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Effectiveness of Subgingivally Delivered 0.4% Moxifloxacin Gel and 0.1% Ofloxacin Gel in the Treatment of Chronic Periodontitis

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Abstract

Background: Local delivery of antimicrobials in sustained or controlled delivery systems are used to enhance the effect of non-surgical periodontal therapy.

Aim: Aim of the present study was to investigate and compare the effectiveness of subgingivally delivered antimicrobial bio-absorbable controlled release 0.4% Moxifloxacin gel and 0.1% Ofloxacin gel as an adjunct to scaling and root planing in the treatment of chronic periodontitis.

Methods and material: A total of 62 patients suffering from chronic periodontitis were randomly divided into group A and group B. The group A were treated with Scaling & Root Planing (SRP) in combination with subgingival application of 0.4% Moxifloxacin gel. The group B received SRP and subgingival application of 0.1% Ofloxacin gel. Probing Depth (PD) and Clinical Attachment Level (CAL) were recorded at baseline, 3, 6 and 9 months.

Statistical analysis: Statistical analysis was done using one way Analysis of Variance (Anova) to test the difference between groups.

Results: The PD scores in experimental group A were 5.22, 3.71 and 3.71 mm and for the experimental group B were 5.30, 3.96 and 3.96 mm at baseline, 3 months, 6 months and 9 months respectively.

Conclusion: Overall, both the therapies led to significant improvements of the investigated parameters. Thus in periodontal pockets with PD of ≥ 5 mm, a single subgingival administration of a 0.4% Moxifloxacin gel and 0.1% of Ofloxacin gel as an adjunct to SRP may result in additional PD reduction compared to SRP alone.

Keywords: Moxifloxacin, Ofloxacin, Periodontitis, Scaling and root planing, W Probing depth

Introduction:

Periodontitis is an infection of the periodontium because of the bacterial etiology and an immune response^[1]. Approximately 500 bacterial taxa inhabit periodontal pockets, which provide a moist, warm, nutritious and anaerobic environment for microbial colonization and multiplication. The microbial etiology of human periodontitis suggests antimicrobial agents as one of the effective treatment options^[2]. The gold standard in the treatment of periodontitis is mechanical debridement of the pockets by scaling

and root planing (SRP)^[3]. However it has limitations, mainly related with the inability to access to deep pockets and to eliminate certain pathogens^[4,5]. To overcome these limitations, the use of systemic or local antimicrobial agents have been proposed^[6,7,8]. Local drug delivery are administered directly into the periodontal pocket providing a high drug concentration and it does not need to be administered daily for a defined time period.

Moxifloxacin is a 4th generation fluoroquinolone antibiotic with a broad antimicrobial activity against aerobic and anaerobic

bacteria.[9,10] It exerts excellent antibacterial activity against a wide range of putative periodontal pathogens. It penetrates well into soft tissues^[11] and is effective against intracellular periodontal pathogens^[12]. Ofloxacin is a quinolone antibiotic modified to include anaerobic bacteria in its antibacterial spectrum. They are considered bactericidal and shows strong antibacterial effects on a wide spectrum of bacteria associated with periodontal disease. There are no studies in the literature comparing the effectiveness of Moxifloxacin and Ofloxacin.

Thus the present study is designed to investigate and compare the effectiveness of subgingivally delivered antimicrobial 0.4% Moxifloxacin gel and 0.1% Ofloxacin gel as an adjunct to scaling and root planing in the treatment of chronic periodontitis.

Materials and methods:

A single center, double blinded, randomized clinical trial was conducted for a period of 9 months. A total of 62 patients (43 males and 19 females) in the age group of 30-75yrs were selected for the study. Patients having probing depth ranging between 5-7mm in different quadrants of the mouth, who have not undergone any periodontal therapy in the previous 6 months and have not taken any antibiotic, steroids and non-steroidal anti-inflammatory drugs which may influence the periodontium in last 1 month were included in the study. Patients with known or suspected allergy to quinolones which is prescribed in this study, existing systemic disease that may influence the severity or progression of periodontitis, in particular Down syndrome, HIV infection, or diabetes mellitus type 1 or type 2, medically compromised, pregnant or lactating women, smokers and sites with overhanging restoration were excluded from the study.

The subjects selected underwent a thorough clinical examination followed by oral prophylaxis and oral hygiene instructions. Patients with probing depth ≥ 5 mm were randomized using computer generated random number table. Group A and Group B will be pre-determined and drug A and drug B will be decided by an examiner. Group A received Scaling and Root Planing [SRP] and subgingivally delivered 0.4% Moxifloxacin gel into periodontal pockets and Group B received Scaling And Root Planing [SRP] and subgingivally delivered 0.1 % Ofloxacin gel into periodontal pockets.

All the selected subjects were examined based on the following clinical parameters at baseline, 3, 6 and 9 months respectively after subgingival application of drugs: Plaque index (PI) - Silness & Loe (1964), Modified Sulcus Bleeding index - A. Mombelli, M.A. Van Oosten, E. Schurch, Jr. N.P. Land, Gingival index - Loe H & Silness (1963), Probing depth (PD) and Clinical attachment level (CAL). All clinical measurements were performed by single examiner who was unaware of treatment carried out for each subject. All the measurements were standardized using customized acrylic stents with grooves, which were prepared on the study model of the patients. The recordings were made using a UNC

15 probe (Hu-Friedy's). The Clinical parameters were recorded at baseline, 3, 6 and 9 months post treatment during the period of 18 months.

Statistical analysis:

One way Analysis of Variance (Anova) to test the difference between groups. To find out which of the two groups means is significantly difference post hoc test of Tukey test is used. The student 't' test was used to determine whether there was a statistical difference between treatment groups in the parameters measured. In all the above test "p" value of less than 0.05 was accepted as indicating statistical significance. Data was analyzed using SPSS (Statistical Package for Social Science, Ver.10.0.5) package.

Results:

62 subjects participated in this study and there were no dropouts from the study. The mean age ($\pm$ standard deviation) of the subjects included in the study was 45.6 ± 14.055 . All patients showed good compliance and the healing period was uneventful for both the treated groups without any signs of inflammation and swelling indicating the biocompatibility of the materials.

The mean reduction in PI scores from baseline to 3, 6 and 9 months was 0.339, 0.429 and 0.554 respectively was seen in group A while in group B, the mean reduction was 0.33, 0.419 & 0.526 respectively. However, the reduction in mean PI score in group A when compared to group B was not significant at 3 months, 6 months and 9 months ($p > 0.05$). The mean reduction in GI score from baseline to 3, 6 and 9 months was 0.289, 0.393 and 0.629 respectively in group A and that in group B was 0.31, 0.397 and 0.614 respectively. However, the mean GI score change was not statistically significant when group A was compared to group B at 3 months, 6 months and 9 months. Also, the mean reduction in MSBI score from baseline to 3, 6 and 9 months 0.057, 0.094 and 0.131 respectively in group A and that in group B was 0.055, 0.092 and 0.134 respectively. The mean MSBI score change was not statistically significant between the group A and group B at follow up visits.

The mean probing depth scores for the group A were 5.22, 3.71, 3.71 and 3.71 mm respectively at baseline, 3 months, 6 months and 9 months. For the group B the mean probing depth scores were 5.30, 3.96, 3.96 and 3.96 mm at baseline, 3 months, 6 months and 9 months respectively. The results obtained in both the groups remained stable after 3 months. Both the groups showed highly significant changes in PD from baseline to 3 months ($p < 0.001$) and remained stable till 9 months. The mean probing depth reduction from baseline to 3 months was 1.51 mm which remained stable thereafter till 9 months for group A ($p < 0.001$); 1.34 mm from baseline to 3 months for group B which remained stable thereafter till 9 months ($p < 0.001$). However when a comparison was made between group A and B, there was no statistically significant difference between both these groups. (Table 1, Graph 1).

Visit	Treatment Group	N	Mean	SD	Min.	Max.	't' value	'p' value
Baseline	Moxifloxacin	65	5.22	0.414	5	6	0.898	0.345
	Ofloxacin	67	5.30	0.578	5	7		
3 months	Moxifloxacin	65	3.71	0.765	2	5	2.847	0.094
	Ofloxacin	67	3.96	0.912	2	6		
6 months	Moxifloxacin	65	3.71	0.765	2	5	2.847	0.094
	Ofloxacin	67	3.96	0.912	2	6		
9 Months	Moxifloxacin	65	3.71	0.765	2	5	2.847	0.094
	Ofloxacin	67	3.96	0.912	2	6		

TABLE 1: COMPARISON OF PROBING DEPTH AT DIFFERENT OBSERVATION PERIODS BETWEEN THE TWO GROUPS

The mean values of CAL scores at baseline, 3 months, 6 months and 9 months for group A were 3.48, 1.98, 1.95 & 1.95 mm whereas that for the group B were 3.60, 2.19, 2.18 and 2.18 mm respectively. CAL gains were statistically significant for both groups in comparison to baseline levels ($p < 0.001$). The mean clinical attach-

ment level (in mm) gain was 1.50 at 3 months, 1.53 at 6 and 9 months for group A ($p < 0.001$); while it was 1.41 at 3 months & 1.42 at 6 and 9 months for group B ($p < 0.001$). When a comparison was made between the groups, there was no statistically significant difference between the two groups (Table 2, Graph 2).

Visit	Trt. Group	N	Mean	SD	Min.	Max.	't' value	'p' value
Baseline	Moxifloxacin	65	3.48	0.812	2	7	0.751	0.388
	Ofloxacin	67	3.60	0.780	2	6		
3 months	Moxifloxacin	65	1.98	1.053	1	6	1.276	0.261
	Ofloxacin	67	2.19	1.076	1	6		
6 months	Moxifloxacin	65	1.95	1.022	1	6	1.525	0.219
	Ofloxacin	67	2.18	1.072	1	6		
9 Months	Moxifloxacin	65	1.95	1.022	1	6	1.525	0.219
	Ofloxacin	67	2.18	1.072	1	6		

TABLE 2: COMPARISON OF CLINICAL ATTACHMENT LEVEL AT DIFFERENT OBSERVATION PERIODS BETWEEN THE TWO GROUPS

Discussion:

Various authors have studied the effect of topical application of Moxifloxacin and Ofloxacin in the form of controlled release drug. They all suggested the use of topical chemotherapy of both these drugs was safe and effective for periodontal therapy. To the best of our knowledge, no study compared the use of 0.4% Moxifloxacin gel and 0.1% Ofloxacin gel as local drug delivery agent in the treatment of chronic periodontitis.

In this double blinded, randomised clinical trial we evaluated the efficacy of adjunctive subgingival administration of 0.4 % Moxifloxacin gel and 0.1% Ofloxacin gel in the treatment of chronic periodontitis. A total of 62 subjects in the age group of 30 to 75 years meeting the inclusion criteria were selected after the completion of initial phases in all the patients. These selected patients were divided randomly into two groups and were treated as follows: Group A - patients treated by 0.4 % Moxifloxacin gel, Group

B - patients treated by 0.1 % Ofloxacin gel. The clinical parameters were recorded at baseline, 3, 6 and 9 months.

In this study, the group A showed statistically significant reductions in PI scores at 3, 6 & 9 months follow up visits when compared to baseline levels. Also, the group B demonstrated statistically significant reductions in PI scores at 3, 6 & 9 months follow up visits when compared to baseline levels. These findings were in agreement with previous study done by Hiroshi Yamagami et al 1992 [13]. The reduced PI scores indicated that the chemical control of subgingival plaque by PT-01 (Ofloxacin) could also have an inhibitory effect on the supragingival plaque.

Also, both the groups showed statistically significant reduction in GI and MSBI scores at 3, 6 & 9 months follow up visits when compared to baseline levels. In a similar study Hiroshi Yamagami et al [13] showed reduction in GI scores during 1 month follow up visit when PT-01 (Ofloxacin) was used. GI and MSBI reflect gingival

inflammation. The significant reduction at the sites indicated that the inflammation had improved with the reduction of pathogenic bacteria. This reduction in pathogenic bacteria was due to PT-01 (Ofloxacin), because PT-01 has proven inhibitory effects on many kinds of pathogenic bacteria present in the subgingival microflora.^[14] All the scores did not show any statistically significant difference during the follow up visit within the group and between the groups.

Reduction in the probing depth is one of the major clinical outcomes measured to determine the success of a treatment. A significant reduction in probing depth was found in both groups compared to baseline at all-time intervals. In the present study the group A exhibited statistically significant reduction in mean PPD at 3 months which remained stable during 6 & 9 month follow up visit. Similar results were confirmed by Isabel Cristina Guzman et al 2012 [15], who demonstrated significant reduction in PPD when compared to baseline while using systemic Moxifloxacin. Arndt Guentsch et al compared SRP with adjunctive Moxifloxacin, SRP with adjunctive doxycycline to SRP alone; they found PD reduction was significantly greater in the MOX group compared to the DOX group and the controls. Thomas F. Flemmig et al (2011)[16], also demonstrated significant reduction in PPD when compared to baseline while using 0.4% Moxifloxacin gel at three months follow up.

The group B also showed significant reduction in PD at 3 months follow up visit and this result remained stable during 6 & 9 months follow up visit. A study was done by J.W.Kleinfelder et al (2000)^[17] where they evaluated the effect of systemic Ofloxacin therapy as an adjunct to flap surgery. At 3 and 12 months following therapy mean PD reduction in test group was 3.6 and 3.8 mm compared to control group which was 4 and 4.1 mm respectively. Furthermore, the uptake of ofloxacin by resting polymorphonuclear leukocytes (PMN) appears to be much higher than the uptake of other quinolones. PMN may serve as vehicles for transport and delivery of fluoroquinolones as they migrate from the bloodstream to infection sites. By this mechanism, PMN have the potential to enhance resolution of an infection by increasing the local quinolone concentration at sites most beneficial to the host. Similar results were showed by Hiroshi Yamagami (1992)[13].

On comparison group A did not show significantly greater reduction in PD than that of group B. However, group A showed slightly more reduction in PD when compared to group B (1.51 ± 0.765 vs 1.34 ± 0.912). This could be attributed to the fact that the first and second generations act only on Gram-negative aerobic bacteria.[18] Newer quinolones, of which the most important representative is Moxifloxacin (MOX), have improved activity against Gram-positives and anaerobes.[19] In vitro studies [12,20] showed good activity against planktonic microorganisms as well as bacteria located within a biofilm or intracellularly.

In the current study, the group A showed statistically significant gain in CAL at 3, 6 & 9 months as compared to baseline. Similarly, Arndt Guentsch et al in 2008 [21] showed that CAL gains were significantly greater in the SRP plus adjunctive MOX group compared to the SRP alone group. Comparing full mouth SRP

plus 0.4% Moxifloxacin gel to SRP alone Thomas F. Flemmig et al in 2011^[16] found a gain in CAL of 0.6 - 0.8 mm in the test group at 12 weeks. In the present study the mean gain in clinical attachment level was comparatively higher in group A. Statistically significant gain in CAL was also observed in group B at 3, 6 & 9 months. Similar results were confirmed by J.W.Kleinfelder et al (2000)[17].

Conclusion:

The findings of the present study suggested that the outcome of the initial periodontal therapy may benefit from the adjunctive subgingival administration of 0.4 % Moxifloxacin gel and 0.1% Ofloxacin gel and both these gels are safe and effective for the treatment of chronic periodontitis. Further studies are needed to evaluate the long term clinical advantage of adjunctive therapy with 0.4% Moxifloxacin gel and 0.1% Ofloxacin gel in larger sample size and microbiological analysis in the treatment of chronic periodontitis. It might be interesting to explore the possible surplus value of subgingival administration of these two gels for other forms of periodontal diseases such as aggressive periodontitis, refractory periodontitis & peri-implantitis. However, long-term studies, using different vehicles and concentrations of Moxifloxacin and Ofloxacin gel should be carried out to affirm the observations of our study.

Clinical interpretation:

Local application of antimicrobials could reduce the risk of adverse events associated with systemic antimicrobials, including the development of bacterial resistance. Also, antimicrobial agents administered directly into the periodontal pocket aim at inhibition of the growth of periodontal pathogenic bacteria or modulate the inflammatory response, thereby limiting periodontal tissue destruction.

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