Journal of Clinical Periodontology
Official Journal of The European Federation of Periodontology
Founded by the British, Dutch, French, German, Scandinavian, and Swiss Societies of Periodontology

J Clin Periodontol 2008; 35: 1011–1012 doi: 10.1111/j.1600-051X.2008.01327.x

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Guest Editorial

Effect of periodontal therapy on general health – is there a missing component in the design of these clinical trials?

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Armitage GC. Effect of periodontal therapy on general health – is there a missing component in the design of these clinical trials? J Clin Periodontol 2008; 35: 1011–1012. doi: 10.1111/j.1600-051X.2008.01327.x.

Accepted for publication 28 August 2008

In the past decade there has been a dramatic increase in literature dealing with the potential impact of periodontal infections on overall general health (Kinane & Bouchard 2008). Strong biologically plausible arguments can be made supporting this connection. In addition, results of many (but not all) epidemiological studies indicate that periodontal infections increase the risk of adverse health outcomes such as cardiovascular disease (Mustapha et al. 2007, Persson & Persson 2008), preterm birth (Xiong et al. 2006, Wimmer & Pihlstrom 2008) and pre-eclampsia (Conde-Agudelo et al. 2008). These association studies are important, but if periodontal infections truly have measurable effects on general health outcomes, treatment of these infections should reduce the incidence and severity of these outcomes.

One of the scientific sessions at the recent International Conference on Periodontal Research held in Ljubljana, Slovenia, dealt with randomized clinical trials (RCT) designed to evaluate the effects of periodontal therapy on general health outcomes. A lively discussion occurred after I pointed out that there appears to be a critically important component missing in the design of these clinical trials. Almost without exception, published intervention trials in this area have *no defined periodontal treatment goals or clinically acceptable endpoints linked to the resolution of periodontal infections*. The ''Material and Methods'' sections of most clinical trials adequately describe the periodontal interventions, but fail to include endpoint criteria that can be used to assess the resolution of periodontal infections.

For example, in a large well-performed RCT on a US population [i.e., the Obstetric & Periodontal Therapy (OPT) study], it was found that periodontal treatment did not significantly alter the rates of pre-term birth, low birth weight or foetal development (Michalowicz et al. 2006). The non-surgical periodontal therapy delivered in the OPT study was appropriate in that it included oral hygiene instructions, scaling and root planing (SRP), monthly evaluation and additional scaling ''as needed.'' Although this treatment regimen was reasonable, the study design did not include pre-determined outcome criteria for successful periodontal therapy. This design problem became apparent after completion of the study when the data showed that the treated subjects still had bleeding on probing (BOP) at an average of 46.9% of sites after treatment. This was a statistically significant decrease in the percentage of sites with BOP compared with baseline values of 69.6%, but most clinicians would regard such a high post-treatment percentage of BOP sites as an unacceptable periodontal outcome. In a non-pregnant population with 68% of the sites exhibiting BOP before SRP, it has been reported that average post-treatment BOP values can be reduced to approximately 10% (Apatzidou & Kinane 2004). It can be argued that it is unreasonable to expect in pregnant individuals that the percentage of sites with BOP can be decreased to levels in the 10–15% range as there are profound perturbations in the maternal immune system during pregnancy (Poole & Claman 2004). However, this argument is difficult to support as non-surgical periodontal therapy in pregnant individuals has been shown to reduce the percentage of sites with BOP to 11–15% (López et al. 2002, 2005, Offenbacher et al. 2006). Interestingly, these studies, which showed a dramatic reduction in BOP, also found that periodontal therapy lowered the risk of adverse pregnancy outcomes.

When RCTs are being designed to evaluate the effect of periodontal therapy on general health outcomes, it is critically important that a clinically acceptable targeted endpoint for successful periodontal therapy be included in the study design. It should not be assumed that simply because periodontal treatment has been performed, it has necessarily been effective in managing the patient's periodontal infection. Inclusion of a defined therapeutic endpoint could be considered impractical as all patients do not respond in an identical or predictable fashion to conventional periodontal therapy. This is a real problem since in a large population-based RCT it is not feasible to include

a wide range of treatment modalities (e.g., SRP alone, SRP+multiple antimicrobial agents, SRP+periodontal surgery). Meaningful analysis of the data would be a nightmare as there would be too many intervention variables. However, it is possible to choose a cost-effective and practical form of periodontal therapy that can be expected to work in the majority of the study population. If clinically relevant periodontal outcomes were used, the patients could be placed into responder quartiles for purposes of data analysis. Alternatively, the patients could be dichotomized in responder and non-responder categories. The important point is that the criteria for successful periodontal therapy (i.e., responder and non-responder criteria) be established before conducting the study.

Establishment of clinically relevant criteria for successful periodontal therapy will require a considerable amount of thought and widespread consultation. Since periodontal infections contribute to the inflammatory–infectious burden carried by the patient, the criteria for successful periodontal therapy must include clinical assessments that are linked to this burden. For example, since a composite of probing depth and BOP has been shown to be related to systemic markers of inflammation (Beck & Offenbacher 2002), these two clinical assessments should probably be included as part of any definition of successful periodontal therapy. It is strongly urged that planners of RCTs seek a consensus from the periodontal community as to what clinical criteria should be used for successful periodontal therapy in future clinical trials.

References

Apatzidou, D. A. & Kinane, D. F. (2004) Quadrant root planing versus same-day full-mouth root planing. I. Clinical findings. *Journal of Clinical Periodontology* **31**, 132–140.

Beck, J. D. & Offenbacher, S. (2002) Relationships among clinical measures of periodontal disease and their associations with systemic markers. *Annals of Periodontology* **7**, 79–89.

Conde-Agudelo, A., Villar, J. & Lindheimer, M. (2008) Maternal infection and risk of preeclampsia: systematic review and metaanalysis. *American Journal of Obstetrics & Gynecology* **198**, 7–22.

Kinane, D. & Bouchard, P. (2008) Periodontal diseases and health: consensus report of the sixth European workshop on periodontology. *Journal of Clinical Periodontology* **35** (Suppl. 8), 333–337.

López, N. J., Da Silva, J., Ipinza, J. & Gutiérrez, J. (2005) Periodontal therapy reduces the rate of preterm low birth weight in women with pregnancy-associated gingivitis. *Journal of Periodontology* **76**, 2144–2153.

López, N. J., Smith, P. C. & Gutierrez, J. (2002) Periodontal therapy may reduce the risk of preterm low birth weight in women with periodontal disease: a randomized controlled trial. *Journal of Periodontology* **73**, 911–924.

Michalowicz, B. S., Hodges, J. S., DiAngelis, A. J., Lupo, V. R., Novak, M. J., Ferguson, J. E., Buchanan, W., Bofill, J., Papapanou, P. N., Mitchell, D. A., Matseoane, S. & Tschida, P. A., for the OPT Study. (2006) Treatment of periodontal disease and the risk of preterm birth. *New England Journal of Medicine* **355**, 1885–1894.

Mustapha, I. Z., Debrey, S., Oladubu, M. & Ugarte, R. (2007) Markers of systemic bacterial exposure in periodontal disease and cardiovascular disease risk: a systematic review and meta-analysis. *Journal of Periodontology* **78**, 2289–2302.

Offenbacher, S., Lin, D., Strauss, R., McKaig, R., Irving, J., Barros, S. P., Moss, K., Barrow, D. A., Hefti, A. & Beck, J. D. (2006) Effects of periodontal therapy during pregnancy on periodontal status, biologic parameters, and pregnancy outcomes: a pilot study. *Journal of Periodontology* **77**, 2011–2024.

Persson, G. R. & Persson, R. E. (2008) Cardiovascular disease and periodontitis: an update on the associations and risk. *Journal of Clinical Periodontology* **35** (Suppl. 8), 362–379.

Poole, J. A. & Claman, H. N. (2004) Immunology of pregnancy. Implications for the mother. *Clinical Reviews in Allergy & Immunology* **26**, 161–170.

Wimmer, G. & Pihlstrom, B. L. (2008) A critical assessment of adverse pregnancy outcome and periodontal disease. *Journal of Clinical Periodontology* **35** (Suppl. 8), 380–397.

Xiong, X., Buekens, P., Fraser, W. D., Beck, J. & Offenbacher, S. (2006) Periodontal disease and adverse pregnancy outcomes: a systematic review. *British Journal of Obstetrics & Gynaecology* **113**, 135–143.

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