

The effectiveness of adjuvant therapy with ciprofloxacin in non-surgical treatment of severe chronic periodontitis

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ABSTRACT

Introduction & Objective: Periodontitis is one of the most common microbial infections in adults known as an inflammatory bacterial disease that affects the protective tissue of the tooth. Ciprofloxacin is a broad-spectrum antibacterial agent that can be used as a systemic drug in the treatment of periodontitis. The aim of this study was to determine the effect of systemic administration of ciprofloxacin antibiotic, along with scaling and root planning (SRP), in the treatment of chronic periodontitis patients. **Methods:** In this double-blind clinical trial study, 80 patients with chronic periodontitis with inclusion criteria into the study were equally divided into two groups of case and control. At first, the consent form was completed by the patient and the GBI, PD and CAL indices in these patients were measured and recorded in the relevant information form. All patients underwent scaling and root planning (SRP), and health education was given to all patients in a similar way. Patients were asked to avoid using any antimicrobial mouthwash during the study period. Immediately after completing the SRP, patients were randomly assigned to two equal groups of test and control using block randomization. For the case group, ciprofloxacin 500 mg was given twice daily for 7 days and placebo capsule was administered with the same dose and timing sequence for control group. The patient and the prescriber were not aware of the type of drug used. In the first months (before intervention), two and four (after intervention) clinical indexes were recorded. The results were analyzed using SPSS 20 software. **Results:** In each group, 55% were female and 45% were male. The mean age in the ciprofloxacin group was 47.44 and in the control group was 47.3 years. Before treatment, there was bleeding in the teeth in all of the patients in the two groups. In the second and fourth months, the frequency of patients with bleeding in the ciprofloxacin treatment group was significantly lower than the control group. The GBI, PD, and CAL values in both case and control groups have a significant reduction in clinical parameters over a period of one to three months. Also, the improvement in parameters of GBI, PD and CAL over time in the case group was significantly better than the control group. On the other hand, PD and CAL levels did not significantly differ between men and women at any time. **Conclusion:** The use of ciprofloxacin with scaling and root planning (SRP) is effective in treating patients with chronic periodontitis.

Keywords: Chronic periodontitis, non-surgical treatment, ciprofloxacin.

Introduction

Pathogenic bacteria present in the microbial plaque are the main cause of chronic periodontitis. A large number of black pigmented gram negative rods and spirochetes are found in deep

periodontal pockets, while natural salicylic of gum are mostly gram-positive cocci [1-3], base therapy in periodontitis includes oral microbial plaque control (oral health education), mechanical debridement of the dental surface (scaling and root planning) and removal of local stimuli. Periodontal surgeries are also used to remove the pocket and, if possible, reconstruction of periodontal tissues later in life. These therapeutic methods are effective in the orientation of the microbial flora to the natural microbial flora of the gum, as well as to the improvement of periodontal clinical indices [4, 5]. However, the penetration of pathogenic bacteria into the gum tissue and even dental tubules has led to ineffective long-term mechanical treatments in many periodontal diseases, and chemical methods such as antibiotic therapy can be used [6, 7].

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Periodontitis is one of the most common microbial infections in adults known as an inflammatory bacterial disease that affects the protective tissue of the tooth. There are a total of 2 major periodontal diseases, including gingivitis and periodontitis. Gingivitis involves a brief inflammation of the non-connective gingiva, which is considered to be relatively reversible and functional, while periodontitis is a generalized inflammatory condition in periodontal tissues that results in apical appendicitis migrating to the root surface and progressive degeneration of periodontal ligaments and alveolar bone.

The periodontal disease is a cycle of intensification, recovery, and delay, which is closely related to the patient's immune response^[8]. Now in recent years, two general trends have been suggested to improve this condition in periodontitis patients:

- 1) The use of adjuvant antibiotics with debridement in a 24-hour period, known as a complete oral anesthetic.
- 2) The use of systemic antibiotics, which is also supported by validated systemic reviews of trials, which is believed to be effective in the treatment of chronic periodontitis^[9].

Ciprofloxacin is an antibacterial agent that, after penetrating into the cell membrane of the bacterium, stops DNA synthesis by inhibiting the DNA gyrase enzyme. This enzyme plays the role of rewinding the two opened DNA strands. By controlling this enzyme by this drug, the two DNA strands that are opened for copying will not be re-connected and will be destroyed^[10].

Paknejad et al. (2010) showed that in patients with periodontitis, the use of erythromycin, along with the scaling and root planning was much more effective than this method without using azithromycin^[11].

On the other hand, research has shown that the combination of metronidazole and ciprofloxacin is effective against A.a^[12]. Metronidazole targets mandatory anaerobes and ciprofloxacin targets optional bacteria that can be an effective and strong method against various infections^[13]. Studies of this drug combination in the treatment of recurrent periodontitis have demonstrated a certain clinical improvement. This drug combination can provide a therapeutic benefit (by reducing or eliminating pathologic organisms) and a prophylactic effect by producing the dominant streptococcal microflora^[14].

Regarding the abovementioned materials, and also the wide-spectrum effect of ciprofloxacin, the present study was conducted with the aim of determining the effect of systemic administration of ciprofloxacin antibiotic with scaling and root planning in the treatment of chronic periodontitis patients.

Materials and Methods

The method of this study is a double-blind placebo-controlled clinical trial. In this study, according to the results of similar studies^[11], using convenience sampling method, 80 chronic periodontitis patients referring to the periodontics department of the Faculty of Dentistry, Zahedan University of Medical Sciences, with inclusion criteria into the study (completion of consent form to participate in the study, aged 18 years and older, suffering from chronic moderate to severe periodontitis,

3-5 mm clinical attachment loss in more than 30% of the oral areas and presence of at least 20 teeth) were selected and equally studied in two groups of case and control. Also, to match the two groups, in each group, half the population was selected from women and half of men. Exclusion criteria include lack of collaboration, antibiotic therapy over the past three months, history of allergy to ciprofloxacin, smokers and tobacco users, systemic diseases affecting periodontal conditions such as diabetes, blood and immune system disorders, pregnant women, periodontal interventions over the past three months and those treated with warfarin, antacidT, and cyclosporine^[1].

Procedures

Gingival bleeding index (GBI), pocket probing depth (PPD), and clinical attachment level (CAL) were recorded in these patients. All patients underwent complete scaling and root planning (SRP) and health education was given to all patients in a similar way (brushing in periodontal patients with modified stilman analysis, and in patients without gingival recession using bas method and the use of dental floss). Patients were asked to avoid using any antimicrobial mouthwash during the study period. Immediately after completing the SRP, patients were randomly assigned to two equal groups of test and control using block randomization. In this study, the drug was provided by the project presenter to researcher, and the researcher delivered them to the patient without knowing which drugs were available. In this study, for the case group, the antibiotic ciprofloxacin 500 mg produced by the Daroo Pakhsh (drug distributing) company was given twice daily for 7 days^[15]. In the control group, placebo capsules were administered with the same dose and timing sequence. The patient and the prescriber were not aware of the type of drug used. In the first month (before intervention), two and four after intervention, patients were referred to assess health status and to measure and record clinical parameters. They also received health education. Index plaque was kept to 25% for all patients (according to the o'leary index)^[16]. If the patient was in trouble, or if they did not observe the health and did not cooperate, they were excluded from the study. It should be noted that during the study, all information was measured and recorded by constant person.

In order to describe the data, the mean and standard deviation were used. In order to compare the measured parameters of each group over time, the Wilcoxon test (due to the lack of normal distribution of data) and for comparison of the parameters in two groups, the Mann-Whitney test (due to the lack of normal distribution of data) was used. The comparison of qualitative parameters and frequency between two groups was done by Chi-square test.

Findings

Equally, 55% (22 subjects) of women and 45% (18 subjects) were male in each of the studied groups. The mean and standard deviation of the age group in the ciprofloxacin group was 44.47 and 10.78, respectively and in the control was 47.3

years with 10.62 years that according to t-test, there was no significant difference in the mean age of the two groups ($t = -18.1, p = 0.24$).

The frequency of patients with bleeding in the two groups of control and case at the time of study is presented in Table 1.

Table 1. Comparison of the frequency of patients with bleeding in the control and case groups at the time of study

	Before Treatment Number (%)	Second Month Number (%)	Fourth Month Number (%)
Case	40 (100%)	1 (2.5%)	1 (2.5%)
Control	40 (100%)	8 (20%)	13 (32.5%)
Chi square test		Value=6.13 P-Value=0.013	Value=12.46 P-Value=0.001

Table 1 shows that before treatment in all patients, there were two groups with bleeding in the teeth. In the second month, one patient in the case group and eight in the control group had bleeding. In the fourth month, one in the case group and 13 in the control group had bleeding. In the second and fourth months, the frequency of bleeding in the ciprofloxacin group was significantly lower than the control group. Comparison of GBI in the control and case groups at the time of study is presented in Table 2.

Table 2. Comparison of GBI in two groups of control and case at the time of study

	Before Treatment Mean ± SD	Second Month Mean ± SD	P-Value	Fourth Month Mean ± SD	P-Value*
Case	1.52±1.3	0.67±0.82	<0.001	0.3±0.51	0.001
Control	1.7±1.15	1.02±1.14	0.001	0.72±0.98	0.114
P-Value**	0.540	0.041		0.018	

P value of the Wilcoxon test to compare the values in the pre-test and the second month

P value * Wilcoxon test to compare values in the second and fourth months

P value ** Mann-Whitney test for comparison in two groups

According to Table 2, GBI examination showed that in the ciprofloxacin-treated group, the mean GBI in the first month was 1.72 ± 1.32 , in the second month 0.67 ± 0.82 and in the third month 0.3 ± 0.51 . The Wilcoxon test shows that there is a significant decrease in GBI over a period of from one month to four months. In the control group, the GBI level was 1.7 ± 1.15 in the first month and 1.02 ± 1.14 in the second month and 0.72 ± 0.98 in the third month. The Wilcoxon test shows that there is a significant decrease in GBI over a period of one month to two months. Also, comparison of GBI in the two groups shows that there is no significant difference between the two groups before treatment. However, in the second and third months, the amount of GBI in the ciprofloxacin treatment group was significantly lower than the control group.

Diagram 1 shows the comparison of GBI in the control and case groups at the time of the study.

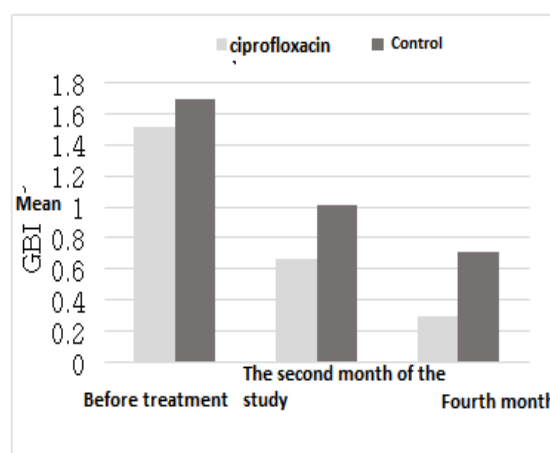


Diagram 1: Comparison of GBI in the control and case groups at the time of study

Table 3 shows PD comparison between the control and case groups at the time of the study.

Table 3: Comparison of PD in two groups of control and case at the time of study

	Before Treatment Mean ± SD	Second ,onth Mean ± SD	P-Value	Fourth Month Mean ± SD	P-Value*
Case	3.52±0.75	2.84±0.44	>0.000	2.87±0.39	0.552
Control	3.63±0.59	3.28±0.31	0.001	3.22±0.34	0.269
P-Value**	0.480	>0.000		>0.001	

P value of the Wilcoxon test to compare the values in the pre-test and the second month

P value * Wilcoxon test to compare values in the second and fourth months

P value ** Mann-Whitney test for comparison in two groups

According to the results of Table 3, in the ciprofloxacin treatment group, the PD levels in the first month was 3.52 ± 0.75 , in the second month 2.84 ± 0.44 in the third month, 2.87 ± 0.39 . The Wilcoxon test shows that there is a significant decrease in PD levels over a period of one month to two months. In the control group, the PD level in the first month was 3.63 ± 0.59 in the second month 3.28 ± 0.31 and in the third month 3.22 ± 0.34 . The Wilcoxon test shows that there is a significant decrease in PD levels over a period of one month to two months.

Also, comparing PD in both groups shows that there is no significant difference before treatment group in the two groups. However, in the second and third months, the level of PD in the ciprofloxacin treatment group was significantly lower than the control group.

Diagram 2 shows PD comparison between the control and case groups at the time of the study.

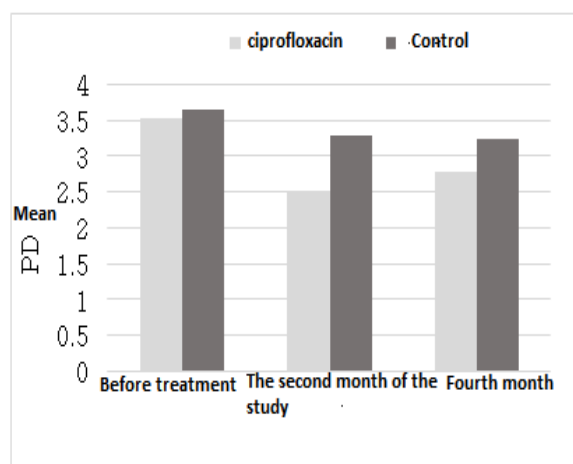


Diagram 2: Comparison of PD in two groups of control and case at the time of study

Table 4 shows the comparison of CAL in the control and case groups at the time of the study.

Table 4. Comparison of CAL in the control and case groups at the time of study

	Before Treatment	Second Month	P-Value	Fourth Month	P-Value*
	Mean \pm SD	Mean \pm SD		Mean \pm SD	
Case	3.97 \pm 0.52	2.94 \pm 0.80	<0.001	2.73 \pm 0.67	<0.001
Control	4.18 \pm 0.42	3.7 \pm 0.69	0.001	3.69 \pm 0.72	0.888
P-Value**	0.055	<0.000		>0.000	

P value of the Wilcoxon test to compare the values in the pre-test and the second month

P value * Wilcoxon test to compare values in the second and fourth months

P value ** Mann-Whitney test for comparison in two groups

According to the results of Table 4, in the ciprofloxacin treatment group, the CAL level in the first month was 3.97 \pm 0.52, in the second month 2.94 \pm 0.80 and in the fourth month 2.73 \pm 0.67. The Wilcoxon test shows that there is a significant decrease in CAL levels over a period of one month to four months. In the control group, the CAL level in the first month was 4.18 \pm 0.42, in the second month 3.7 \pm 0.69 and the fourth month 3.69 \pm 0.72. The Wilcoxon test shows that there is a significant decrease in CAL over a month to two months. Also, comparing the CAL in the two groups showed that there was no significant difference in the pre-treatment in the two groups. However, in the second and fourth months, CAL levels were significantly lower in the ciprofloxacin treatment group than in the control group.

Diagram 3 shows PD comparison between the control and case groups at the time of the study.

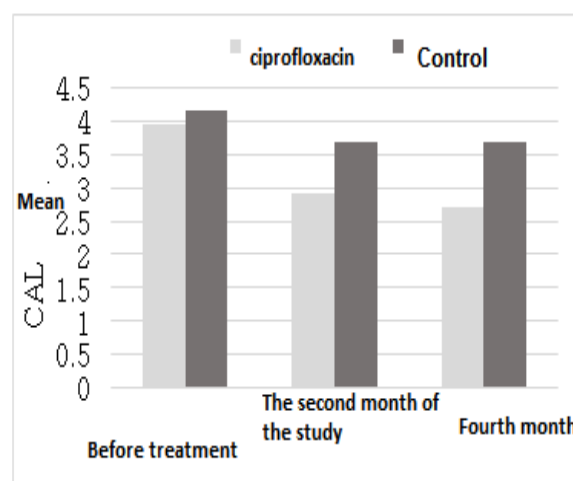


Diagram 3: Comparison of CAL in the control and case groups at the time of study

To answer this question, is the effect of the drug above different between the two groups of women and men? Mann-Whitney test was used for comparison in two groups (Table 5).

Table 5: Comparison of clinical parameters in the ciprofloxacin group among women and men

		Before Treatment	Second Month	Fourth Month
		Mean \pm SD	Mean \pm SD	Mean \pm SD
GBI	Female	1.73 \pm 1.28	0.91 \pm 0.87	0.45 \pm 0.60
	Male	1.28 \pm 1.32	0.39 \pm 0.70	0.11 \pm 0.32
	P-Value	0.055	0.041	0.001
PD	Female	3.66 \pm 0.79	2.89 \pm 0.45	2.85 \pm 0.42
	Male	3.36 \pm 0.69	2.80 \pm 0.43	2.9 \pm 0.37
	P-Value	0.473	0.055	0.336
CAL	Female	4.04 \pm 0.52	2.91 \pm 0.87	2.76 \pm 0.67
	Male	3.90 \pm 0.53	2.99 \pm 0.73	2.70 \pm 0.69
	P-Value	0.465	0.770	0.932

P value * Mann-Whitney test for comparison in two groups

According to Table 5, the comparison of clinical parameters in the ciprofloxacin group among men and women showed that (1) in two and four months after intervention, GBI in women was significantly higher than in men, and (2) There was no significant difference in PD and CAL between women and men at any time of study.

Finally, Spearman correlation coefficient was used to answer the question of is the response to ciprofloxacin treatment depended on age? (Table 6)

Table 6: Relationship between clinical parameters in the 4th month and patient's age in the ciprofloxacin group

	GBI	PD	CAL
correlation coefficient	-0.084	-0.079	0.000
P value	0.605	0.626	0.998
Number	40	40	40

As shown in Table 6, in the ciprofloxacin group, there is no significant relationship between the patient's age and the clinical

parameters PD, CAL and GBI. In other words, the response to treatment with ciprofloxacin is not dependent on age.

Discussion and Conclusion

In the present study, GBI level in the ciprofloxacin group decreased from 1.52 ± 1.3 before intervention to 0.3 ± 0.51 in the fourth month after treatment. In the control group, from 1.7 ± 1.15 before intervention was reduced to 0.72 ± 0.98 in the fourth month after treatment. Also, in the second and fourth months, GBI was significantly lower in the ciprofloxacin group than in the control group.

Isfahanizadeh and Khalilnezhad in 2010 showed that bleeding during probing was significantly lower in the third and sixth months after treatment in the ciprofloxacin and metronidazole treatment group than in the control group^[17]. The results of this study are similar to the present study.

Erdemir et al. (2013) did not show any significant difference in the measured parameters in the two groups despite improvement of the condition in the two groups^[18]. Soleimani Shayesteh et al. (2004) did not show any difference between ciprofloxacin and control groups on gum index on the 10th day after treatment^[19].

The results of these studies are inconsistent with the present study. Patients did not receive mechanical periodontal treatments and health education and only received systemic treatment with the antibiotics mentioned. While the effect of drug treatments is now questioned without mechanical treatment. In the current study, the patients in both case and control groups received mechanical treatments and then received medication and seemingly the difference in the way research is conducted is the cause of the inconsistency. Another reason for the inconsistency is the time taken to measure clinical parameters. In regular dentistry, regular examinations and evaluation of the results of initial periodontal treatments are usually done three months after initial treatment, and this evaluation period seems to be appropriate for a clinical study^[20]. In this study, the first measurement after the intervention was 2 months after the treatment, and the ciprofloxacin administration lasted 7 days, while Soleimani and colleagues compared the clinical parameters on the 10th day after treatment, which is a very short time to examine the course of the disease.

In the present study, PD in the ciprofloxacin group decreased from 3.52 ± 0.75 before the intervention decreased to 2.87 ± 0.39 in the fourth month after treatment. In the control group, from 3.63 ± 0.59 before the intervention decreased to 3.22 ± 0.34 in the fourth month after treatment. Also in the second and fourth months, PD in the ciprofloxacin group was significantly lower than the control group.

Ahmadi et al. (2012) showed a significant difference in the PD between the combination therapy group (scaling and root planning along with antibiotics) and the SRP group (scaling and root planning), which confirms the current study. Prakasam et al. (2012) stated that ciprofloxacin is the only antibiotic in

periodontal treatment that is sensitive to all A-Actinobacillus species and recommended the best treatment for invasive periodontitis as a combination of conventional therapy with antimicrobial therapies (use of antibiotics)^[21].

In the present study, CAL levels in the ciprofloxacin group decreased from 3.97 ± 0.52 before intervention to 2.73 ± 0.67 in the fourth month after treatment. In the control group, from 4.8 ± 0.42 before intervention was decreased to 3.69 ± 0.72 in the fourth month after treatment. Also, in the second and fourth months, CAL levels were significantly lower in the ciprofloxacin group than in the control group.

According to Tezel et al. (2005) use of ciprofloxacin significantly reduced the clinical adhesion level of subjects with periodontitis on day 21 and third month^[22], which is consistent with the present study. Isfahanizadeh and Khalilnezhad (2010) showed that the clinical attachment level was similar in the third and sixth months after treatment in the ciprofloxacin and metronidazole treatment group and in the control group^[17], which contradicts the present study. The reason for this inconsistency can be the severity of the initial CAL in patients and the rate of drug use. Kapoor et al. (2012) emphasized the administration of antimicrobial regimen, with regard to periodontal disease status^[23]. Guerrero et al (2005) considered effective 7-day use of metronidazole and systemic amoxicillin in reducing the duration of non-surgical periodontitis treatment^[9]. In this study also, ciprofloxacin was taken for 7 days and there was a significant decrease in clinical parameters of patients. Patil et al. (2013) also stated that antimicrobial therapy can be used as a complement to mechanical therapy in patients with invasive periodontitis, who do not respond to mechanical treatments that have an acute or severe periodontal infection. Compared to the dose of ciprofloxacin, they emphasized on the type of use and the duration of drug use in cardiovascular disease, asthma, seizure, or diabetes^[24].

Finally, in response to the research questions, the present study showed that there was not a significant difference between PD and CAL in men and women at any time of study, but in two and four months after intervention, GBI in women was significantly higher of men. In the conducted studies, the difference in recovery rates between men and women has not been compared, and therefore there was no background for this research goal. Also, the results of this study indicate that the response to treatment with medioprofloxacin is not dependent on age.

Conclusion

The findings showed that (1) GBI, PD, CAL values in both case and control groups have a significant decrease in clinical parameters over a period of one month to three months. (2) The improvement in parameters of GBI, PD, CAL over time in the case group was significantly better than the control group; and (3) There was no significant difference between PD and CAL in both men and women at any time of study. In general, the administration of ciprofloxacin antibiotics is systemically

effective, along with scaling and root planning in the treatment of chronic periodontitis patients

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