Effect of periodontal treatment on serum C-reactive protein levels: a systematic review and meta-analysis
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CRD summary
The authors concluded that the evidence does not support the concept that periodontal treatment can reduce systemic serum C-reactive protein levels. The results were based on three small randomised controlled trials and three before-and-after studies. This limited evidence from a small number of studies suggests that a more cautious conclusion might be more appropriate.

Authors' objectives
To evaluate the effects of periodontal treatment on serum C-reactive protein (CRP) levels.

Searching
MEDLINE (1966 to July 2005) and the Cochrane CENTRAL Register; the search terms were reported. In addition, reviews were screened. Studies were only included if they were published in full and in the English language.

Study selection
Study designs of evaluations included in the review
Studies of any design were eligible for inclusion in the review. The included studies were randomised controlled trials (RCTs) and single-cohort studies.

Specific interventions included in the review
Studies that evaluated periodontal treatment were eligible for inclusion. The included studies evaluated the following interventions, either alone or in combination: scaling and root planning (all but one study), oral hygiene instructions, flurbiprofen, local delivery of minocycline hydrochloride, metronidazole, and surgery plus systemic antibiotics. Treatment duration ranged from 2 to 24 months. No details were provided of the control treatments (where these existed).

Participants included in the review
Inclusion criteria were not specified in terms of the participants. Where reported, the mean age of the participants in the included studies ranged from 40.5 to 49.6 years (individual ages ranged from 20 to 94) and the mean baseline CRP ranged from 0.317 to 4.33 mg/L. Some of the included studies included smokers (27% to 46%, where reported), some included patients with a family history of heart disease and some included healthy patients. One study excluded smokers and included patients who had had a myocardial infarction less than 6 months before study entry.

Outcomes assessed in the review
Studies that measured serum CRP using a high-sensitivity assay at least 2 months after periodontal treatment were eligible for inclusion. The review also assessed the efficacy of periodontal treatment reported in terms of the probing depth.

How were decisions on the relevance of primary studies made?
Two reviewers independently selected the studies. Any disagreements were resolved by discussion.

Assessment of study quality
Two reviewers independently assessed validity. Any disagreements were resolved by discussion. The validity of the RCTs was assessed using a published checklist that included an assessment of allocation concealment, blinding, intention-to-treat analysis and loss to follow-up. The authors did not state that the validity of single-cohort studies was
assessed.

Data extraction
The data were extracted onto a standardised form, but the authors did not explicitly state how many reviewers performed the data extraction. For each study, the mean change in CRP level and variance were extracted or estimated (details of estimation methods were reported). Where required, authors were contacted for clarification and additional data.

Methods of synthesis
How were the studies combined?
The studies were pooled using the DerSimonian and Laird random-effects model. If studies had more than one treatment arm, all comparisons were included in the meta-analysis (see CRD Commentary). For data from single-cohort studies, the overall effect was weighted by individual studies (no other details were provided).

How were differences between studies investigated?
For RCTs, statistical heterogeneity was assessed using the chi-squared statistic. Other differences between the studies were discussed in the text or were apparent from the tables.

Results of the review
The review included three RCTs (n=159) and five studies that provide single-cohort data for six treatment arms (n=209).

RCTs.
One RCT randomised patients using a block method and reported allocation concealment; the other two did not report methods of randomisation or allocation concealment. One RCT was double-blind, one was single-blind and the other provided no details. One RCT used intention-to-treat analysis. The three studies reported attrition rates of 0% or 2.5%.

Two RCTs (three treatment-control comparisons) provided sufficient data for meta-analysis. There was no significant difference between periodontal treatment and control in the change in CRP levels from baseline (-0.18 mg/L, 95% confidence interval, CI: -0.70, 0.35, p=0.49). No statistically significant heterogeneity was detected (p=0.71). The third RCT did not report before and after CRP values for each treatment group.

Data from single-cohort studies.
Over all treatment arms, the change in CRP from baseline ranged from -0.3 to 0.7 mg/L. Three studies provided sufficient data for meta-analysis. There was no significant change in CRP levels from baseline (0.2 mg/L, 95% CI: -0.15, 0.55, p>0.05).

Authors' conclusions
The review findings provided no support for the concept that periodontal treatment can reduce systemic CRP levels.

CRD commentary
The review question was clearly defined in terms of the outcome, broadly defined in terms of the study design and intervention, and not defined in terms of the participants. By limiting the search to English language publications listed in two databases, the authors might have missed some relevant studies. Methods were used to minimise reviewer error and bias in the selection of studies and assessment of validity, but it was unclear whether similar steps were taken at the data extraction stage. The validity of the RCTs was assessed and the results reported; the quality of the single-cohort studies was not assessed.

Studies differed with respect to population and treatment characteristics, and it might not have been appropriate to pool
the data. In addition, the authors should not have pooled data from the same study where there was more than one treatment arm. The results were based on three small RCTs and three before-and-after studies. This limited evidence from a small number of studies suggests that a more cautious conclusion might be more appropriate.

**Implications of the review for practice and research**

Practice: The authors did not state any implications for practice.

Research: The authors stated the need for well-designed, adequately powered RCTs to evaluate the effects of periodontal treatment (including other methods of treatment) on systemic inflammation in the general population, and to determine if modifying the systemic inflammatory process can influence the atherothrombotic process in patients with periodontal disease.

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