

Linking Research to Clinical Practice

Treating Aggressive Periodontitis

Denise M. Bowen, RDH, MS

The purpose of Linking Research to Clinical Practice is to present evidence based information to clinical dental hygienists so that they can make informed decisions regarding patient treatment and recommendations. Each issue will feature a different topic area of importance to clinical dental hygienists with A BOTTOM LINE to translate the research findings into clinical application.

Griffiths GS, Ayob R, Guerrero A, et al. Amoxicillin and metronidazole as an adjunctive treatment in generalized aggressive periodontitis at initial therapy or re-treatment: a randomized controlled clinical trial. J Clin Periodontol. 2011;38(1):43-49.

Background: Previously, we showed that systemic metronidazole and amoxicillin significantly improved the outcomes of non-surgical debridement in generalized aggressive periodontitis patients. This study aimed to observe whether re-treatment with adjunctive antimicrobials would give the placebo group benefits comparable with the test group.

Methods: Thirty-eight of 41 subjects, from the initial 6 month trial, completed the second phase, the re-treatment of sites with remaining pockets of 5 mm. Subjects on placebo in phase 1 received adjunctive antibiotics for 7 days. Clinical parameters were collected at 2 months post-treatment (8 months from baseline).

Results: Patients who received antibiotics at initial therapy showed statistically significant improvement in pocket depth reduction and in the percentage of sites improving above clinically relevant thresholds, compared with patients who received antibiotics at re-treatment. In deep pockets (7 mm), the mean difference was 0.9 mm ($p=0.003$) and in moderate pockets (4 to 6 mm) it was 0.4 mm ($p=0.036$). Pockets converting from 5 to 4 mm was 83% compared with 67% ($p=0.041$), and pockets converting from 4 to 3 mm was 63% compared with 49% ($p=0.297$).

Conclusion: At 8 months, patients who had antibiotics at initial therapy showed statistically significant benefits compared with those who had antibiotics at re-treatment.

Commentary

Current classifications of periodontal diseases were developed at the 1999 World Workshop for the Classification of Periodontal Diseases and Conditions.¹ Aggressive periodontitis, formerly known as early-onset periodontitis/rapidly progressive periodontitis/juvenile periodontitis, was defined as rapid attachment loss and bone destruction in otherwise healthy individuals, with a familial pattern and microbial deposits that are inconsistent with severity of tissue destruction. The localized form occurs around puberty and affects incisors and first molars. The generalized form often affects people under 30 years of age, but patients may be older. In generalized aggressive periodontitis (GAgP), generalized interproximal attachment loss affects at least 3 permanent teeth other than the incisors and first molars. Invasive periodontal pathogens, neutrophil abnormalities and a poor serum antibody response to infecting agents are frequently identified. These characteristics provide the impetus for consideration of adjunctive antimicrobials in the treatment of aggressive periodontitis.²

In a previous study, these authors concluded that a 7 day regimen of systemic metronidazole and amoxicillin (500 mg each, 3 times per day) significantly improved clinical outcomes of non-surgical debridement in subjects with GAgP when administered in conjunction with initial therapy.

Those findings have been replicated in other studies of initial therapy for GAgP. The focus of this study was to assess whether systemic antibiotics in conjunction with full mouth root surface debridement (FMRSD) improve periodontal disease parameters better than FMRSD with a placebo in patients with GAgP when administered at re-treatment.

Several questions arise about this design. Why would the researchers want to test the antibiotics at re-treatment if they knew that the regimen was effective in initial therapy? Why are antibiotics considered in treatment of GAgP and not for treatment of chronic periodontitis? How does a clinician know when to include systemic antibiotics in a treatment plan for nonsurgical periodontal therapy?

Research findings indicate that FMRSD for chronic periodontitis is effective without prescribing antibiotics as adjuncts. Unnecessary use of antibiotics is also discouraged due to concerns about development of resistant strains of pathogens rendering drugs ineffective, risks and adverse reactions and cost. As a result, most clinicians attempt initial therapy for periodontitis without antibiotics and consider their use at re-evaluation if it is determined that FMRSD was ineffective.

The researchers had previously treated one group of subjects without antibiotics. These individuals could serve as the group receiving antibiotics at retreatment in phase 2, and those subjects who received antibiotics in the first trial would receive FMRSD alone. Although there was improvement in most subjects after phase 1, sites with ≥ 5 mm pockets remained. The first phase of the study included initial therapy with 2 and 6 month follow-ups, and this study was implemented 2 months later at reevaluation. Nineteen subjects in each group entered the second phase of the study. The authors reported, based on a power analysis, that 17 subjects in each group would be an adequate sample size for power needed to detect a difference of 1 mm in pocket depth (in deep pockets ≥ 7 mm), assuming 1 mm variation is normal. The sample size is only one of several factors in assuring there is enough power to detect a difference in outcomes if one exists, and generally a larger sample increases statistical power. Current guidelines for reporting clinical trials require authors to report this information.

Results indicated that antibiotics administered at initial therapy were more effective than administration of the same antibiotics at re-evaluation based on pocket depth reduction and percentage

of sites that improved above clinically relevant thresholds. In periodontal therapy studies, it is important to determine whether results are clinically relevant or just statistically significant. For example, a statistically significant reduction of 0.5 mm in pocket depths from 7 mm to 6.5 mm would not provide a good prognosis for health. A clinician would not want to adopt the intervention for their patients, even though a study may have found a significant difference. These researchers conducted an analysis to identify reductions in pockets by ≥ 2 mm or reductions in the number of pockets that would require additional treatment (≥ 5 mm to ≤ 4 mm or ≥ 4 mm to ≤ 3 mm). These parameters represent criteria used in practice to assess success of periodontal therapy at re-evaluation. Findings from a comparison of both groups indicated that, in deep pockets (7 mm), the mean difference in probing depth reduction was 0.9 mm ($p=0.003$), and in moderate pockets (4 to 6 mm) it was 0.4 mm ($p=0.036$). For pockets converting from ≥ 5 mm to ≤ 4 mm, the group receiving antibiotics at initial therapy had 83% of sites improved compared with 67% ($p=0.041$) at reevaluation. For pockets converting from ≥ 4 mm to ≤ 3 mm reduction, the percentage was 63% compared with 49% ($p=0.297$). The authors also reported a high incidence (42%) of adverse effects from the medication with the majority being minor such as mild nausea, vomiting, diarrhea, metallic taste or headache. These risks need to be weighed against the advantages of using systemic antibiotics in periodontal therapy, thereby reinforcing their potential use in GAgP cases and not in chronic periodontitis cases. It is interesting to note that none of the possible side effects of 0.2% chlorhexidine mouthrinse were reported, possibly because the subjects only were required to use it for 2 weeks following the debridement.

Although a statistically significant difference in pocket depth reduction was found from 0 to 8 months, it was found in both groups, perhaps because both groups had been exposed to antibiotics at some point in therapy. The main effect was found in phase 1 (0 to 6 months) when antibiotics were administered with initial therapy. These findings would not support the common approach of delivering initial therapy and waiting to see if it worked before prescribing antibiotics in patients with GAgP. Prescribing amoxicillin and metronidazole (500 mg each, 3 times a day) with FMRSD is more effective when administered with initial therapy. A careful periodontal assessment with consideration of all criteria for an accurate periodontal disease classification is indicated for appropriate care planning.

Varela VM, Heller D, Silva MX, Torres MC, Colombo AP, Feres-Filho EJ. Systemic antimicrobials adjunctive to a repeated mechanical and antiseptic therapy for aggressive periodontitis: a 6-month randomized controlled clinical trial. J Periodontol. 2011;82(8):1121-1130.

Background: The purpose of this study is to compare the additional benefit of systemic antimicrobials versus placebos to a repeated mechanical instrumentation combined with comprehensive local chemical plaque control for the periodontal treatment of GAgP.

Methods: This was a 6 month, randomized, double-masked, placebo-controlled clinical trial. All GAgP patients received full-mouth disinfection followed by staged scaling and root planing without (placebo group, n=17) or with (test group n=18) systemic antimicrobials (500 mg amoxicillin [AMX] + 250 mg metronidazole [MET], 3 times a day for 10 days). Clinical parameters were measured at baseline and 3 and 6 months post-therapy. Significant differences between groups at baseline were sought by using the Mann-Whitney U test, whereas comparisons over time were examined by using a general linear model repeated measures procedure.

Results: Both groups demonstrated similar improvements in most parameters over time. The test group presented a greater mean probing depth reduction and clinical attachment level (CAL) gain at sites with initially moderate probing depth at 6 months ($p < 0.03$). No differences were seen between groups regarding mean reductions and mean gains, respectively, for probing depth and CAL initially ≥ 7 mm. The test group presented a higher percentage of sites that improved ≥ 2 mm and ended up with a probing depth ≤ 4 mm, or a lower percentage of sites that worsened ≥ 2 mm and remained with probing depth > 4 mm at 3 months ($p < 0.01$). No differences were noticed between groups for these parameters at 6 months.

Conclusion: AMX and MET brought additional clinical effects to the repeated mechanical and antiseptic treatment of GAgP in a very short time (3 months), which tended to fade away over time (6 months).

Commentary

This study assessed the adjunctive use of systemic antibiotics (500 mg amoxicillin [AMX] + 250 mg metronidazole [MET], 3 times a day for 10 days) in conjunction with full mouth disinfection followed by quadrant scaling and root planing for patients with GAgP. As mentioned in the discussion of the

preceding abstract, systemic antibiotics are considered in periodontal therapy for treatment of GAgP and not typically included in care plans for chronic periodontitis. All subjects received full-mouth ultrasonic debridement complemented by 0.2% chlorhexidine (CHX) irrigation in a 24 hour period, and home care instructions including daily use of 0.12% CHX twice a day as a mouthrinse and for tongue brushing. The test group received the antibiotics, and the control group was given a placebo to take for 10 days immediately following. Within a week, all subjects began quadrant scaling and root planing sessions with Gracey curets and 0.2% CHX irrigation of all pockets, with all quadrants completed within 4 to 6 weeks.

The sample included 17 control group subjects and 18 test group subjects. The authors reported that a power analysis indicated 17 in each group provided adequate power to detect differences of 1 mm in pockets ≥ 7 mm.

Probing depth and CAL were measured pre-intervention and post-intervention at 3 and 6 months. Although both groups showed improvement, the group taking the antibiotics with initial periodontal therapy showed a significantly greater average reduction in probing depth and gain in CAL at sites with initially moderate probing depth (≤ 6 mm) at 6 months. These pockets would be most appropriate for nonsurgical periodontal therapy. This same improvement in probing depth and CAL was found in deeper pockets (≥ 7 mm) at 3 months, but there was no difference between subjects receiving the antibiotic and those who did not at 6 months. These areas would normally require periodontal surgery for adequate response and long-term stability. When comparing both groups' improvement in percentage of sites reduced by ≥ 2 mm or reduced to ≤ 4 mm, the test group had more sites showing these clinically relevant changes than the control group at 3 months. However, these changes were not found at 6 months. This finding combines clinical results of treating moderate and deep pockets. The fact that those changes were not sustained over time might have been related to the need for surgical correction of the deeper pockets (≥ 7 mm).

The regimen for antibiotics differed in this study from the standard protocol used in the previously discussed study. These subjects were prescribed 500 mg AMX and 250 mg MET, 3 times a day for 10 days. The standard protocol is 500 mg AMX and 500 mg MET, 3 times a day for 7 days. The side-effects reported in this study were more varied, possibly due to the longer regimen prescribed or perhaps due to the requirement in this study that subjects complete a compliance document daily and record

any adverse effects. Several of the side-effects also could be attributed to the long-term CHX use in this study as compared to the 2 week regimen used post-therapy in the former study. Side-effects included oral ulcerations, metallic taste, dizziness, nausea, diarrhea, tongue staining, teeth staining, taste alterations and mouth burning. The lower dose of MET was intended to reduce side effects; however, the authors note that it is possible that the 250 mg of MET 3 times a day is less effective than at a higher dosage, and could explain the minimal effect in the test group in this study.

The conclusion drawn by the authors was that the use of AMX and MET brought some additional clinical benefits to repeated SRP and antiseptic therapy for GAgP in the short term (3 months), which had a tendency to disappear at 6 months. This conclusion is related to the authors' identified primary outcome measure of deep pockets (≥ 7 mm) and the clinically relevant measures which included the percentage of sites reduced by ≥ 2 mm or reduced to ≤ 4 mm. It does not draw a conclusion about the moderate pockets (4 mm to 6 mm) which did maintain successful reductions at 6 months.

The Bottom Line

Each of these studies addressed the adjunctive use of antibiotics in patients with GAgP. Although this classification of periodontitis is less common than chronic periodontitis, prevalence has been estimated to be 2% for GAgP and 4% for localized aggressive periodontitis in individuals between the ages of 18 and 30 years.³

Both of these studies provide support for use of systemic antibiotics in the initial nonsurgical treatment of GAgP. Both authors also emphasize the importance of prudent use of antibiotics in periodontal therapy because of concerns about side effects/adverse reactions, development of resistant strains rendering the antibiotics ineffective and cost. Based on the findings of these studies, the following conclusions can be drawn:

- For patients with GAgP, adjunctive therapy with systemic antibiotics (500 mg amoxicillin and 500 mg metronidazole, 3 times a day for 7 or 10 days) with nonsurgical periodontal therapy (full mouth debridement, scaling and root planing) results in greater reduction of pocket depths and clinical attachment gains in moderate pockets (4 to 6 mm) when compared to nonsurgical periodontal therapy alone. For pockets ≥ 7 mm, this improvement was found at 6 months in one study, and detected only at 3 months in another. Deep pockets should be referred for periodontal

surgery. Systemic antibiotics added a benefit, especially in the moderate categories of probing depth and CAL.

- Adjunctive systemic antibiotic therapy is more effective when administered with initial nonsurgical periodontal therapy than when administered at reevaluation.
- A thorough periodontal examination with consideration given to characteristics of aggressive periodontitis should be performed for all patients between the ages of 18 and 30 years. Bone and attachment loss in the mandibular incisors and first molars, as well as 3 other sites, presence of deposits inconsistent with degree of attachment loss and a familial pattern suggest a classification of GAgP. When GAgP is found, consultation with the dentist or periodontist and the adjunctive use of antibiotics should be considered in conjunction with initial nonsurgical periodontal therapy rather than waiting to see if periodontal debridement/scaling/root planing alone will be effective at reevaluation.

Summary

Evidence presented in this column indicates that adjunctive antibiotics should be considered in treatment plans for GAgP, despite the fact that they are not recommended for initial treatment of chronic periodontitis. Both of these studies were well-designed and provide support for dental hygienists to alter normal care planning and treatment considerations for GAgP cases.

Denise M. Bowen, RDH, MS, is Professor Emerita in Dental Hygiene at Idaho State University. She has served as a consultant to dental industry, as well as numerous government, university and private organizations and presently is a member of the National Advisory Panel for the National Center for Dental Hygiene Research in the U.S.

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