Meta-analysis of the effect of systemic metronidazole as an adjunct to scaling and root planing for adult periodontitis

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Authors' objectives
To assess the use of systemic metronidazole (S-MET) as an adjunct to scaling and root planing (SRP) in the treatment of adult periodontitis.

Searching
MEDLINE was searched from 1980 to 1995 using the following keywords: 'periodontal therapy', 'periodontitis', 'metronidazole', 'drug therapy', 'antibiotics', 'randomised controlled (control) trials' and 'controlled clinical trial'.

Current issues of journals specific to periodontal research (1995 to 1996) and the bibliographies of identified papers were also examined for additional studies.

Study selection

Study designs of evaluations included in the review
Randomised clinical trials that evaluated the effect of S-MET on humans, where the studies randomised persons, quadrants, or mouths to treatment groups. The participants were treated with metronidazole for up to 4 weeks, and had to be followed up for between 4 and 26 weeks.

Specific interventions included in the review
S-MET (200, 250, 400 or 500 mg, three times per day, over periods of between 5 days and 4 weeks) in combination with SRP was compared with SRP alone. Oral hygiene instruction was provided to the intervention group in two trials.

Participants included in the review
Adults undergoing treatment for periodontitis were included.

Outcomes assessed in the review
The primary outcome measures were differences in pocket depth (PD) or clinical attachment level (CAL). PD was measured by a reduction in mm depth, while CAL was measured by a gain in mm of attachment.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the authors performed the selection.

Assessment of study quality
The authors did not state that they assessed validity. However, they did consider some of the more important methodological aspects, such as randomisation and blinding.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the authors performed the data extraction.

Methods of synthesis
How were the studies combined?
For studies measuring outcomes on the same continuous scale, a fixed-effect meta-analysis was performed according to the method described by Petitti (see Other Publications of Related Interest).
Changes in the mean PD and mean CAL, and the time to evaluation, were obtained for each of the individual trials. The weighted overall differences between the treatment groups were calculated, along with their 99% confidence intervals. The analyses were conducted both including and excluding crossover studies.

**How were differences between studies investigated?**
The chi-squared test for homogeneity of the results among studies was performed for each stratum, to determine the feasibility of meta-analysis. Heterogeneity was considered to exist if the p-value was less than or equal to 0.10.

Evidence for a dose-response relationship for S-MET was evaluated by applying a weighted least-squares regression to strata consisting of at least 3 studies.

**Results of the review**
Eight randomised controlled trials with 552 participants were included. The distribution of patients between the treatment and control groups was not provided.

The results for each outcome were stratified by the initial PD (1 to 3 mm, 4 to 6 mm, or 7 mm) and the length of follow-up (4 to 6 weeks, 9 to 13 weeks, or 14 to 26 weeks). The number of studies in each stratum ranged from 1 to 3.

S-MET in conjunction with SRP was superior to SRP alone in reducing PD where the initial PD was 4 to 6 mm and the follow-up was 9 to 13 weeks.

There was no significant advantage of S-MET for reducing PD where the initial PD was less than 4 mm or the follow-up was longer than 13 weeks.

No significant heterogeneity of effect was present at any level of initial PD or length of follow-up (p<0.01).

No significant dose-response was observed between the total dose of S-MET and the effect measure of studies within the strata.

**Authors’ conclusions**
These results suggested that S-MET in conjunction with SRP may offer benefit over SRP alone, in the treatment of adult periodontitis patients with pockets of at least 4 mm. However, the additional benefit was not evident if the PD was less than 4 mm or the follow-up was beyond 13 weeks. Further research is required to corroborate these findings.

**CRD commentary**
The authors conducted a reasonable review of studies that varied in their treatment protocols, follow-up times and outcome measures. However, the inclusion criteria for the review were well set, details of the studies were provided, and an appropriate statistical pooling was conducted. On the other hand, the search was restricted to English language studies identified in MEDLINE and relevant studies could, therefore, have been missed. No attempt was made to identify unpublished articles or to contact researchers in this field.

There was no discussion of how judgements were made about the relevance of the included studies. The authors did not assess the quality of of the included studies, or describe their criteria and methods for the data extraction.

The results reported in the abstract for probing depth do not match those reported in the results table in the article. The results of the review should be viewed with caution because of the following limitations: the literature search; the lack of a quality review of the selected articles; discrepancies in the reporting of the results; and the possibility of the effect sizes being influenced by the wide differences between the study characteristics, despite the mitigating stratification performed by the authors.

**Implications of the review for practice and research**
The authors state that further long-term study is needed to corroborate these findings and to ascertain which clinical
parameters influence the clinical decision-making process. The authors believe that these studies should be of at least 9 months' duration.

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