Effects of Amoxicillin – Metronidazole Combination Versus Ciprofloxacin as an Adjunct to Nonsurgical Periodontal Therapy of Chronic Generalized Periodontitis

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ABSTRACT

Introduction: Periodontitis is an infectious disease caused by bacteria residing in biofilms at or below the gingival margin. Periodontal disease appears to be caused by subgingival infection by specific microbial agent(s). The objective of this study was to evaluate the short-term clinical benefits of two different systemic antibiotic regimes added to the nonsurgical periodontal treatment of chronic generalized periodontitis.

Material and Methods: 40 patients were selected and divided into the following two groups: SRP plus metronidazole and amoxicillin (M + A group), and SRP plus Ciprofloxacin (C group); The periodontal indexes were recorded at baseline and 3-month post therapy.

Results: The periodontal parameters were improved in both groups -month post therapy. The scores were decreased more in the M + A group than C group, but the differences between two groups were not significant. In addition, the decrease in the plaque index from baseline to 3-month in the M + A group was not significant.

Conclusion: Nonsurgical therapy like scaling and root planning reduces the probing depth, clinical attachment level, and clinical inflammation findings. Better healing was observed in the M + A group despite the baseline plaque scores. Therefore, M + A might be active against the bacteria in dental biofilms.

Key words: Ciprofloxacin, Chronic Generalized Periodontitis, Metronidazole and Amoxicillin, Nonsurgical Periodontal Therapy, Scaling and Root Planning.

INTRODUCTION

Previous therapy for periodontitis involved elimination or suppression of subgingival microbial complexes by mechanical debridement such as scaling and root planning or surgical procedures. However, the pathogenic microorganisms becomes more complex with time, so systemic antibiotics can be given as an adjunct in controlling bacterial infections. These bacteria invade periodontal tissues, so mechanical therapy alone is sometimes ineffective.[1] In our case, the microbial aetiology of periodontal diseases provides the rationale for using systemic antimicrobial medication in periodontal therapy. The structure of the periodontal biofilm, consisting of multiple bacterial colonies residing in a glycocalyx matrix, has been well described by Marsh.[2] It has been seen that once bacteria attach to a tooth surface and reside within a mature biofilm structure, they are less susceptibile to antimicrobials compared with planktonic or free-floating bacteria.[3] Therefore, it is important to mechanical disrupt the biofilm when using systemic antibiotics to treat periodontitis. The rationale for use of adjunctive systemic antimicrobials is to reduce the bacterial load, enabling resolution of the inflammation in the periodontal pocket. Antibiotics can be prescribed for periodontal patients who do not respond to conventional mechanical therapy like scaling and root planning, for patients with acute periodontal infections associated with systemic manifestations, for prophylaxis in medically compromised patients, and as an adjunct to surgical and non-surgical periodontal therapy. Application of systemic antibiotic therapy focuses on the pathogenic microorganisms, the patient, and the choice of drug.

There has been seen that the use of adjunctive antibiotics results in increase in attachment levels than mechanical therapy alone.[4,5] However, it depends on the optimum type, dosage, duration of treatment, and mix of antibiotics for combination therapy.[6]

The combined use of amoxicillin (AMX) and metronidazole (MTZ) is bactericidal, and spectral efficacy compared with monotherapy with either drug.[7,8] The combination of MTZ and AMX in the treatment of chronic periodontitis has higher efficacy, mostly due to its effectiveness against Aggregatibacter actinomycetemcomitans, a periodontal pathogen closely associated with the etiology of this infection.[9,10] This combination is also active against Treponema denticola, Tannerella forsythia, Porphyromonas gingivalis, Fusobacterium nucleatum, and Prevotella intermedia.[11-13]

Ciprofloxacin is active against gram-negative rods, including all facultative and some anaerobic putative periodontal pathogens. Since it demonstrates minimal

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effect on Streptococcus species, which are associated with periodontal health. At present, ciprofloxacin is the only antibiotic in periodontal therapy to which all strains of A. actinomycetemcomitans are susceptible. It has been used in combination with metronidazole.[14]

Ciprofloxacin is a quinolone antibiotic and is bactericidal due to its action on DNA replication. Generally, ciprofloxacin like most quinolones is well tolerated. Its side effects are generally nausea, headache, abdominal discomfort or epigastric upset, photosensitivity, dizziness and light headedness. Ciprofloxacin is contraindicated during lactation and pregnancy as it is excreted in human breast milk and may cross the placental barrier.

Therefore, this prospective study was done to find out the clinical short-term effects of C and a combination of MTZ and AMX.

MATERIALS AND METHODS

The study protocol was approved by the Ethics Committee of Govt Dental College and Hospital Srinagar The clinical records of chronic generalized periodontitis patients were seen from April 2016 to August 2016 in the Department of Periodontics were reviewed to identify patients diagnosed with "CGP" according the criteria of Armitage,[15] who were nonsmokers, systemically healthy, with no medication use in the previous 6 months, and no previous periodontal treatment. The records of 30 patients were examined; and all met the inclusion criteria. The clinical parameters were scored at six sites per tooth (mesiobuccal, midbuccal, distobuccal, mesiolingual, midlingual, and distolingual) at baseline at the time of scaling and root planning and 12 weeks after SRP: Probing depth (PD)[16], clinical attachment level (CAL)[17], plaque index (PI)[18], and bleeding on probing (BOP).[19] The control group underwent full-mouth SRP and Ciprofloxacin only, whereas the test group received two systemic antibiotic regimens in addition to SRP. The control group (C group; n = 20) was given C 500 mg, twice per day, for 8 days, and the test group was given MTZ + AMX 250 mg each, 2 times/day (M + A group; n = 20)

Index	M+A	C	P
PD	3.43±0.59	3.65±1.46	NS
CAL	3.77±1.09	3.88±1.51	NS
PI	1.05±0.73	0.71±0.57	NS
BOP	64.47±26.49	57.53±31.46	NS

M+A = SRP + Metronidazole + Amoxicillin; C= SRP + Ciprofloxacin. PD=Probing depth; CAL=Clinical attachment level; PI=Plaque index; BOP=Bleeding on probing; NS=Nonsignificant.

Table-1: parameters of the subjects at baseline

RESULTS

Table 1 presents the mean baseline clinical parameters. Differences were non significant among groups in terms of age, gender, or clinical periodontal parameters, confirming that the groups were well matched.

The mean of average change per-group in periodontal parameters from baseline to 3 months after SRP is shown in Table 2. Improvements were seen in almost all parameters at 3 months for both groups. The PD, CAL, GI, and BOP reduced significantly in both groups. The PI showed a significant clinical improvement for the M + A (–0.19 ± 0.61, $P \geq 0.05$) However, PI did not change significantly at 3 months in the C group (–0.71 ± 0.64, $P < 0.01$). All of the treatment procedures significantly reduced the PD in both groups. However, more reduction in PD was seen in the test group compared with the control group (–1.29 ± 1.39 and -1.27 ± 0.51 (for M + A and C respectively).

Discussion

This study shows the short-term clinical benefits of two treatment protocols for nonsurgical periodontal therapy of GCP. Many studies have compared antibiotic regimens as adjuncts to SRP.[20-23] We reviewed their findings to assess the use of antimicrobials administered after an initial period of oral hygiene motivation.

In Our study has control and test groups. The differences among groups in terms of age, gender, and initial periodontal parameters were negligible. All patients were nonsmokers. Our data from this study indicate that both therapies improved the PD, CAL, GI, and BOP at the 3-month follow-up.

Scaling and root planning is an initial therapy to induce the resolution of inflammation by removal of plaque, calculus, and endotoxins from the root surfaces. In our study, all clinical parameters improved in the control group. In most studies which were done previously, M + A combined with SRP leads to significantly greater reductions in clinical periodontal parameters.[20,24,25] Guerrero et al.in his study found the adjunctive benefits of M + A in the nonsurgical treatment of GCP and found that all clinical parameters were improved at 2 and 6 months in both the test and placebo groups.[23] However, the M + A therapy resulted in an additional 1.4-mm PD and 1-mm CAL gain. Similarly, Casarin et al. treated GCP patients with full-mouth ultrasonic debridement with or without administering M + A.[20] Their results showed improved clinical and microbiological benefits of combination group (M + A) administration 3 and 6 months post therapy. In another study, two grops like aggressive periodontitis and chronic periodontitis were treated similarly by using M + A in addition to nonsurgical

Groups	PD	CAL	PI	BOP
M+A	−1.29±1.39*	−1.56±1.74**	−0.19±0.61NS	−38.18±28.78***
C	−1.27±0.51***	−1.56±0.96***	−0.71±0.64**	−50.88±26.83***

**P<0.01, ***P<0.001. Results of one-way ANOVA comparing the two groups M+A=SRP + metronidazole + amoxicillin; C= Ciprofloxacin only; NS=Statistically nonsignificant. PD=Probing depth; CAL=Clinical attachment level; PI=Plaque index; BOP=Bleeding on probing; ANOVA=Analysis of variance

Table-2: The average changes in periodontal parameters for T3-T0

treatment like scaling and root planning alone ; the use of M + A resulted in additional clinical benefits.[25] In this study, the pocket depth (PD) decreased from 3.5 ± 0.7 to 2.5 ± 0.5 mm at 12 weeks time. In addition, the gingival bleeding index, plaque control record, and BOP all decreased significantly in these groups. Silva-Senem et al. also showed significant improvements in most parameters at 1-year in the nonsurgical treatment of GAP and GCP patients using M + A in one group and not in other, although the M + A group had shallower residual pockets than the placebo group.[26] Another randomized and clinical trial evaluated the short-term effects of nonsurgical treatment of aggressive periodontitis with M + A and photodynamic therapy (PT); in this study both treatments improved the clinical parameters after 3-month, but the systemic administration of antibiotics resulted in a greater reduction in PD compared to the PT group.[27] In this study our results were similar to these reports in that the clinical periodontal parameters improved in both the M + A and control groups. The PD was seen reduced significantly ($P < 0.001$) by 1.27 ± 0.51 and 0.79 ± 0.55 for the respective groups but reduction was higher in the M + A group.

In contrast, similar results of SRP and SRP plus systemic Ciprofloxacin was also seen.[28-30] GCF concentration of ciprofloxacin was found significantly higher than its serum concentration according to various studies.[31] Ciprofloxacin is particularly effective against many invasive pathogens as it penetrate cells and produce bactericidal effects.[32] In controlled trials evaluating the clinical and microbiological effects of quinolone antibiotics and periodontal treatment combination shows positive contributions of the systemic drug administration to the improvement of periodontal parameters.[33,34] When the clinical indices were seen both treatment approaches were found effective in the elimination of periodontal inflammation in the present study. However, adjunctive use of antibiotic have influence on the clinical results in addition to non-surgical periodontal treatment of mild to moderate level chronic periodontitis. Our results in this study were in accordance with the results of Serrano et al.[35] and Dannewitz et al.[36]

In our study, the clinical periodontal parameters improve significantly in the M + A combination group. On comparing whole groups, the parameters improved. However, the reduction in PD was higher in the M + A combination group than the control, not significantly so (–1.29 ± 1.39 and –1.27 ± 0.51, for the M + A combination and, C group, respectively). The CAL, GI, and BOP parameters showed similar trends to the PD. The PI also decreased compared to baseline, not significantly. M + A combination is effective against the bacteria in dental plaque,[16] which gives good results. Although clinicians attempt to motivate, patients to perform plaque control, maintaining a high level of oral hygiene can be difficult. Thus, M + A combination administration might be useful for the treatment of periodontitis.

Mechanical treatment only may not be effective on periodontal pathogens such as A. actinomycetomcomitans at inaccessible areas and periodontal soft tissues.[5] So in patients with aggressive periodontitis and chronic periodontitis will be benefited with the adjunctive use of antibiotics as adjunct to treatment. There are various antibiotic regimes that recommended but we compared two of them. Hence, the results may be a useful guide about the choice of antibiotics. In addition, the patient records were selected according to protocol for this study.

CONCLUSION

The CGP patients had been treated in the same clinic by the same treatment protocol as standardized.

However, the limitations to this study are; the short follow-up time and no immunological or microbiological parameters were evaluated. So further research is needed to find optimum adjunctive antibiotic therapy for the nonsurgical treatment of GCP.

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