received a second application of 1% chlorhexidine gel.

Group 3: Included 133 sites; here the sites received mechanical debridement as above alone on day 0 and repeated after 7days.

Statistical analysis:

The data was processed and analysed using (SPSS). Both descriptive statistics (means, standard error and percentage) and inferential statistics (ANOVA and Post Hoc test) were conducted.

Results:

A total of 394 sites on 124 teeth were selected. The mean number of teeth per patient was (12.4).

The statistical analysis comparing each group at each visit to baseline regarding the mean (GI, BOP, PPD& CAL) showed gradual reduction, except mean PLI scores was fluctuated between visits as shown in Table (1).

Intergroup comparison by ANOVA test for (PLI, GI, BOP, PPD & CAL) showed no significant difference between all the groups for all parameters as shown in Table (1), except for GI when group 1 compared with group 3 the result revealed a significant difference at week 4, highly significant differences at week 6 and week 8 by using Bonferroni test as shown in Table (2).

Discussion:

Scaling and root planing is an effective mechanical approach for reducing bacterial colonization and for controlling the progression of periodontal disease, and as periodontitis is an infectious disease, the use of antimicrobials has rendered attention in periodontal treatment. Since antimicrobials show low potential to penetrate subgingival biofilms, therefore, it is

suggested that the use of antimicrobials in the treatment of periodontitis should be used as an adjunct to mechanical debridement and not as an alternative therapy⁽²⁴⁾.

Metronidazole gel and CHX gel are known for having antimicrobial effects against most periodontal pathogens^(25, 26). In order to assess the clinical effects of subgingivally applied antimicrobial agents, it should be consider that the factors rather than the drug alone may affect the results obtained, such factors are: effects of supragingival plaque control, effects of the adjunct mechanical debridement of subgingival area. Therefore, the present study was designed to evaluate the effects of the three alternative treatment modalities: RP plus 25% metronidazole gel, RP plus 1% CHX gel and RP alone in the same patients. Therefore, a split - mouth design was used. This design is advantageous in that all sites can be compared under the same conditions of the oral hygiene, host immune response.

Effect of treatment modalities on clinical parameters:

All subjects attending this study showed statistically significant improvement in clinical parameters in response to the three treatment modalities except the plaque score as follows:

Plaque index:

When the mean plaque score compared with baseline for all treatment fluctuated although the oral hygiene instruction was consistently reinforced throughout the study. This indicated that optimal plaque control by the patient was mainly affects on the level of the mean plaque index and minimally affected by the use of specific subgingival treatment⁽²⁶⁾. Non-significant differences were also observed between the groups at week 2, 4, 6, and 8; this was in agreement with Quirynen et al., 2000⁽²⁷⁾.

Gingival index:

A gradual reduction in the gingival index from the baseline values to the end of the 2 months experimental period was observed, and this improvement was noticed by improvement in the condition of marginal gingival tissue by decrease of inflammation.

The combination of root planing plus metronidazole gel was significantly reduced the mean GI and this result was consistent with Awartani et al.,1998 ⁽²⁸⁾. This result could be attributed to the action of metronidazole gel on the microorganisms by a reduction in their numbers. At week 2, on comparing group 1 with group 3, a non- significant difference was observed in GI, but this difference was significant at week 4, 6, and 8, this indicate that tissues are still under healing process (stage of epithelialization), and this was in agreement with Pietrusk et al., 2006⁽²⁹⁾. CHX gel plus RP reduced gingival index; this was owing to the additional effect of adjunct antimicrobial effect of

Table 1: Comparison of means of clinical parameters (PLI, GI, BOP, PPD and CAL) scores to baseline

Clinical Parameters	Visits	Type of treatment			F.	Sig.
		Group 1	Group 2	Group 3		
		Mean± S.E	Mean± S.E	Mean± S.E		
PLI	Baseline	0.59	0.58	0.59		
	2w	0.58±0.100	0.54±0.100	0.56±0.100	0.070	NS
	4w	0.53±0.106	0.59±0.106	0.57±0.106	0.191	NS
	6w	0.46±0.090	0.57±0.090	0.57±0.090	0.987	NS
	8w	0.48±0.083	0.58±0.083	0.55±0.083	0.768	NS
GI	Baseline	1.90	2.02	1.91		
	2w	1.40±0.102	1.53±0.102	1.53±0.102	0.935	NS
	4w	1.10±0.071	1.24±0.071	1.33±0.071	4.380	S
	6w	0.96±0.063	1.15±0.063	1.33±0.063	5.145	HS
	8w	0.96±0.055	1.09±0.055	1.21±0.055	8.481	VHS
BOP	Baseline	0.100	0.100	0.100		
	2w	0.53±0.112	0.58±0.112	0.62±0.112	1.953	NS
	4w	0.39±0.061	0.45±0.061	0.50±0.061	1.404	NS
	6w	0.26±0.041	0.36±0.041	0.37±0.041	1.806	NS
	8w	0.20±0.055	0.28±0.055	0.30±0.055	1.056	NS
PPD	Baseline	5.43	5.43	5.39		
	2w	4.55±0.150	4.75±0.150	4.37±0.150	0.973	NS
	4w	3.83±0.152	3.98±0.152	4.19±0.152	2.349	NS
	6w	3.54±0.143	3.60±0.143	3.83±0.143	5.017	NS
	8w	3.28±0.145	3.38±0.143	3.53±0.143	6.611	NS
CAL	Baseline	8.64	8.44	8.33		
	2w	8.07±0.211	8.22±0.211	8.08±0.211	0.337	NS
	4w	7.85±0.186	7.91±0.186	7.96±0.186	0.126	NS
	6w	7.73±0.175	7.90±0.175	7.85±0.175	0.540	NS
	8w	7.65±0.275	7.64±0.275	7.51±0.275	1.084	NS

NS=not significant $P>0.05$, S=significant $P<0.05$, HS=highly significant $P<0.01$, VHS=very highly significant $P<0.001$.

CHX gel that suppress the bacterial microflora harbored at the periodontal pocket. At week 2, 4, 6, and 8 when group 1 compared with group 2, the comparison revealed non- significant differences and also a non- significant difference was observed when group 3 compared with group 2. The latter was in contrast to Vinholis et al., 200⁽³⁰⁾, who revealed a significantly greater reduction in GI in the CHX gel group.

Bleeding on probing:

Statistical analysis of data showed improvements in all three groups that was demonstrated by a decrease in the percentage of sites with bleeding on probing from the baseline and persisted throughout the 2 months experimental period.

Table 2: Comparison of mean GI between group 1 and group 3 (The significant result only)

Visit	Mean difference	S.E	Sig
4w	-0.227	0.78	S
6w	-0.362	0.085	HS
8w	-0.257	0.088	VHS

S=significant P<0.05, HS=highly significant P<0.01, VHS=very highly significant P<0.001.

Reduction in percentage of sites with bleeding on probing (BOP) following treatment with scaling and root planing was observed, because subgingival mechanical debridement not only decrease plaque mass but also radically changes the composition of the subgingival microbiota⁽³¹⁾, and decreasing the prevalence of pathogens responsible for disease progression⁽³²⁾, so has been used as the main therapy for treating the periodontitis⁽³⁰⁾. This reduction in the percentage of sites with BOP was increased when metronidazole gel used as the adjunctive therapy to scaling and root planing through the bactericidal effect of metronidazole gel⁽³³⁾. At week 2, 4, 6, and 8, when group 1 compared with group 3, a non-significant difference was observed and this was consistent with the results obtained by Leiknes et al.,2007⁽³⁴⁾. The limited effect of metronidazole gel might be due to the high clearance rate of the drug from the periodontal pocket under the high turnover rate of gingival crevicular fluid (GCF)⁽³⁵⁾. RP in combination with CHX gel reduced the percentage of bleeding sites; this might be due to the antimicrobial effect of CHX gel that improved the effect of RP treatment. When group 2 compared with group 3, a non-significant difference was observed, and this might be due to the fact that presented bacteria was not exposed to CHX because no longer the drug remain at the sites, and this was in accordance with the results obtained by Unsal et al., 1994⁽²²⁾. A non-significant difference was also observed when group 1 compared with group 2, this is due to the antimicrobial effect of both metronidazole and CHX and their positive role in reduction of microorganism and decreasing inflammation and promoting healing process of the deeper tissue structure.

Probing pocket depth:

Analysis of data showed a gradual reduction in mean PPD in all sites as compared with the baseline values, which persisted throughout the experimental period. RP plus metronidazole gel group demonstrated that scaling and RP was effective in reducing subgingival plaque, calculus and endotoxin attached to the root cementum and reduced bacterial colonization⁽³⁶⁾, but when metronidazole gel was used as adjunctive to scaling and RP this provided an additional effect on decreasing the rate of bacterial recolonization⁽³⁷⁾.

CHX gel has the ability to reduce the bacterial population and changing subgingival microflora toward aseptic environment. However some did not observe benefits with its use⁽³⁸⁾. The explanation of this result may be due to the low frequency of administration as a result of the single application of gel or low drug concentration. At week 2, 4, 6, and 8 when (group 1) was compared to (group 3), there was non-significant difference, this indicates that the debridement of the contaminated soft pocket wall and planing the root is quite enough to eliminate the causative pathogens and enhance reattachment process that result in significant pocket depth reduction, and the latter result was in agreement with Riep et al., 1999⁽³⁹⁾. Also, there were non-significant differences when RP treated sites alone compared with RP plus CHX gel in reduction of mean PPD and this was in accordance with Unsal et al., 1994⁽²²⁾.

Also at week 2, 4, 6, and 8 when (group 1) was compared to (group 2), there were no significant differences in reduction of mean PPD and this was in agreement with Perinetti et al., 2004⁽⁴⁰⁾, this indicated that both subgingival administrations of CHX gel and/or metronidazole gel could lead to getting an equal clinical result in reduction of pocket depth .

Clinical attachment level:

This study showed that there was a gain in attachment level was observed in all three experimental group at all subsequent visits as compared with the baseline values. This gain in attachment level obtained in root planing plus metronidazole gel treated sites was explained in follow that metronidazole gel application into the periodontal pocket and after its contact with crevicular fluid, metronidazole will directly crystallize and step by step it will be released to reach a high concentration in sulcus solution⁽⁴¹⁾. At week 2, 4, 6, and 8, when the group 1 compared with group 2 a non-significant difference was observed, and when compared with group 3 also there was a non-significant difference and this was in agreement with Riep et al.⁽³⁹⁾ and Palmer et al.⁽⁴²⁾. Gains in attachment level in root planing plus CHX gel treated sites were observed and it indicates that CHX contribute to bacterial elimination in deep pockets and attenuates the adhesion of Porphyromonas gingivalis to the epithelial cells⁽⁴³⁾. Also at week 2, 4, 6, and 8 also when group 2 compared with group 3 a non-significant difference was observed in gain of attachment and this was in accordance with Unsal et al., 1994⁽²²⁾.

Conclusions:

- 1-The 3 treatment modalities employed in the study found to be similarly effective in treating site showing ≥ 5 mm probing depth.
- 2-Scaling and root planing was able to cure gingival inflammation and improve the clinical attachment level without the adjunctive application of metronidazole or chlorhexidine gel.

3-This study also determined that both metronidazole and chlorhexidine gel showed no significant difference in improvement of clinical periodontal parameters.

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