Evidence Report/Technology Assessment
Number 88

Effectiveness of Antimicrobial Adjuncts to Scaling and Root Planing Therapy for Periodontitis

Volume 1. Evidence Report and Appendixes

Prepared for:
Agency for Healthcare Research and Quality
540 Gaither Road
Rockville, Maryland 20850
www.ahrq.gov

Contract No. 290-97-0011

Prepared by:
RTI International-University of North Carolina Evidence-based Practice Center
Research Triangle Park
North Carolina

Investigators
Arthur J. Bonito, Ph.D.
Kathleen N. Lohr, Ph.D.
Linda Lux, M.P.A.
Sonya Sutton, B.S.P.H.
Anne Jackman, M.S.W.
Lynn Whitener, Dr.P.H.
Christian Evensen, M.S.

AHRQ Publication No. 04-E014-3
March 2004

This document is in the public domain and may be used and reprinted without permission except those copyrighted materials noted for which further reproduction is prohibited without the specific permission of copyright holders.

Suggested Citation:

Arthur J. Bonito AJ, Lohr KN, Lux L, Sutton S, Jackman A, Whitener L, Evensen C. Effectiveness of Antimicrobial Adjuncts to Scaling and Root Planing Therapy for Periodontitis Vol. 2. Evidence Tables. Evidence Report/Technology Assessment No. 88 (Prepared by RTI International-University of North Carolina Evidence-based Practice Center under Contract No. 290-97-0011) AHRQ Publication No. 04-E014-3. Rockville, MD: Agency for Healthcare Research and Quality. March 2004.

Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-Based Practice Centers (EPCs), sponsors the development of evidence reports and technology assessments to assist public- and private-sector organizations in their efforts to improve the quality of health care in the United States. This report, *Effectiveness of Antimicrobial Adjuncts to Scaling and Root-Planing Therapy for Periodontitis*, was requested and funded by the National Institute of Dental and Craniofacial Research. The reports and assessments provide organizations with comprehensive, science-based information on common, costly medical conditions and new health care technologies. The EPCs systematically review the relevant scientific literature on topics assigned to them by AHRQ and conduct additional analyses when appropriate prior to developing their reports and assessments.

To bring the broadest range of experts into the development of evidence reports and health technology assessments, AHRQ encourages the EPCs to form partnerships and enter into collaborations with other medical and research organizations. The EPCs work with these partner organizations to ensure that the evidence reports and technology assessments they produce will become building blocks for health care quality improvement projects throughout the Nation. The reports undergo peer review prior to their release.

AHRQ expects that the EPC evidence reports and technology assessments will inform individual health plans, providers, and purchasers as well as the health care system as a whole by providing important information to help improve health care quality.

We welcome written comments on this evidence report. They may be sent to: Director, Center for Outcomes and Evidence, Agency for Healthcare Research and Quality, 540 Gaither Road, Rockville, MD 20850.

Carolyn M. Clancy, M.D.
Director
Agency for Healthcare Research and Quality

Jean Slutsky, P.A., M.S.P.H.
Acting Director, Center for Outcomes and Evidence
Agency for Healthcare Research and Quality

Lawrence Tabak, D.D.S., Ph.D.
Director
National Institute of Dental and Craniofacial Research

The authors of this report are responsible for its content. Statements in the report should not be construed as endorsement by the Agency for Healthcare Research and Quality or the U.S. Department of Health and Human Services of a particular drug, device, test, treatment, or other clinical service.

Acknowledgments

This study was supported by Contract 290-97-0011 from the Agency of Healthcare Research and Quality (Task No. 6). We acknowledge the continuing support of Jacqueline Besteman, JD, MA, director of the AHRQ Evidence-based Practice Program, Ernestine Murray, RN, MAS, the AHRQ Task Order Officer for this project, and Isabel Garcia, DDS, MPH, the National Institute for Dental and Craniofacial Research representative.

We are deeply appreciative of the clinical and research assistance for this systematic review provided by James D. Bader, DDS, MPH, and Daniel A. Shugars, DDS, PhD, of the University of North Carolina at Chapel Hill School of Dentistry and Cecil G. Sheps Center for Health Services Research (Dr. Bader). Both were instrumental in advising on the key questions, designing literature search strategies, selecting critical outcomes, identifying consultants, reviewing titles and abstracts, and initially reviewing clinical articles (Dr. Bader, tetracycline; Dr. Shugars, minocycline). Dr. Bader in addition was extremely helpful with data abstraction and abstractor training and provided a thoughtful review of the draft evidence report. We are singularly indebted to Anne Jackman, MSW, of UNC's Cecil G. Sheps Center for Health Services Research for her unwavering project management and research support. We thank our abstractors, Nancy Fan Lenfestey, MHA, of RTI and Laura Sterling, MD, and Gerald Gartlehner, MD, of the University of North Carolina at Chapel Hill. Finally, the investigators deeply appreciate the considerable support, commitment, and contributions from RTI staff Ghada Homsi, ME, Loraine Monroe, and Terri Kissiah.

In addition, we would like to extend our appreciation to the members of our Technical Expert Advisory Group (TEAG), who served as vital resources throughout our process. They are: Gary Armitage, DDS, Division of Periodontology, University of California at San Francisco School of Dentistry, San Francisco, Calif.; Jack Caton, DDS, Eastman Dental Center, Rochester, NY; Daniel Fine, DMD, Department of Oral Biology, University of Medicine and Dentistry of New Jersey, Newark, NJ; Sarah D. Grossi, DDS, MS, Department of Oral Biology, State University of New York at Buffalo, Buffalo, NY; Marjorie Jeffcoat, DDS, Department of Periodontology, University of Alabama-Birmingham, Birmingham, Ala.; and Anthony Neely, DDS, School of Dentistry, University of Detroit Mercy, Detroit, Mich.

We owe our thanks as well to our external peer reviewers, who provided constructive feedback and insightful suggestions for improvement of our report. Our peer reviewers included Drs. Armitage, Caton, Fine, and Neely from the TEAG, and Dr. Debora Matthews, DDS, Dipl. Periodontics, MSc, Division of Periodontics, Dalhousie University, Nova Scotia, Canada. Our Federal Reviewers included Dr. William Maas of the Centers for Disease Control and Prevention, David Atkins, MD, Chief Medical Officer at ARHQ and David Lewin, of the AHRQ editorial staff, and several other anonymous reviewers from NIDCR and AHRQ.

Structured Abstract

This systematic review concerns chronic periodontitis (bacterial infections of the soft tissue and bone supporting the teeth), which affects many adults in the United States, some severely enough to threaten loss of teeth. The key question is whether, in adults with chronic periodontitis, scaling and root planing (SRP) accompanied by an adjunctive antimicrobial agent when compared to SRP alone improves outcomes that persist over time. Adjunctive antimicrobials include systemic and/or locally applied tetracycline, minocycline, metronidazole, metronidazole plus amoxicillin, chlorhexidine, a grouping of other antibiotics, and a grouping of other antimicrobials. Primary outcomes are reductions in probing depth (PD), gains in clinical attachment level (CAL), and decreases in selected pathogens, especially spirochetes.

Search Strategy. The RTI-UNC Evidence-based Practice Center did a series of MEDLINE searches covering 1966 through December 2002 and an EMBASE search through February 2002 to identify published primary research on this key question; we conducted hand searches of relevant leading journals and used literature identified by clinical experts that the searches did not identify.

Selection Criteria. We included clinical trials published in English that (a) involved adults with chronic periodontitis but no serious comorbidities, (b) tested one or more chemical antimicrobial agents as an adjunct to SRP alone (or with a placebo), (c) had a concurrent control group that received the same SRP as the treatment group, (d) reported outcomes for specified, fixed time periods, and (e) if multiple antimicrobials were tested, reported outcomes for each agent separately.

Data Collection and Analysis. From a pool of nearly 11,000 articles, we retained 599 for independent dual reviews; we retained 70 of these articles, although we used some more than once because they involved more than one antimicrobial arm. A single abstractor abstracted data that were then entered into evidence tables; at least one author independently confirmed data in the evidence tables against original articles and verified data in text and text tables.

We did descriptive and qualitative syntheses of this evidence, focusing on the PD, CAL, and microbiological outcomes, mainly percentage change in spirochetes, reported for the longest time period of each trial. We conducted several meta-analyses of PD and CAL effect sizes when we had necessary data on at least three studies at 6-month follow-up (plus or minus 3 months).

Main Results. Findings differed markedly by antimicrobial and mode of delivery. While this literature has numerous limitations, locally administered adjunctive drugs appear to be more efficacious than systemic drugs; most positive results occurred for tetracycline, minocycline, metronidazole, and chlorhexidine. Adjunctive therapies generally reduced PD levels; differences between treatment and SRP-only groups in the baseline-to-follow-up changes typically favored treatment groups but usually only modestly (e.g., from about 0.1 mm to nearly 0.5 mm) even when the differences between groups were statistically significant. Effects for CAL gains were smaller and statistical significance less common.

Conclusions. Some antimicrobials show promise as adjunctive therapies to SRP for treating non-aggressive chronic periodontitis in patients without other comorbid conditions such as diabetes or immune deficiency, but the marginal improvements in PD and CAL are a fraction of the improvements from SRP alone. Thus, whether such improvements, even if statistically significant, are clinically meaningful remains a question. A substantial agenda of future research to address that and other issues (e.g., costs, patient-oriented outcomes) remains.

Table of Contents

Summary **1**
Objectives 1
Methodology 1
Search Strategy 1
Selection Criteria 1
Data Collection and Analysis 2
Findings 2
Conclusions 5

Evidence Report

1. Introduction **9**
Periodontal Disease and Periodontitis 9
Controlling Periodontal Infections 10
Origins of this Evidence Report 11
Technical Expert Advisory Group 12
Organization of the Report 13

2. Methods **17**
Overview 17
Key Question and Causal Pathway 17
Literature Search and Analysis Strategy 18
Literature Searches 18
Inclusion/Exclusion Criteria 19
Title, Abstract, and Article Review 20
Data Abstraction 20
Meta-Analysis 21
Comparisons 22
Outcomes 22
Preparing Study Data for Meta-Analysis 22
Analysis 22
Quality Rating of Articles 23
Development of the Evidence Report 23

3. Results **29**
Overview 29
Description of the Evidence 29
Limitations of the Evidence 30
Organization of this Chapter 32
Tetracycline 33
Systemic Tetracycline 33
Local Tetracycline 34
Minocycline 37

Systemic Minocycline 37
Local Minocycline 37
Metronidazole 40
Systemic Metronidazole 40
Local Metronidazole 41
Metronidazole with Amoxicillin 43
Chlorhexidine 44
Irrigation and Mouthwash 45
Direct Gingival Applications 46
Other Antibiotics 48
Systemic Antibiotics 48
Local Antibiotics 49
Other Antimicrobials 50

4. Conclusions 81
Overview 81
Summary of Results 82
Overall Comments 82
Therapy-Specific Findings 83
Concluding Comments 85

5. Recommendations for Future Research 89
Clinical Issues Concerning Antimicrobials 89
Types of Antimicrobials 89
Clinical Significance of Potential Benefits 90
Other Research Questions 91
Improving Study Design and Conduct 91

6. References 95

7. Full Bibliography 103

Figures

Figure 1. Diagrammatic Representation of Mechanical and/or Antimicrobial Therapy on Both the Microbial Load and Disease Risk 15
Figure 2. Added Effectiveness of Therapies Adjunctive to Scaling and Root Planing for Treatment of Chronic Periodontitis: Causal Pathway 25
Figure 3. Meta-analysis of Systemic Tetracycline and SRP versus SRP Alone: Probing Depth 72
Figure 4. Meta-analysis of Local Tetracycline and SRP versus SRP Alone: Probing Depth 73
Figure 5. Meta-analysis of Local Tetracycline and SRP versus SRP Alone: Clinical Attachment Level 74
Figure 6. Meta-analysis of Local Minocycline and SRP versus SRP Alone: Probing Depth 75

Figure 7. Meta-analysis of Local Minocycline and SRP versus SRP Alone: Clinical Attachment Level....76
Figure 8. Meta-analysis of Local Metronidazole and SRP versus SRP Alone: Probing Depth....77
Figure 9. Meta-analysis of Local Metronidazole and SRP versus SRP Alone: Clinical Attachment Level....78
Figure 10. Meta-analysis of Local Chlorhexidine and SRP versus SRP Alone: Probing Depth....79
Figure 11. Meta-analysis of Local Chlorhexidine and SRP versus SRP Alone: Clinical Attachment Level....80

List of Tables

Table 1. Technical Expert Advisory Group for the Evidence Report on Effectiveness of Adjuncts to Scaling and Root Planing Therapy for Periodontitis....14
Table 2. Strategy and Results of Original and Follow-up MEDLINE Searches....26
Table 3. Strategy and Results of EMBASE Search....27
Table 4. Inclusion/Exclusion Criteria For Studies of Added Effectiveness of Periodontitis Therapies Adjunctive to Scaling and Root Planing....28
Table 5. Main Features and Findings on Probing Depth and Clinical Attachment Level: Trials of Systemic Tetracycline....53
Table 6. Main Features and Findings on Probing Depth and Clinical Attachment Level: Trials of Local Tetracycline....54
Table 7. Main Features and Findings on Probing Depth and Clinical Attachment Level: Trials of Systemic Minocycline....57
Table 8. Main Features and Findings on Probing Depth and Clinical Attachment Level: Trials of Local Minocycline....58
Table 9. Main Features and Findings on Probing Depth and Clinical Attachment Level: Trials of Systemic Metronidazole....60
Table 10. Main Features and Findings on Probing Depth and Clinical Attachment Level: Trials of Local Metronidazole....62
Table 11. Main Features and Findings on Probing Depth and Clinical Attachment Level: Trials of Systemic Metronidazole plus Amoxicillin....64
Table 12. Main Features and Findings on Probing Depth and Clinical Attachment Level: Trials of Local Chlorhexidine....65
Table 13. Main Features and Findings on Probing Depth and Clinical Attachment Level: Trials of Other Systemic Antibiotics....68
Table 14. Main Features and Findings on Probing Depth and Clinical Attachment Level: Trials of Other Local Antibiotics....70
Table 15. Main Features and Findings on Probing Depth and Clinical Attachment Level: Trials of Other Antimicrobials....71
Table 16. Summary of Qualitative and Quantitative Results for Probing Depth and Clinical Attachment Level....88

Appendixes

Appendix A. Dental Abstraction Form……..141

Appendix B. Quality Review Checklist ……159