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Evaluation of the Efficacy of Ciprofloxacin as Topical Adjunctive Therapy in Non-Surgical Treatment of Stage I and II Grade A Periodontitis (Clinical and Biochemical Study)

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ABSTRACT

Aims: This study was performed to evaluate clinically and biochemically the efficacy of ciprofloxacin as adjunctive in non-surgical treatment of stage I and II Grade A periodontitis, through evaluation of the clinical parameters as well as IL-6 level in GCF.**. Subjects and Methods:** 20 patients of both sex divided into two groups. Group 1 included 10 patients were treated by only conventional periodontal therapy (scaling and root planing). Group 2 included 10 patients were treated by scaling and root planing followed by topical intra pocket application of Ciprofloxacin gel 1%. Evaluated clinically at baseline, 1 month and 3 months. The biochemical evaluation of interleukin 6 was done at baseline, 1 month and 3 months. **Results:** Clinical parameter showed a statistically significant differences in both groups at the different intervals when compared to the baseline. All parameter showed in group 2 statistically significant difference between 1 month and 3 month. When groups 2 was compared to group 1 all parameter showed statistically reduction at 1 month and 3 months in relation to baseline. Biochemical marker showed a statistically significant differences were showed in both groups at the different intervals when compared to the baseline with statistically significant difference between 1 month and 3 month. **Conclusion:** The topically applied ciprofloxacin seamed to exhibit a synergistic action in treatment of stage I and II grade A periodontitis.

KEYWORDS

Ciprofloxacin, periodontitis, synergistic action ,root scaling , root planning.

INTRODUCTION

Periodontal diseases are a multifactorial inflammatory conditions caused by interaction between oral bacteria organized in complex communities that form biofilms, adhering to dental structure and infecting the tooth supporting tissue and the local host defense response[(1)].

According to 2017 workshop to develop a new classification framework for periodontitis [(2)], Stage I; is the borderland between gingivitis and periodontitis and represents the early stages of attachment loss as a response to gingival inflammation and biofilm dysbiosis. The

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interdental stage I CAL is between 1-2 mm, the radiographic bone loss found in the coronal third >15% mostly horizontal bone loss with maximum 4 mm probing depth. Stage II; represents established periodontitis in which a carefully performed clinical periodontal examination identifies the characteristic damages that periodontitis has caused to tooth support. The interdental stage II CAL is between 3-4 mm, the radiographic bone loss found in the coronal third 15% to 33% mostly horizontal bone loss with maximum 5 mm probing depth[3].

While Grade A, is a primary criteria depend on no evidence of bone loss over 5 years, the percentage of bone loss to patient age is >0.25 and there is heavy biofilm deposit with low level of destruction[4].

IL-6 has a significant effect in inflammatory process as pro-inflammatory cytokine [5]. It has been found in elevated levels in the gingival fluid and tissue in patients with periodontitis and associated with attachment loss and tissue destruction due to its effect on osteoclast differentiation [6].

The treatment of periodontitis is focused on arresting destruction of the periodontal support of the teeth by eliminating pathogenic bacteria present in the inflamed pocket. It is performed by mechanical scaling and root planning (SRP) and the efficacy of this procedure is well documented[7]. However, variations in the depth of periodontal pockets often result in variable effectiveness of SRP and in many cases, mechanical therapy alone cannot completely eliminate periodontal pathogens present in periodontal pockets, as they are inaccessible to the instruments and the use of systemic or local antibiotics may enhance treatment effects and overcome the limited efficacy of conventional treatment [8].

Ciprofloxacin (CPF) is a second-generation fluoroquinolone antibiotic. It has been used as an adjunctive therapy for periodontal disease treatment as its spectrum of activity includes most strains of bacteria such as gram negative rods in periodontal disease[9].

METHODOLOGY

This study was designed as randomized controlled clinical trial carried out on 20 patients of both sex (ranged in age from 20 -45 years) with Stage I or II Grade A Periodontitis with probing pocket depth ≤ 5mm and clinical attachment loss 1-4mm. All patients were selected from those attending at the out-patient clinic, Oral Medicine and Periodontology Department, Faculty of Dental Medicine, Al- Azhar University, Assiut Branch.

All subject were

1. All patients were free from any systemic diseases according to American dental academy general guideline for referring dental patients to specialist and other setting for care[10].
2. Patients with stage I to stage II, grade A periodontitis. Stage I have CAL 1 to 2mm with no tooth loss and probing depth ≤4 mm. Stage II have CAL 3 to 4mm with no tooth loss and probing depth ≤5 mm. Grade A: no evidence of CAL or bone loss over 5 years, the patient is nonsmoker and no evidence of diabetes.
3. Weren't subjected to previous periodontal therapy, received antibiotics or non-steroidal anti-inflammatory for at least three months prior to sample collection.

Group 1: Included 10 patients with stage I to stage II, grade A periodontitis patients were treated by only conventional periodontal therapy (scaling and root planing).

Group 2: Included 10 patients with stage I to stage II, grade A periodontitis patients were treated by scaling and root planing followed by topical intra pocket application of Ciprofloxacin gel 1%.

Periodontal evaluation The periodontal conditions were evaluated for all patients at base line, 1 and 3 month after treatment using the following parameters: Plaque Index (PI), Gingival Index (GI), Probing Pocket Depth (PPD), Clinical Attachment Level (CAL) [11-14].

Sample collection and preparation

- GCF samples were obtained from the site which showed the highest probing depth (range 3-5mm).
- The teeth selected for sampling were isolated with cotton roll, and supra gingival plaque was removed without touching the marginal gingiva.
- GCF sampling was obtained from all patients at baseline, 1 and 3 months after treatment.

Assessment of IL-6 in GCF samples The samples were assayed for IL6 levels using enzyme-linked immune-sorbent assay (ELISA).

Preparation of Ciprofloxacin gel 1%:

- Buffer solution was prepared by dissolving 9.08 gm of potassium dihydrogen phosphate in sufficient distilled water to make one liter. The pH was adjusted to 7.2.
- Gels were prepared by dispersing the polymer at different concentrations in water by continuous stirring for a period of 2 hours. The ciprofloxacin powder was dissolved in propylene glycol and the solution was added gently to the above polymer dispersion, under continuous stirring. The mixture was stirred gently until a homogeneous gel was formed. The gels prepared were stored in wide mouthed bottles. Entrapped air bubbles were removed by keeping the gels in a vacuum oven for 2 hours.

RESULTS

Changes in plaque Index (PI) and GI:

Group 1 and 2 showed statistically significant difference between baseline, 1 month and 3 month where ($p<0.001$), significant reduction when comparing the 1 month and 3 month with the baseline ($p<0.001$). Group 1 showed no statistically significant difference between 1 month and 3 month where ($p=0.843$) and ($p=0.343$) respectively, however group 2 showed statistically significant difference ($p=0.005$) and ($p= 0.037$) respectively. No significant difference between groups at baseline and 1 month. However at 3 months PI showed statistically significant difference when group 1 was compared with group 2 ($p= 0.026$), However GI showed no significant difference between the two groups when compared with each other.

Changes in Probing pocket depth (PPD):

Group 1and 2 showed statistically significant difference between baseline, 1 month and 3 month where ($p<0.037$) and ($p=0.001$) respectively, significant reduction when comparing the 1 month and 3 month with the baseline ($p<0.001$) and ($p=0.001$) respectively. Group 1 showed no statistically significant difference between 1 month and 3 month where ($p= 0.591$), however group 2 showed statistically significant difference where ($p= 0.005$).

Changes in Clinical attachment level (CAL):

Group 1and 2 showed statistically significant difference between baseline, 1 month and 3 month where ($p=0.024$) and ($p=0.001$) respectively, significant reduction when comparing the 1 month and 3 month with the baseline for group1 ($p<0.001$), group 2 ($p=0.001$) and ($p>0.001$) respectively. Group 1 showed no statistically significant difference between 1 month and 3 month where ($p= 0.443$), however group 2 showed statistically significant difference where ($p= 0.015$).

PPD and CAL showed no significant difference between groups at baseline and 1 month. At 3 months there was no significant difference between the two groups when compared with each other.

Changes in Interleukin-6 (IL-6):

Group 1 and 2 showed statistically significant difference between baseline, 1 month and 3 month where ($p<0.001$), significant reduction when comparing the 1 month and 3 month with the baseline ($p<0.001$), statistically significant

difference was found between 1 month and 3 month where (*p >0.001*).

At baseline there was no significant difference between groups (*p=0.927*). At 1 month there was statistically significantly different between groups (*p<0.001*).

At 3 months there was statistically significantly different between groups (*p<0.001*).

Table (1) *Showing means ± SD and Paired sample t- test of PI, GI, PPD, CAL and IL-6*

Parameters	Group	Baseline	I Month	3 Months	Base vs 1 month	Base vs. 3 month	I month vs 3 month
		Mean±SD	Mean±SD	Mean±SD	(P-value)	(P -value)	(P -value)
Plaque Index	Group I	2.61±0.5	0.65±0.1	0.65±0.1	<0.001	<0.001	= 0.843
	Group 2	2.53±0.5	0.63 ± 0.2	0.48±0.1	<0.001	<0.001	= 0.005
Gingival Index	Group I	2.34 ± 0.7	0.63 ± 0.2	0.58±0.2	<0.001	<0.001	0.343
	Group 2	2.33±0.5	0.55 ± 0.2	0.45±0. 2	<0.001	<0.001	0.037
Probing Pocket Depth	Group I	4.67±0.5	3.25 ± 0.7	3.21±00.7	<0.001	<0.001	- 0.591
	Group 2	4.58±0.7	3.13 ± 0.7	2.54±0.7	=0.001	<0.001	0.005
Clinical Attachment Level	Group I	3.61± 0.5	2.34 ± 0.7	2.10±0.8	<0.001	<0.001	0.443
	Group 2	3.64± O. 7	2.21 ± 0.7	1.70±0.6	=0.001	<0.001	0.015
Interleukin 6	Group I	165.5±17.1	154.4±12.9	139.6±10.8	<0.001	<0.001	0.001
	Group 2	161.5±14.4	144.1±9.1	127.9+ 10.1	<0.001	<0.001	0.001

DISCUSSION

Non-surgical mechanical periodontal treatment (scaling and root planing) is main and the first recommended approach to the control of periodontal disease. It has proven to be the gold standard of periodontal therapy for most patients specially with stage I and stage II periodontitis. However it was showed to have significant limitations including difficulty in accessing deep and tortuous pockets, furcation and vertical defects [15].

Systemic antimicrobial agents can be used as adjuncts to conventional mechanical therapy [16].

There are multiple advantages of local drug delivery route that it can attain in sub-gingival site 100-fold higher concentrations of an antimicrobial agent in comparison with systemic drug regimen. Therefore, the present study was designed to use intra-pocket topically applied antimicrobial as adjunctive to mechanical debridement [17].

In this study the mean age of the patient participant was 32.8±5.9 years old as it was reported that periodontitis commonly affected age is 30 years or more [18].

Regarding to the plaque index, there were statistically significant differences when the results of the different intervals were compared with baseline. There were statistically significantly differences between the two groups at 3 month only.

For the interaction between time and treatment group, the reduction in PI was more evident in ciprofloxacin group than controlled group.

The gingival index results illustrated statistically significant difference between the different evaluations intervals when compared with each baseline in two groups. There was no significant difference between the two group at baseline, 1 month and 3 months. For the interaction between time and treatment group, no significant difference was found for the interaction between the two groups.

These results are in agreement with different clinical studies that used ciprofloxacin as adjunctive monotherapy to scaling and root planning stating that, there were statistically significant improvement in PI and GI after treatment with or without the use of antimicrobial. In addition, there was no statistically significant difference between the treatment groups in PI and GI after 3 months. The showed marked reduction in PI and GI, in all groups could be due to the combined effect of the drug and scaling with root planing [19].

The present study exhibited statistically significant reduction in the probing pocket depth and clinical attachment level in two groups after 3 months when compared to baseline. For the interaction between time and treatment group, the reduction in PPD and CAL was more evident in ciprofloxacin group than control group.

Similar results were reported by a study on ciprofloxacin gel but with statistically significant to test group after 30 days[19].

Regarding to GCF level of Interleukin-6, statistically significant differences were illustrated in the different intervals when compared with baseline in the two groups.

Most of the studies that used antimicrobial local delivery drugs specially ciprofloxacin evaluated its antimicrobial activity on periodontal pathogenesis but not on the inflammatory process. While different studied evaluated the IL-6 level following conventional periodontal therapy or one stage full mouth scaling and root planing and reported that IL-6 level decreased significantly after 6 to 8 weeks[20].

CONCLUSION

The topically applied ciprofloxacin seamed to exhibit a synergistic action in treatment of stage I and II grade A periodontitis. Interleukin-6 (IL-6) is appeared as a good biomarker not only to determine periodontal disease activity but also to evaluate the outcomes following periodontal treatment through the strong correlation with the clinical parameters.

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تقييم فعالية السيبروفلوكساسين كعلاج مساعد موضعي في العلاج غير الجراحي للمرحلة الأولى والثانية من التهاب اللثة من الدرجة الأولى {دراسة سريرية وكيميائية حيوية}

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الملخص :

الهدف: م إجراء هذه الدراسة لتقييم فعالية السيبروفلوكساسين سريريًا وكيميائيًا كعامل مساعد في العلاج غير الجراحي للمرحلة الأولى والثانية من التهاب اللثة من الدرجة الأولى، من خلال تقييم المعلمات السريرية بالإضافة إلى مستوى IL-6 في GCF.

المواد والأساليب: 20مريضا من كلا الجنسين تم تقسيمهم إلى مجموعتين. المجموعة الأولى شملت 10 مرضى تم علاجهم عن طريق علاج اللثة التقليدي فقط (تجريف وتخطيط الجذر). المجموعة الثانية شملت 10 مرضى تم علاجهم عن طريق التقشير وتخطيط الجذر يليه تطبيق موضعي داخل الجيب لجيل سيبروفلوكساسين 1٪. تم تقييمه سريريًا عند خط الأساس، شهر واحد و3 أشهر. تم إجراء التقييم الكيميائي الحيوي للإنترلوكين 6 عند خط الأساس، بعد شهر واحد و3 أشهر.

النتائج: أظهرت المعلمات السريرية وجود فروق ذات دلالة إحصائية في كلا المجموعتين على فترات مختلفة بالمقارنة مع خط الأساس. أظهرت جميع المعلمات في المجموعة 2 فروق ذات دلالة إحصائية بين شهر واحد و 3 أشهر. عند مقارنة المجموعات 2 بالمجموعة 1، أظهرت جميع المعلمات انخفاضًا إحصائيًا عند شهر واحد و3 أشهر بالنسبة إلى خط الأساس. أظهرت العلامة البيوكيميائية وجود فروق ذات دلالة إحصائية في كلا المجموعتين على فترات مختلفة بالمقارنة مع خط الأساس مع وجود فرق ذو دلالة إحصائية بين شهر واحد و 3 أشهر.

الخلاصة: إن دواء سيبروفلوكساسين المطبق موضعياً يظهر تأثيراً تآزرياً في علاج المرحلة الأولى والثانية من التهاب اللثة من الدرجة الأولى.

الكلمات المفتاحية: سيبروفلوكساسين، التهاب اللثة، عامل معزز، كحت الجذر، تخطيط الجذر.