Does adjunctive use of metronidazole plus amoxicillin benefit patients receiving non-surgical scaling and root planning for the treatment of generalised aggressive periodontitis?

Authors:
Andre W. van Zyl[1]
Johan Hartshorne[1,2]
Alonso Carrasco-Labra[3,4]

Affiliations:
[1]Department of Periodontics and Oral Medicine, University of Pretoria, South Africa

[2]Private practice, Tyger Valley, South Africa

[3]Department of Oral and Maxillofacial Surgery and Evidence-Based Dentistry Unit, Universidad de Chile, Chile

[4]Department of Clinical Epidemiology and Biostatistics, McMaster University, Canada

Correspondence to:
Johan Hartshorne

Email:
jhartshorne@kanonberg.co.za

Postal address:
PO Box 6223, Welgemoed 7538, South Africa

How to cite this article:
Van Zyl A, Hartshorne J, Carrasco-Labra A. Does adjunctive use of metronidazole plus amoxicillin benefit patients receiving non-surgical scaling and root planning for the treatment of generalised aggressive periodontitis? Open J Implant Dent. 2013;1(1), Art. #7, 3 pages. http://dx.doi.org/10.4102/ojid.v1i1.7

Read online:
Scan this QR code with your smart phone or mobile device to read online.

This article describes a double-blinded, placebo-controlled randomised clinical trial that involved 30 eligible subjects experiencing generalised aggressive periodontitis. Subjects were randomly assigned to either the test group (scaling and root planning + metronidazole [400 mg]) and amoxicillin [500 mg]) or the control group (scaling and root planning without the adjunctive antibiotics combination). Both antibiotics and placebos were administered three times per day for 14 days. Participants were examined at baseline, and again six months and one year after therapy. Both therapies led to a statistically significant improvement in all clinical parameters as measured after one year. However, subjects who received the metronidazole–amoxicillin combination showed the greatest reduction in mean probing depth, an improved clinical attachment level and a lower mean number of residual sites after one year. The investigators concluded that the non-surgical treatment of generalised aggressive periodontitis was markedly improved by the adjunctive use of metronidazole and amoxicillin up to one year after treatment.

Focus article

Mestnik MJ, Feres M, Figueiredo LC, et al. (2012) The effects of adjunctive metronidazole plus amoxicillin in the treatment of generalized aggressive periodontitis: a 1-year double-blinded, placebo controlled, randomized clinical trial. Journal of Clinical Periodontology 39, 955–961.

Background

Generalised aggressive periodontitis (GAP) is a distinct type of periodontitis, which affects people who, in most cases, appear healthy, have a familial aggregation tendency and a pronounced episodic and rapid rate of destruction of clinical attachment and alveolar bone.[1] It usually affects people younger than 30, but patients may also be older. There is typically a generalised interproximal attachment loss affecting at least three permanent teeth other than the first molars and incisors. The disease is frequently associated with the periodontal pathogens *Aggregatibacter actinomycetemcomitans* and *Porphyromonas gingivalis*, and neutrophil function abnormalities.[1]

A. actinomycetemcomitans is an important periodontal pathogen implicated in the aetiology of GAP.[2] There is general agreement that scaling and root planning (SRP) alone cannot eliminate or significantly suppress the levels of this pathogen in patients with periodontal disease.[3,4,5] Therefore, it is generally accepted that the use of a combination of metronidazole (MTZ) and amoxicillin (AMX) as an adjunct to SRP will benefit the treatment of GAP. However, to date no double-blinded, placebo-controlled clinical trials have been conducted beyond six months of follow-up to validate this therapy in patients with GAP.

Appraisal of study methodology and validity of the results

A sample of 30 subjects who met the study criteria were selected from a population of 200 patients diagnosed with GAP and who had been referred to a university clinic.

Subjects were randomly assigned to intervention groups using a computer-generated table. The allocation sequence of subjects was concealed from those assigning the subjects to the intervention groups. The test and control groups were well balanced and similar with respect to known prognostic factors.

All study personnel, including the examiner, biostatisticians and participants were blinded as to patient assignment, thus maintaining prognostic balance as the study progressed.

Prior to the study, all subjects received full-mouth supra-gingival scaling and instructions on proper home-care oral hygiene techniques. They were also given a single type of dentifrice to use during the study. All subjects received full-mouth SRP performed under local anaesthesia over the course of four to six appointments of approximately 1 h each. Treatment of the entire oral cavity was completed within 10–14 days. SRP was performed by a single trained periodontist using manual instruments. The antibiotic and placebo therapies and chlorhexidine (CHX) rinses started immediately after the first session of mechanical instrumentation. Compliance with medication was checked once a week. Supra-gingival biofilm control in both groups was achieved by rinsing with a 0.12% CHX solution twice daily for 60 days. Subjects were also called every two days to monitor compliance. This ensured that the groups maintained their prognostic balance at completion of the study.

Participants were examined at baseline and again after 6 and 12 months by a different calibrated clinician. Periodontal maintenance was conducted 3, 6 and 12 months after therapy.

All subjects who completed the study reported full adherence to the prescribed course of the antibiotic and/or placebo and the CHX rinse regimen. The investigators followed the intention-to-treat principle, including all subjects in the group to which they were randomised. There were two subjects from each group who did not return for the 12-month follow-up visit. Although this rendered the trial under-powered, the trial still yielded consistent results, as most of the clinical parameters measured showed statistically significant differences between the two groups, always in favour of the antibiotic treatment.

This randomised clinical trial satisfied all the validity assessment criteria; therefore, the results likely yielded an accurate and unbiased assessment of the treatment effect.

Results

The presence of residual sites with a probing depth (PD) ≥ 5 mm is generally considered to be the most important parameter for evaluating treatment success and to predict disease recurrence and the need for further treatment. In the control group (SRP + placebo) the mean number of residual sites with PD ≥ 5 mm decreased from 42.7 (SD ± 15.4) at baseline to 23.1 (SD ± 13.4) after one year. In comparison, after one year the mean number of residual sites with PD ≥ 5 mm decreased from 54.3 (SD ± 17.3) to 6.4 (SD ± 7.2) in the test group (SRP + MTZ + AMX). The majority of evaluated clinical parameters showed statistically significant differences between the two groups, always in favour of the antibiotic treatment.

Adverse events and the short-term microbiological profile of this study were reported previously by the investigators.[6] Two subjects, one from the test group and one from the control group, reported adverse events (diarrhoea and vomiting) during the study. No statistically significant differences were observed between the groups with regard to the number of subjects reporting adverse events. Subjects who received systemic antibiotics presented with the most favourable changes in the subgingival microbial profile after treatment. A manuscript reporting on the long-term (one-year) effects of the therapies on the microbiological profile is currently being prepared by the investigators.

Applicability of the results

Patients who participated in this study are quite similar to those treated in everyday general practice. Patients who receive treatment for GAP in general dental practice could therefore receive additional clinical benefit from the adjunctive use of a MTZ–AMX combination. The cost of MTZ and AMX is less than 2% of the cost of SRP, which renders the treatment affordable. Clinicians should, however, be aware of possible allergic reactions to MTZ and AMX in patients. This intervention could possibly also be used for treating other forms of periodontitis.

Clinical resolution

This study clearly demonstrated that the adjunctive use of an MTZ–AMX combination in patients receiving non-surgical SRP to treat GAP had a significant beneficial effect on all the clinical parameters evaluated up to one year after the treatment.

However, a general medical assessment to determine if systemic disease is present, as well evaluation and counselling of family members, is necessary. Microbial identification and antibiotic sensitivity testing may need to be considered prior to treatment. Patient compliance and regular periodontal maintenance care are critically important for ensuring a successful and predictable long-term outcome.

Acknowledgements

AOSIS is thanked for contributing towards the copyediting and publishing costs of this article.

Competing interests

The authors declare that they have no financial or personal relationship(s) that may have inappropriately influenced them in writing this article.

Authors' contributions

J.H. was the project leader. A.v.Z., J.H. and A.C-L. made conceptual contributions towards the methodological quality and synthesis of the study within the relevant clinical context.

References

1. American Academy of Periodontology. Parameters on aggressive periodontitis. J Periodotol. 2000;71(5 Suppl.):867–869. http://dx.doi.org/10.1902/jop.2000.71.5-S.867, PMid:10875695
2. Faveiri M, Figueiredo LC, Duarte PM, et al. Microbiological profile of untreated subjects with localized aggressive periodontitis. J Clin Periodontol. 2009;36:739–749. http://dx.doi.org/10.1111/j.1600-051X.2009.01449.x, PMid:19637996

3. Renvert S, Wikström M, Dahlén G, et al. Effect of root debridement on the elimination of *Actinobacillus actinimycetemcomitans* and *Bacteroides gingivalis* from periodontal pockets. J Clin Periodontol. 1990;17:345–350. http://dx.doi.org/10.1111/j.1600-051X.1990.tb00029.x, PMid:2204636

4. Takamatsu N, Yano K, He T, et al. Effect of initial periodontal therapy on the frequency of detecting *Bacteroides forsythus*, *Porphyromonas gingivalis*, and *Actinobacillus actinomycetemcomitans*. J Periodontol. 1999;70:574–580. http://dx.doi.org/10.1902/jop.1999.70.6.574, PMid:10397511

5. Mombelli A, Schmid B, Rutar A, Lang N. Persistance patterns of *Porphyromonas gingivalis*, *Prevotella intermedia/nigrescens*, and *Actinobacillus actinomycetemcomitans* after mechanical therapy of periodontal disease. J Periodontol. 2000;71:14–21. http://dx.doi.org/10.1902/jop.2000.71.1.14, PMid:10695934

6. Mestnik MJ, Feres M, Figueiredo LC, et al. Short-term benefits of the adjunctive use of metronidazole plus amoxicillin in the microbial profile and in the clinical parameters of subjects with generalized aggressive periodontitis. J Clin Periodontol. 2010;37:353–365. http://dx.doi.org/10.1111/j.1600-051X.2010.01538.x, PMid:20447259