Locally Applied Antimicrobial Therapy

Position Statement

Introduction and Background

The use of locally applied antimicrobial therapy (LAA) has expanded to become almost routine by some dental offices (ADA code 4381) in conjunction with scaling and root planing (S/RP) for periodontal treatment. If there is no or limited clinical significance derived from the use of these products the cost associated with these procedures would represent wasted benefit dollars which could be used for more proven therapies. Stakeholders in this discussion include general dentists, periodontists, patients, payers and product manufacturers.

The key question that needs to be answered is whether the use of LAA in conjunction with S/RP results in a clinically significant way to improve the periodontal condition. Is it effective for routine use when treating periodontal disease?

METHODS: This paper is a literature search, a meta analysis, reviewing many papers (some collated many articles) involving more than 5000 patients. More than 700 articles were selected that had been published in English in peer reviewed journals ie: j.perio, j. clinical perio, and j. perio research.

The 8 references contained the many articles encompassed in the selected references.

Summary of Evidence

There are many products used for LAA along with S/RP including tetracycline, minocycline, metronidazole, chlorhexidine, combination of metronidazole and amoxicillin, and other antibiotics/antimicrobials.

These products are delivered in various forms including: impregnated strings, chips, rinses, intra-crevicular injection etc. The following studies were reviewed in the development of this position paper to determine the efficacy of these agents when delivered in conjunction with S/RP.

1) LOCAL ANTI-INFECTIVE THERAPY: PHARMACOLOGICAL AGENTS. A SYSTEMATIC REVIEW

32 studies, 3,705 subjects. Conclusions – S/RP alone resulted in significantly reduced probing depths and gains in clinical attachment level. Findings from the meta-analysis indicate that the average amount of PD reduction achieved by the addition of sustained-release antimicrobials to S/RP is quite small, although highly statistically significant. Is this amount of an additional PD reduction worth the extra time and expense required to insert the antimicrobial system? (per authors, p92, pp 3)

2) LOCALLY DELIVERED DOXYCYCLINE DURING SUPPORTIVE PERIODONTAL THERAPY: A 3 YEAR STUDY

Significant reductions in bleeding on probing (BOP), pocket depths (PD), and residual attachment loss (RAL) and the mean counts of a number of target species between baseline and 3 years were documented for both treatment groups Whereas plaque scores remained unchanged, a statistically significant difference in favor of the adjunctive doxycycline therapy was found between the two groups only at the 3 month examination for BOP, PD, and RAL and for a minority of bacterial species at 2 years.

Although short-term effects on clinical parameters were found with the adjunctive use of locally delivered doxycycline, repeated applications annually had no clinical microbiologic effects beyond those observed with mechanical debridement alone in maintenance patients. (study’s conclusion)

3) IMPACT OF LOCAL ADJUNCTS TO SCALING AND ROOT PLANING IN PERIODONTAL DISEASE THERAPY: A SYSTEMIC REVIEW.

Among the locally administered adjunctive antimicrobials, the most positive results occurred for tetracycline, metronidazole, and chlorhexidine. Adjunctive local therapy generally reduced pocket depth (PD) levels. Differences between treatment and S/RP only groups in the baseline-to-follow-up period typically favored treatment groups but usually only modestly (e.g. from about 0.1 mm to nearly 0.5 mm) even when the differences were statistically significant. Effects for clinical attachment levels (CAL) gains were smaller and statistical significance less common. The marginal improvements in PD and CAL were a fraction of the improvement from SRP alone.

Whether such improvements, even if statistically significant, are clinically meaningful remains a question. A substantial agenda of future research to address this and other issues (e.g. costs, patient-oriented outcomes) is suggested. (study’s conclusion)

4 & 5) TREATMENT OF PERIODONTITIS BY LOCAL ADMINISTRATION OF MINOCYCLINE MICROSPHERES; A CONTROLLED TRIAL

LOCALLY DELIVERED MINOCYCLINE MICROSPHERES FOR THE TREATMENT OF PERIODONTITIS IN SMOKERS
Two clinical studies, similar format and method. Baseline measurement; S/RP alone; with microspheres. Measurements at baseline, 1,3,6 and 9 months. Experimental patients seen multiple times and S/RP only at beginning.

The results were statistically significant. However, clinical significance was very small.

6) CLINICAL AND MICROBIOLOGICAL CHANGES ASSOCIATED WITH THE USE OF COMBINED ANTIMICROBIAL THERAPIES TO TREAT “REFRACTORY” PERIODONTITIS

Study of 14 subjects with refractory periodontitis. Patients treated with S/RP, locally delivered tetracycline and systemically administered amoxicillin and metronidazole and professional removal of supragingival plaque weekly for 3 months.

Some modest clinical improvements after 6 months but regrowth of bacteria after.

7) EFFECTIVENESS OF ANTIMICROBIAL ADJUNCTS TO SCALING AND ROOT-PLANING THERAPY FOR PERIODONTITIS

Review of many papers involving use of tetracycline. Minocycline, Metronidazole, combination of metronidazole and amoxicillin, Chlorhexidine, and other antimicrobials. All were used in treatment with S/RP.

The key question is whether S/RP accompanied by an antimicrobial agent, as a supplemental of adjunct treatment, results in improved outcomes that persist over time in adults with chronic periodontitis when compared with S/RP alone.

Of the antimicrobials investigated, studies of locally applied tetracyclines and minocycline and locally delivered chlorhexidine have fairly consistent results in moderately large studies that often reach statistical significance; improvements observed in these studies typically average in the neighborhood of 0.3mm to 0.6 mm. The question remains, the authors note, whether such improvements are clinically meaningful.

8) AMERICAN ACADEMY OF PERIODONTOLOGY STATEMENT OF LOCAL DELIVERY OF SUSTAINED OR CONTROLLED RELEASE ANTIMICROBIALS AS ADJUNCTIVE THERAPY IN THE TREATMENT OF PERIODONTITIS

The existing data appear insufficient to conclude that adjunctive sustained or controlled release locally delivered antimicrobial (LDA) treatment can either reduce the need for surgery or improve long-term tooth retention, or is cost effective. Additional studies are needed to support the use of LDA in special sites.

Discussion

A review of the published papers representing many studies revealed that S/RP is effective in the routine treatment of periodontal disease. Addition of LAA was tested to determine if adjunctive therapy would add to improvement. The studies involved use of many different agents in a variety of delivery systems. Results were measured at baseline and various intervals.

All studies showed some improvement with S/RP alone that was clinically significant. Most studies reported no significant improvement with adjunctive therapy involving LAA. A few studies claimed some “statistically significant” improvement of between 0.3mm to 0.6mm. The majority of the studies reported that any improvements were of little or no clinical significance for treatment of non-surgical periodontitis.

"Numerous clinical trials have demonstrated that manual probing without benefit of a stent results in a standard error of measurement for PD and Cal of +/- 1.0 mm” (from C.Cobb, Presentation at AADC workshop, 5/11). When allowing for the standard error of the measurement, the results of the studies are no better than SRP alone.

One additional paper titled “Treatment of Periodontitis by Local Administration of Minocycline Microspheres: A Controlled Trial” (Williams RC, Paquette D et al, J Periodontol, November 2001) was presented and reviewed. This paper studied patients with more advanced chronic periodontal disease and, therefore, was not included in our review to determine the efficacy of adjunctive use of LAA for routine treatment of nonsurgical periodontal disease patients. However, it is presented to show an important possibility of bias which could influence researchers. The following statement is from the

Acknowledgments at the end of the report:

This study was supported by a grant from OraPharma, Inc., Warminster Pennsylvania. Drs.Cochran, Ofenbacher, Van Dyke and Williams are members of the Scientific Advisory Board for OraPharma, Inc., and in that role have been given equity in the company. Drs. Santucci, Rodda, and Lessern are in the Clinical Research Division of OraPharma, Inc.

This is not to say that the research is not valid, only that both researchers and readers should be aware of the possible conflict of interest which could influence the findings. Papers #4 & 5 were conducted by many of the same researchers.

Position Statement

Based on review of the published papers as summarized above, scientifically based evidence does not support the use of locally applied antimicrobial therapy as adjunctive therapy for the routine treatment of periodontal disease. Additional studies are recommended to
determine the value of LAA for the treatment of periodontal disease with specific recalcitrant pockets that have not responded to conventional periodontal treatment modalities.

References

4. TREATMENT OF PERIODONTITIS BY LOCAL ADMINISTRATION OF MINOCYCLINE MICROSPHERES; A CONTROLLED TRIAL Williams RC, Paquette D, J. Periodontol, 2001 Nov; 72(11):1535-44
7. EFFECTIVENESS OF ANTIMICROBIAL ADJUNCTS TO SCALING AND ROOT-PLANING THERAPY FOR PERIODONTITIS Evidence report/technology assessment: Number 88 RTI International UNC
8. AMERICAN ACADEMY OF PERIODONTOLOGY STATEMENT OF LOCAL DELIVERY OF SUSTAINED OR CONTROLLED RELEASE ANTIMICROBIALS AS ADJUNCTIVE THERAPY IN THE TREATMENT OF PERIODONTITIS

The AAP statement was developed under the direction of the Task Force on Local delivery of Antimicrobials as Adjunct Therapy and approved by the Board of Trustees of the American academy of Periodontology in May 2006.

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Dr. Michael D.L. Weisenfeld (Chair and Principal Author)
Dr. George Koumaras
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