Source: Journal of Dental Hygiene, Vol. 81, No. 2, April 2007
Copyright by the American Dental Hygienists' Association

Effect of Treating Periodontal Disease on Cardiovascular Markers

Karen B Williams, RDH, PhD

Karen B. Williams is a professor and director of the Clinical Research Center at the University of Missouri-Kansas City. She received her Certificate in Dental Hygiene and B.S. in Education at The Ohio State University, her M.S. in Dental Hygiene Education at the University of Missouri-Kansas City, and Ph.D. in evaluation, measurement and statistics at the University of Kansas. Dr. Williams has been active in clinical dental hygiene for over 30 years and in clinical research for 20 years. Her areas of specialization include research design and statistics, educational methods, dental product efficacy, health services and health outcomes research, oral manifestations of eating disorders, and clinical dental hygiene. She is a research consultant for numerous dental manufacturers. Dr. Williams has presented papers and continuing education programs throughout the United States and internationally.

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.

Periodontal infections cause changes in traditional and novel cardiovascular risk factors: results from a randomized controlled clinical trial

D'Aiuto, Francesco. Parkar, Mohamed. Nibali, Luigi. Suvan, Jean. Lessem, Jan. Tonetti, Maurizio S. American Heart Journal. 151(5):977-84, 2006 May.

Department of Periodontology, Eastman Clinical Investigation Centre, University College London, London, United Kingdom.

Abstract

Background. Chronic infections, such as periodontitis, are associated with increased risk of systemic diseases driven by a persistent low-grade systemic inflammation and metabolic changes. Severity of periodontitis has also been associated with increased systolic blood pressure (BP). However, the issue remains poorly investigated. We aimed to estimate the effect of periodontal therapy on traditional and novel cardiovascular risk factors in systemically healthy individuals who have periodontitis.

Methods. We enrolled 40 otherwise healthy patients with severe chronic generalized periodontitis in a 6-month pilot intervention trial. Individuals were randomized either to a standard course of periodontal therapy (subgingival scaling and root planing) or an intensive one including the adjunctive use of a locally delivered antimicrobial (IPT).

Results. Compared to control, IPT produced significant reductions in a cluster of inflammatory markers at 1 month (P = .041) and 2 months (P = .006) months together with an improvement in lipid markers at 2 months (P = .032) and 6 months (P = .043) after therapy. Intensive periodontal therapy (IPT) produced greater reductions in IL-6 at 1 (0.4 ± 0.2 ng/L difference, 95% CI 0.03-0.9, P = .0284) and 2 months (0.3 ± 0.2 ng/L difference, 95% CI 0.1-0.8, P = .028), together with decreases in C-reactive protein (0.4 ± 0.2 mg/L difference, 95% CI 0.01-0.8, P = .044) and total cholesterol (0.3 ± 0.1

mmol/L difference, 95% CI 0.04-0.6, P = .025). Moreover, a 7 ± 3mm Hg decrease in systolic BP was observed at 2 months in the IPT group (95% CI 1-12, P = .021), and this difference was greater in current smokers (14 ± 5 mm Hg 95% CI 3-25, P = 0.012). Intensive periodontal therapy subjects exhibited a 1.53% ± 1.20% (95% CI 1.05-2.24, P = .029) and 2.00% ± 1.42% (95% CI 0.98-4.09, P = .057) decreases in cardiovascular risk scores (Framingham) at 2 and 6 months, respectively, when compared to those in the standard group.

Conclusions. Our findings suggest that intensive periodontal treatment reduces systemic inflammatory markers and systolic BP, and improves lipid profiles with subsequent changes in cardiovascular risk when compared to standard therapy.

Commentary

In recent years, considerable attention has been given to the link between periodontal infections and cardiovascular health. Much of the current knowledge regarding the association between periodontitis and cardiovascular problems has been derived from observational studies (primarily cohort and case-control designs). While these studies suggest that periodontitis may increase the risk of myocardial infarction and stroke, as well as be a contributing factor to atherosclerosis and endothelial function, there is also the possibility that these associations are confounded by other common risk factors for cardiovascular diseases. This study was one of the first to experimentally examine the impact of 2 periodontal treatment interventions on common systemic markers of inflammation (that are related to adverse cardiovascular outcomes). The key feature of this study was the random assignment of subjects, who had at least 50% of their dentition with pocket depths exceeding 4 mm and radiographically evident bone loss, to either the 'standard of care' or 'intensive' intervention. The standard of care intervention was comprised of scaling and root planing with local anesthesia completed at one visit lasting between 4 hours and 6 hours. The intensive intervention included scaling and root planing similar to standard of care but with adjunctive use of local delivery of minocycline microspheres (Arestin®, OraPharma). Patients were reexamined and had blood drawn for assessment of inflammatory markers at 2 months and 6 months. An important factor in this study was that the authors determined that the groups were equivalent with respect to their demographic, systemic health, and inflammatory marker values. This is important because any changes that are observed at 2 months and 6 months are more likely attributed to the effect of the intervention, not the fact that groups were not equal at the onset of the project. Results from this study suggest that the addition of Minocycline microspheres resulted in minimal differences in clinical outcomes between the groups at 6 months. Change in periodontal pathogens was not evaluated in this study, so one cannot determine if this lack of difference between the 2 treatments extended to subgingival flora. However, there was a different pattern observed for markers of inflammation. Six months after treatment was completed, the C-reactive protein, IL-6, and lipid markers were significantly lower for the intensive treatment group compared to the standard treatment group. Since C-reactive protein, IL-6, and lipid markers have been shown to be significant predictors of future cardiovascular events, reduction of these markers could have clinical implications. One cannot necessarily conclude that intensive periodontal treatment will reduce future adverse cardiovascular events in all patients; however, reducing systemic inflammation by aggressively treating periodontal infections may be important as part of an overall plan for reducing risk in otherwise healthy patients. The authors caution readers not to over generalize these results to all patients with generalized periodontitis as the sample was small and because this study did not establish that severe periodontitis has a systemic effect.

Treatment of Periodontitis and Endothelial Function

Maurizio S. Tonetti, D.M.D., Ph.D., Francesco D'Aiuto, D.M.D., Ph.D., Luigi Nibali, D.M.D., Ph.D., Ann Donald, Clare Storry, B.Sc., Mohamed Parkar, M.Phil., Jean Suvan, M.Sc., Aroon D. Hingorani, Ph.D., Patrick Vallance, M.D., and John Deanfield, M.B., B.Chir. New Eng J Med 356(9): 911-920; 2007 March.

Department of Oral Health and Diagnostic Sciences, University of Connecticut Health Center, Periodontology Unit, Eastman Dental Institute and Hospital, University College London, Center for Clinical Pharmacology, University College London, and the Vascular Physiology Unit, University College London and Great Ormond Street Hospital for Sick, London.

Abtract

Background. Systemic inflammation may impair vascular function, and epidemiologic data suggest a possible link between periodontitis and cardiovascular disease.

Methods. We randomly assigned 120 patients with severe periodontitis to community-based periodontal care (59 patients) or intensive periodontal treatment (61). Endothelial function, as assessed by measurement of the diameter of the brachial artery during flow (flow-mediated dilatation), and inflammatory biomarkers and markers of coagulation and endothelial activation were evaluated before treatment and 1, 7, 30, 60, and 180 days after treatment.

Results. Twenty-four hours after treatment, flow-mediated dilatation was significantly lower in the intensive-treatment group than in the control-treatment group (absolute difference, 1.4%; 95% confidence interval [CI], 0.5 to 2.3; P=0.002), and levels of C-reactive protein, interleukin-6, and the endothelial-activation markers soluble E-selectin and von Willebrand factor were significantly higher (P<0.05 for all comparisons). However, flow-mediated dilatation was greater and the plasma levels of soluble E-selectin were lower in the intensive-treatment group than in the control-treatment group 60 days after therapy (absolute difference in flow-mediated dilatation, 0.9%; 95% CI, 0.1 to 1.7; P=0.02) and 180 days after therapy (difference, 2.0%; 95% CI, 1.2 to 2.8; P<0.001). The degree of improvement was associated with improvement in measures of periodontal disease (r=0.29 by Spearman rank correlation, P=0.003). There were no serious adverse effects in either of the two groups, and no cardiovascular events occurred.

Conclusions. Intensive periodontal treatment resulted in acute, short-term systemic inflammation and endothelial dysfunction. However, 6 months after therapy, the benefits in oral health were associated with improvement in endothelial function.

Commentary

This recently reported study provides additional experimental evidence that periodontal treatment of patients with severe generalized periodontitis has an impact on systemic health. Otherwise healthy subjects (n=120) were invited to participate if they had probing pocket depths of > 6 mm and alveolar bone loss of > 30% evident on more than 50% of their teeth. Patients were randomly assigned to receive either supragingival scaling and polishing (control) or intensive periodontal therapy, comprised of scaling and root planing with anesthesia, removal of hopeless teeth, and local drug delivery with minocycline microspheres (Arestin®, OraPharma). At baseline and again at 2 months and 6 months, subject received comprehensive periodontal examinations along with assessment of their endothelium-dependent vasodilatation and serum samples of endothelium activating factors and markers of systemic inflammation. Endothelium-dependent vasodilatation (a measure of vascular function) is an important marker as it occurs early in the development of arterial disease, and like the collected inflammatory markers, has been shown to be a predictor of future cardiovascular events. Once again, groups were equivalent at the beginning of the study with regard to factors that might influence the markers of inflammation and vascular function outcomes. Results showed that the intensive periodontal treatment resulted in significantly ($p<.05$) lower plaque scores, less gingival bleeding, and fewer periodontal lesions than observed in the control group. Additionally, vascular function was significantly better in the intensive treatment group than in the control group at both 2 months and 6 month evaluations; although, at 24 hours after the periodontal intervention, the intensive group had a transient decrease in function compared to the control. Markers of endothelium activating factors followed the same trend as vascular function measures. Markers of systemic inflammation (C-reactive protein and IL-6) showed a transient increase at 24 hours, but were not different between the 2 intervention groups at 2 months and 6 months. This study adds to the body of evidence regarding the periodontal-cardiovascular connection. The authors hypothesized that one possible mechanism for this effect may relate to direct effect of pathogens and their by-products on endothelial cells during the transient post-treatment bacteremia. Laboratory studies have shown that P. gingivalis has the potential to invade endothelial cells. Also, periodontal pathogens might initiate a systemic inflammatory response that affects the cells lining vascular pathways. Clinically, these results suggest that aggressive treatment of periodontal disease does impact predictors of cardiovascular events; whether these changes would contribute to actual differences in disease rates of atherosclerosis and cardiovascular events in the population remains to be determined.

Copyright by the American Dental Hygienists' Association

The Bottom Line

There continues to be a large body of evidence investigating the possible relationship between periodontal disease and adverse cardiovascular outcomes. Early studies showing equivocal results on the relationship between chronic periodontal infections and systemic health often did not have clear criteria for the diagnosis of periodontitis. These 2 studies can certainly be considered best evidence based on numerous factors. The diagnostic criteria for study entry allow readers to have a clear understanding that participants in the 2 studies had moderate and severe chronic periodontal infections, respectively, when the studies were initiated. Additionally, the experimental designs, which used random assignment for allocation of subjects to treatment groups, along with assessment of baseline equivalence between groups, provides further confidence that the observed differences at the end of the study can be attributed to the interventions. The clinical implications of this study to day to day dental hygiene practice may not be directive for treatment planning but have logical value to patient management. Logically, these results suggest that chronic periodontitis is an inflammatory event that may have both direct and indirect effect on systemic markers of inflammation. Systemic inflammation is known to predispose individuals to various health risks. Any intervention that reduces chronic infection and reduces signs of systemic inflammation cannot be bad. This suggests that intensive treatment (scaling and root planing with anesthesia and local drug delivery) for subjects with moderate to severe disease may have a positive impact on systemic inflammation. For dental hygienists, this is critically important. Recent literature suggests that patients with moderate to severe periodontal disease are not receiving appropriate care, nor continuing supportive care at appropriate intervals in general dental practices (Cobb et al and Dockter et al). Since this is the most common practice site in which dental hygiene care is rendered, this also suggests that hygienists may be responsible for the substandard care. The literature is unequivocal about the need for anesthesia for providing thorough scaling and root planing. When patients express discomfort with scaling and root planing, clinicians back off and opt for less aggressive care, even when it's indicated. Dental hygienists must consider periodontitis a chronic infection that requires intensive therapy with anesthesia and local drug delivery when appropriate. Routine prophylaxes at 6-month intervals, then, would not only be considered inappropriate but would constitute neglect.

Therefore the following recommendations can be made based on the findings in these 2 studies:

Intensive treatment of moderate and severe periodontal disease has an impact on markers of systemic inflammation at 2 months but has the greatest effect 6 months after treatment.

Markers of systemic inflammation have been shown to be predictive of adverse cardiovascular future events. Although the evidence does not directly support that treating periodontitis intensively will improve cardiovascular health, it does suggest that treatment is associated with concomitant reductions in systemic inflammation.

Summary

Dental hygiene clinicians must begin to think of periodontitis as a chronic disease, similar to diabetes or hypertension, that requires a different approach to management. Historically, the culture of dentistry has been procedure-based rather than disease-based. If patients have caries or fractured teeth, defined restorative procedures can "repair" the dental defects. A prophylaxis will not "repair" the chronic periodontal infection any more than cleaning an infected wound will cure the infection. Thinking of periodontitis as a chronic infection that can impact systemic health is a different paradigm for practice. Dental hygienists are responsible for the level of care most patients in general practice receive, and need to be aware of the implications of less than ideal care. Intensive periodontal therapy for moderate to severe disease may serve to reduce risk factors for adverse systemic conditions.