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Mean Probing Pocket Depth and Bleeding Index by Comparing Azithromycin and Amoxicillin/Metronidazole After Non-Surgical Periodontal Therapy for Chronic Periodontitis: A Randomized Controlled Trial

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ABSTRACT

Background: Chronic periodontitis (CP) is a prevalent inflammatory condition leading to the progressive destruction of periodontal tissues. Non-surgical periodontal therapy (NSPT), often combined with systemic antibiotics, is an effective treatment for CP. This study aimed to compare the effectiveness of Azithromycin versus Amoxicillin/Metronidazole in reducing probing pocket depth (PPD) and bleeding index (BI) following NSPT in chronic periodontitis patients.

Methods: A randomized controlled trial was conducted with 60 patients diagnosed with chronic periodontitis. These participants were randomly assigned to receive either Azithromycin (500 mg per day for 3 days) or a combination of Amoxicillin (500 mg) and Metronidazole (400 mg), administered three times a day for 7 days, alongside non-surgical periodontal therapy (NSPT). Clinical outcomes, specifically probing pocket depth (PPD) and bleeding index (BI), were assessed at baseline and again 3 months post-treatment. Statistical analyses included paired t-tests for intra-group comparisons and independent t-tests for inter-group differences.

Results: Both treatment groups showed significant reductions in PPD and BI at 3 months. However, the Azithromycin group demonstrated a more significant reduction in PPD (mean reduction: 3.5 mm vs. 2.9 mm, $p < 0.05$) and BI (mean reduction: 1.3 vs. 1.0, $p < 0.05$) compared to the Amoxicillin/Metronidazole group.

Conclusion: when combined with NSPT, Azithromycin showed superior clinical outcomes compared to Amoxicillin/Metronidazole in treating chronic periodontitis. Azithromycin can be a more effective adjunctive treatment for improving periodontal health post-NSPT.

Keywords: Azithromycin, Periodontitis, Amoxicillin, Non-surgical

INTRODUCTION

Chronic periodontitis (CP) is a common and progressive inflammatory condition affecting the supporting structures of the teeth, including the gingiva, periodontal ligament, cementum, and alveolar bone. CP is characterized by the destruction of periodontal tissues, leading to pocket formation, tooth mobility, and, eventually, tooth loss if untreated.[1,2] Globally, CP is a significant public health concern, with a prevalence that increases with age and has substantial implications for oral health and overall well-being.[3] The pathogenesis of CP involves a complex interplay between microbial biofilms and the host immune response. Periodontal pathogens such as *Porphyromonas gingivalis*, *Tannerella forsythia*, and *Treponema denticola* play a central role in initiating and sustaining inflammation in the periodontal tissues.[4,5] The inflammatory response, while aimed at controlling infection, can result in tissue destruction due to an imbalance between pro-inflammatory and anti-inflammatory mediators, along with oxidative stress.[6] Systemic conditions such as diabetes mellitus and cardiovascular disease further exacerbate the progression of CP, highlighting its bidirectional relationship with systemic health.[7]

Non-surgical periodontal therapy (NSPT), primarily comprising scaling and root planing (SRP), is the cornerstone of CP management. The mechanical removal of plaque and calculus aims to disrupt the biofilm and reduce the bacterial load within periodontal pockets.[8] While NSPT is effective in halting disease progression in mild-to-moderate cases, it may be less effective in managing severe or refractory periodontitis. Deep periodontal pockets and complex root anatomy often limit the mechanical accessibility of SRP, necessitating the adjunctive use of systemic antibiotics to enhance clinical outcomes.[9,10]

Systemic antibiotics have been extensively studied as adjuncts to NSPT. The combination of Amoxicillin and Metronidazole is considered a gold standard due to its broad-spectrum efficacy against anaerobic bacteria. Several studies have demonstrated the benefits of this combination in reducing probing pocket depth (PPD) and bleeding on probing (BOP).[11] However, the frequent dosing schedule and gastrointestinal side effects may pose challenges for patient compliance.[12] Azithromycin, a macrolide antibiotic, has emerged as a promising alternative due to its unique pharmacological properties. It exhibits excellent tissue penetration, particularly in inflamed periodontal tissues, and has a prolonged half-life, allowing for a shorter dosing regimen.[13] Additionally, Azithromycin has immunomodulatory effects, reducing pro-inflammatory cytokines and promoting periodontal healing.[14] Recent clinical trials have suggested that Azithromycin may provide superior outcomes in terms of reducing PPD and inflammatory markers when compared to conventional antibiotic regimen.[15] Despite these promising findings, limited studies have directly compared the clinical efficacy of Azithromycin with the traditional combination of Amoxicillin and Metronidazole as adjunctive therapies to NSPT in the treatment of CP. This study aims to address this gap by evaluating and comparing the effects of these two antibiotic regimens on PPD and bleeding index (BI) over three months. PPD and BI are widely used clinical parameters that reflect the severity of periodontal disease and the effectiveness of therapeutic interventions.[16,17] This study hypothesizes that Azithromycin, due to its pharmacological advantages and ease of administration, will demonstrate superior clinical outcomes compared to the Amoxicillin/Metronidazole combination. The findings of this trial are expected to provide valuable insights into optimizing adjunctive antibiotic therapy for CP, thereby improving treatment protocols and patient outcomes.

METHODOLOGY

This study was a randomized controlled trial conducted at a tertiary care dental facility. The study received ethical approval from the Institutional Review Board, and informed consent was obtained from all participants. A total of 60 patients diagnosed with chronic periodontitis were enrolled, with an age range of 35-60 years. Patients were excluded if they had systemic diseases, were pregnant, or had been treated with antibiotics within the last 6 months. Using a computer-generated randomization list, participants were randomly assigned to one of two treatment groups. The two groups were Group A: Azithromycin 500 mg/day for 3 days, combined with NSPT. Group B: Amoxicillin 500 mg and Metronidazole 400 mg three times a day for 7 days, combined with NSPT. Baseline clinical parameters were recorded at the time of enrollment. This included probing pocket depth (PPD) and bleeding index (BI), which were measured at six sites around each tooth. The measurements were repeated at 3 months post-treatment to assess the outcomes. Data were analyzed using SPSS version 22.0. Descriptive statistics were computed for baseline characteristics. Paired t-tests were used to compare the changes in PPD and BI within each group. Independent t-tests were used to compare the differences between groups at the 3-month follow-up. A p-value of <0.05 was considered statistically significant.

RESULTS

A total of 60 patients were enrolled, with 30 patients in each treatment group. The mean age was 47.5 ± 8.2 years. There was no significant difference in baseline PPD or BI between the two groups ($p > 0.05$). Both groups had similar clinical characteristics at baseline. At the 3-month follow-up, both treatment groups showed significant reductions in PPD compared to baseline (Table 1). However, the Azithromycin group exhibited a significantly greater reduction in PPD compared to the Amoxicillin/Metronidazole group ($p < 0.05$). The mean reduction in PPD was 3.5 mm in the Azithromycin group, compared to 2.9 mm in the Amoxicillin/Metronidazole group.

Table 1: Mean Probing Pocket Depth at Baseline and 3 Months

Group	Baseline PPD (mm)	3-month PPD (mm)	Mean Reduction (mm)	p-value
Azithromycin	5.6 ± 1.2	2.1 ± 0.9	3.5	<0.05
Amoxicillin/Metronidazole	5.7 ± 1.0	2.8 ± 1.1	2.9	<0.05

A significant reduction in BI was observed in both groups after treatment. The Azithromycin group showed a greater reduction in BI (mean reduction: 1.3) compared to the Amoxicillin/Metronidazole group (mean reduction: 1.0), with a statistically significant difference ($p < 0.05$).

Table 2: Mean Bleeding Index at Baseline and 3 Months

Group	Baseline BI	3-month BI	Mean Reduction	p-value
Azithromycin	2.2 ± 0.5	0.9 ± 0.3	1.3	<0.05
Amoxicillin/Metronidazole	2.3 ± 0.4	1.3 ± 0.4	1.0	<0.05

Both PPD and BI showed statistically significant improvements within each group ($p < 0.05$). When comparing the two groups, the Azithromycin group demonstrated superior clinical outcomes, with a more significant reduction in both PPD and BI ($p < 0.05$).

DISCUSSION

The findings of this randomized controlled trial suggest that the adjunctive use of Azithromycin with non-surgical periodontal therapy (NSPT) yields superior clinical outcomes compared to the combination of Amoxicillin and Metronidazole in the treatment of chronic periodontitis (CP). Both treatment regimens resulted in significant reductions in probing pocket depth (PPD) and bleeding index (BI) after three months, but the Azithromycin group demonstrated a statistically greater improvement. Several studies have examined the efficacy of systemic antibiotics as adjuncts to NSPT in managing CP. The combination of Amoxicillin and Metronidazole has been the gold standard due to its efficacy in targeting anaerobic pathogens such as *Porphyromonas gingivalis*, *Tannerella forsythia*, and *Treponema denticola*.[18,19,20] However, our findings align with recent studies highlighting Azithromycin's potent antimicrobial and anti-inflammatory properties. Azithromycin's superior penetration into periodontal tissues and extended half-life may explain its enhanced efficacy. A study by Feres et al. demonstrated similar results, with Azithromycin showing greater reductions in clinical parameters compared to Amoxicillin/Metronidazole combination.[21] Additionally, Azithromycin's immunomodulatory properties likely contributed to the significant reduction in BI observed in this study. Azithromycin, a macrolide antibiotic, exerts a bacteriostatic effect by inhibiting bacterial protein synthesis. Its ability to concentrate within inflamed periodontal tissues allows for effective eradication of periodontal pathogens.[22] Furthermore, Azithromycin has demonstrated anti-inflammatory effects by modulating cytokine production and neutrophil activity, which may contribute to improved healing outcomes following NSPT.[23] In contrast, the

Amoxicillin/Metronidazole combination provides a broad-spectrum antimicrobial effect but lacks the anti-inflammatory benefits associated with macrolides. While effective against anaerobic bacteria, its requirement for frequent dosing (three times daily for seven days) may also pose adherence challenges compared to Azithromycin's simpler regimen of once daily for three days.[24] The greater reduction in PPD and BI observed with Azithromycin underscores its potential as a preferred adjunctive antibiotic in the management of CP. Notably, PPD reduction is a critical determinant of periodontal stability and reduced disease progression risk. Similarly, a lower BI indicates decreased inflammation and improved periodontal health.[25,26] The findings are particularly relevant in settings where patient compliance with complex dosing regimens may be a concern. Azithromycin's shorter course and convenient dosing schedule could improve adherence, ultimately enhancing treatment outcomes.

Limitations and Future Directions

While this study provides valuable insights, several limitations warrant consideration. First, the sample size was relatively small, and larger studies are necessary to validate these findings. Additionally, the follow-up period was limited to three months; long-term studies are required to assess the sustainability of the observed clinical improvements. Microbiological assessments were not included, which could have provided a deeper understanding of the antibiotics' effects on subgingival microbiota. Future studies should incorporate microbiological and immunological analyses to elucidate the mechanisms underlying Azithromycin's efficacy. Finally, potential side effects of the antibiotics were not thoroughly explored. While both regimens are generally well-tolerated, adverse reactions such as gastrointestinal disturbances associated with Amoxicillin/Metronidazole should be evaluated in future trials.

CONCLUSION

This study demonstrates that Azithromycin, when used as an adjunct to NSPT, provides superior clinical outcomes compared to the combination of Amoxicillin and Metronidazole in treating CP. The significant reductions in PPD and BI highlight its potential as an effective and patient-friendly therapeutic option. These findings contribute to the growing body of evidence supporting the role of Azithromycin in periodontal therapy. Further research is needed to confirm these results and explore long-term outcomes.

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