A Comparative Evaluation of Systemic Azithromycin and Ornidazole - Ofloxacin Combination as an Adjunct to Scaling and Root Planning In the Treatment of Chronic Generalised Periodontitis

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Abstract

**Background:** It is a well-established fact that various periodontal diseases are caused by bacteria, some of which are tissue invasive. It has been suggested that an antibiotic strength 500 times greater than the usual therapeutic dose may be needed to be effective against bacteria arranged in biofilm. However, so far, the literature shows that the ideal treatment is mechanical removal of local factors followed by systemic anti-infective therapy.

**Aims and Objective:** To evaluate and compare the clinical effects of systemic Azithromycin (AZM) and Ornidazole–Ofloxacin combination as an adjunct to Scaling and Root Planning in the treatment of patients with chronic periodontitis.

**Materials and Method:** This was a comparative randomized clinical Study in which 30 patients with chronic periodontitis participated. Patients were randomly divided into 3 groups: The group 1 received Scaling and Root Planning plus Azithromycin, group 2 received Scaling and Root Planning plus Ornidazole–Ofloxacin combination and the group 3 (control) which received Scaling and Root Planning only. Clinical indices including Probing Pocket Depth (PPD), Relative Attachment Level (RAL), Gingival Index (GI), and Plaque Index (PI) were measured at the baseline, 4 and 8 weeks after treatment.

**Results:** Comparison of the clinical parameters showed statistically significant improvement in all the three groups. SRP plus Azithromycin group showed additional benefit than SRP plus Ornidazole-Ofloxacin and SRP alone.

**Keywords:** Azithromycin; Ornidazole; Ofloxacin

Introduction

Chronic periodontitis is an infectious disease with a bacterial etiology causing inflammation and progressive destruction of the tooth supporting tissues [1,2]. Pocket formation, loss of gingival attachment and alveolar bone desorption are some of its characteristics. The conventional therapy for periodontal diseases consists of scaling and root planning or surgical treatment in order to gain a better access for root instrumentation [3,4]. However, considering the tissue invasive properties of certain periodontic pathogens, it has been suggested that administration of antibiotics adjunctively to scaling and root planning can achieve better clinical and microbial results in comparison to scaling root planning alone [5-8].

Azithromycin is a macrolide antibiotic. It has a considerable potency against gram negative organisms. However, it has a few side effects like mild diarrhea, nausea, vomiting, abdominal pain [9-11]. Azithromycin is quickly absorbed by neutrophils, macrophages and fibroblasts. This helps in the fast delivery of the drug in infected tissues. The concentration of AZM is 10-100 times higher in tissues than in serum. Besides, it has a long half-life which allows it to be recommended for a short period of time [12,13]. Several investigators have reported the clinical results of using AZM as an adjunct to SRP. Mascarenhas et al. [14] have reported the beneficial effects of AZM in decreasing probing depth and increasing attachment levels compared to SRP alone in smokers with periodontitis. Hirsch et al. [15] have also demonstrated the effectiveness of AZM in the treatment of periodontal diseases. On the other hand, Angaji et al. [16] showed that there was inadequate evidence for supplementary effect of adjunctive antibiotic therapy on chronic periodontitis in smokers.

Ofloxacin belongs to the fluoroquinolone group of antibiotic. It inhibits the multiplication of bacteria by inhibiting the production and repair of DNA. Ornidazole is a nitroimidazole which is an antibacterial and antiprotozoal used to treat anaerobic enteric protozoa. It is effective against a wide variety of gram positive, gram negative aerobic bacteria. Metallic taste, abdominal cramps, nausea, vomiting are the few side effects of this combination. There is no literature showing the beneficial effect of ornidazole ofloxacin as an adjunct to SRP.

Periodontal infections may contain a wide array of bacteria; hence, no single antibiotic is effective against all putative pathogens. Indeed, difference exists in the microbial flora associated with periodontal diseases [17]. These “mixed” infections can include a variety of aerobic, microaerophilic and anaerobic bacteria, both gram positive and gram negative. It may thus be necessary to use more than one antibiotic, serially or in combination [18].

Systemic antibiotic therapy for periodontal treatment usually involves monotherapy based on metronidazole, tetracycline, clindamycin, ciprofloxacin and the β-lactams antibiotic. Antibiotics and chemotherapeutics have been prescribed for periodontal patients; who do not respond to conventional mechanical therapy, for patients with acute periodontal infections associated with systemic manifestations, for prophylaxis in medically-compromised patients, as an adjunct to surgical and non-surgical periodontal therapy.

The aim of the present study is to evaluate and compare the clinical effects of systemic Azithromycin (AZM) and Ornidazole-Ofloxacin...
Materials and Methods

This study was a single-blinded, randomized and comparative clinical trial. Eligible patients were selected from those with chronic periodontitis who had reported in the Department of Periodontics at M.A. Rangoonwala College of Dental Science and Research Centre, Pune, India. 30 patients with chronic periodontitis were assessed and oral examination and medical history review were gathered to confirm eligibility. The study was approved by the Medical Ethical Committee of M.A. Rangoonwala College of Dental Science and Research Centre.

Inclusion Criteria: Systemically healthy patients with untreated chronic periodontitis, having more than 12 teeth (excluding third molars and teeth with orthodontic appliance, bridges, crowns, and implants) with at least 4 posterior teeth having PPD>4 mm and clinical attachment loss (CAL)>2 mm

Exclusion criteria: Patient who has undergone antibiotic therapy within 6 months prior the study, allergic to any medication, suffering from debilitating systemic disease/condition, diabetics, smokers, pregnant or lactating mother.

Patients were randomly divided into 3 therapeutic groups. Group 1 (10 patients) received SRP plus Azithromycin (one tab 500 mg OD) for three days after scaling. Group 2 (10 patients) received SRP plus Ornidazole-Ofloxacin combination (one tab 500 mg bd) for three days after scaling. Group 3 (10 patients) received SRP only.

Assessment of subjects

Clinical parameters including: PPD (Probing Pocket Depth), RAL (Relative Attachment Level), GI (Gingival Index -Silness, J. and Löe), PI (Plaque Index -Silness, J. and Löe) [22]. They were measured at baseline, 4 and 8 weeks after the treatment. PPD was recorded from the gingival margin on the mesial, buccal, distal and lingual aspects of teeth with a William’s periodontal probe. RAL was measured from a gingival margin on the mesial, buccal, distal and lingual aspects of teeth. GI was determined according to established GI criteria. PI was measured according to Silness and Löe. Patients were informed about the important role of dental plaque in periodontal diseases.

Periodontal treatment

Before the first treatment visit, each subject was given a code number. Patients’ medical history and prescribed medicines were recorded. Both the groups of antibiotics (Azithromycin and orindazole-ofloxacin combination) were presented in apparently identical package. The package was given to the patients who were blind throughout the study. At the first visit, before SRP, all clinical parameters were recorded. Then the scaling and root planning was performed. All patients were recalled at 4 and 8 weeks after the baseline treatment. The above mentioned clinical parameters including GI, PI, RAL, and PPD were measured and recorded.

Statistical analysis

A sample size of 30 was derived using the formulas $n = 2 (Z_α/2 + Z_{1–β})^2/(μ_1 – μ_2 / σ)^2$ with the SABA software. Data analysis performed by using SPSS (Statistical Package for Social Science) version 19.0.ANOVA test was used to find the significance in the groups. Turkey’s test was used to find significance between pairwise comparisons. P value <0.05 was considered as significant.

Results

30 patients participated in the study. These subjects were divided into three groups. Patients in group 1 received SRP plus azithromycin, patients in group 2 received SRP plus Ornidazole-Ofloxacin, patients in group 3 received only SRP.

Gingival index

Mean gingival index score (±) SD of all three groups at baseline, 4 weeks and 8 weeks post treatment are given in Table 1. There was a statistically significant reduction in the gingival index score from baseline to 4 weeks post treatment (p value=0.017). However no further reduction was observed from 4 weeks to 8 weeks (p value=0.420) post treatment. In inter group comparison using Tukey’s test; SRP plus Azithromycin group showed significant improvement in comparison with SRP plus Ornidazole-Ofloxacin group (p value =0.027) and SRP group (p value =0.042) .

Plaque index

Mean plaque index score (±) SD of all three groups at baseline, 4 weeks and 8 weeks post treatment are given in Table 2. There was a statistically significant reduction in the plaque index score from baseline to 4 weeks post treatment (p value=0.087). However no further reduction was observed from 4 weeks to 8 weeks (p value=0.133) post treatment. In inter group comparison using Tukey’s test; no group showed better results in comparison with other.

Probing pocket depth

Mean PPD score (±) SD of all three groups at baseline, 4 weeks and 8 weeks post treatment are given in Table 3. There was a statistically significant reduction in probing pocket depth score from baseline to 4 weeks post treatment (p value=0.004). However no further reduction was observed from 4 weeks to 8 weeks (p value=0.133) post treatment. In inter group comparison using Tukey’s test; no group showed better results in comparison with other.
8 weeks post treatment are given in Table 3. There was a statistically significant reduction in the plaque index score from baseline to 4 weeks post treatment (p-value=0.002), further reduction was also observed from 4 weeks to 8 weeks (p-value=0.003) post treatment. In inter group comparison using Tukey’s test; SRP plus Azithromycin group showed significant improvement in comparison with SRP plus Ornidazole-Ofloxacin group (p-value=0.001) and SRP group (p-value=0.003).

## Relative Attachment Level

Mean PPD score (±) SD of all three groups at baseline, 4weeks and 8 weeks post treatment are given in Table 4. There was a statistically significant reduction in the plaque index score from baseline to 4 weeks post treatment (p-value=0.001), further reduction was also observed from 4 weeks to 8 weeks (p-value = 0.001) post treatment. In inter group comparison using Tukey’s test; SRP plus Azithromycin group showed significant improvement in comparison with SRP plus Ornidazole-Ofloxacin group (p-value=0.001) and SRP group (p-value=0.002).

Comparing the clinical parameters showed statistically significant improvement in all the three groups from baseline to 4 weeks post treatment. Further reduction was not observed in the gingival index and plaque index from 4 weeks to 8 weeks post treatment. PDD reduced significantly from 4 weeks to 8 weeks post treatment in all three groups. A significant gain in RAL was also observed from 4 weeks to 8 weeks post treatment in all three groups. SRP plus Azithromycin group showed significant reduction in gingival index score, pocket depth reduction, gain in RAL comparison with SRP plus Ornidazole-Ofloxacin group and SRP group.

## Discussion

The present study evaluated the clinical effects of Azithromycin and Ornidazole-Ofloxacin combination as an adjunct to scaling and root planning in the treatment of patients with chronic periodontitis. It is well established that the various periodontal diseases are caused by bacterial infection. In a periodontal pocket the bacteria are highly structured. As this process continues, the bacterial biofilm extends so far subgingivally that the patient cannot reach it during oral hygiene efforts. Additionally this forms a complex biofilm which may offer some protection from host’s immunologic mechanism in extracellular compartment. Azithromycin is actively transported to periodontal lesions is significantly higher than that of normal gingiva. It has been proposed that azithromycin penetrates fibroblasts and phagocytes in concentration 100 to 200 times greater than the extracellular compartment. Azithromycin is actively transported to sites of inflammation by phagocytes and then released directly into the sites of inflammation as the phagocytes rupture during phagocytosis.

In the present study SRP plus Azithromycin group showed significant reduction in gingival index score, pocket depth reduction, gain in RAL comparison with SRP plus Ornidazole-Ofloxacin group and SRP group. In a study by Oteo and Herrea [24], the adjunctive use of systemic azithromycin in the treatment of P gingivalis periodontitis demonstrated significant clinical and microbiological benefits when compared to SRP plus placebo. In a study by Pradeep et al. [25], local drug delivery of 0.5% azithromycin in the treatment of chronic periodontitis among smokers was done. The study concluded that when

<table>
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<th>Probing depth</th>
<th>Number of patients</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>P-value</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
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<tr>
<td>Baseline</td>
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<td>6.77</td>
<td>0.45</td>
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<tr>
<td>4th week</td>
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<td>4.60</td>
<td>0.49</td>
<td>5.79</td>
<td>0.72</td>
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<tr>
<td>8th week</td>
<td>10</td>
<td>4.70</td>
<td>0.41</td>
<td>5.78</td>
<td>0.72</td>
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Table 3: Comparison of probing depth in group 1, group 2 and group 3.

<table>
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<th>RAL Number of patients</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>Baseline</td>
<td>10</td>
<td>5.70</td>
<td>0.95</td>
<td>6.00</td>
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<tr>
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</tr>
<tr>
<td>8th week</td>
<td>10</td>
<td>3.80</td>
<td>0.79</td>
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</table>

Table 4: Comparison of RAL in group 1, group 2 and group 3.
compared to the placebo, the adjunctive use of 0.5% AZM resulted in significant improvement in clinical outcome in the treatment of chronic periodontitis among smokers. Emingil et al. studied the effectiveness of azithromycin in combination with nonsurgical periodontal therapy on clinical and microbiological parameters, and on the MMP-8 and TIMP-1 levels in gingival crevicular fluid, over a 6-month time-period in patients with generalized aggressive periodontitis. They concluded that adjunctive azithromycin therapy provides no additional benefit over nonsurgical periodontal treatment on clinical parameters, microbiological parameters and gingival crevicular fluid biochemical markers investigated in patients with generalized aggressive periodontitis [26]. Mammdoh studied clinical effects of systemic azithromycin as an adjunct to scaling and root planing (SRP) and compared it with metronidazole in the treatment of chronic periodontitis. In this study it was observed that adjunctive use of azithromycin with SRP had potential to improve periodontal health over SRP alone, and could be an effective alternative to metronidazole in patients with chronic periodontitis [27].

Periodontal infections contain a wide variety of bacteria, hence, no single antibiotic is effective against all periopathogens. In these cases it may be necessary to use more than one antibiotic, either serially or in combination.

There is no literature showing the beneficial effect of Ornidazole-Ofloxacin as an adjunct to SRP. Thus in the present study an attempt was made to evaluate the added effect of Ornidazole-Ofloxacin combination as an adjunct to SRP, however, no such added benefit was documented with the adjunctive use of this combination.

Limitations of the Study

To enhance the reproducibility of these results, a larger sample size with a longer follow up period should be included in further trials. Before combinations of antibiotics are used, periodontal pathogens being treated must be identified and antibiotic – susceptibility testing should be done. However, no antibiotic sensitivity was done in the present study.

Conclusion

According to the present study, the adjunctive use of systemic azithromycin showed a significant clinical benefit in the treatment of chronic periodontitis in comparison to SRP alone. However no added improvement was obtained with Ornidazole-Ofloxacin combination as an adjunct to SRP.

References