Sinomenine versus NSAIDs for the treatment of rheumatoid arthritis: a systematic review and meta-analysis
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CRD summary
This review compared sinomenine with non-steroidal anti-inflammatory drugs for treatment of rheumatoid arthritis and concluded that sinomenine may be effective and safe for clinical treatment. Although the findings were limited by a lack of good-quality data, the authors' conclusions were suitably cautious and are likely to be reliable.

Authors' objectives
To evaluate the efficacy and safety of sinomenine compared with non-steroidal anti-inflammatory drugs (NSAIDs) for treatment of rheumatoid arthritis.

Searching
Forty three databases were searched without language or publication restrictions to December 2007, including CENTRAL, MEDLINE, CINAHL, AMED, China National Knowledge Infrastructure, VIP, CBMdisc, Chinese Medical Current Contents, Wanfang, Traditional Chinese Medicine Database, China Proceedings of Conference Databases and China Doctorate/Master Dissertations Full Text Databases. Search terms were reported. Additional studies were sought through the reference lists of included studies and handsearches of periodicals, journals and symposium abstracts.

Study selection
Randomised controlled trials (RCTs) and controlled clinical trials (CCTs) that compared the efficacy and/or safety of sinomenine with NSAIDs for treatment of rheumatoid arthritis were eligible for inclusion. Oral sinomenine comparators were any type of NSAID, either individually or in combination. For most of the included studies sinomenine dose ranged from 100mg/day to 240mg/day for adults and 4mg/kg/day for children. The most frequent comparators were aspirin or indometacin. Also included were oxaprozin, ibuprofen and diclofenac. Included outcomes comprised: number of improved patients; number of rheumatoid-factor-disappeared patients; adverse events; morning stiffness; painful joints; swollen joints; grip strength; erythrocyte sedimentation rate; C-reactive protein; joint tenderness score; and articular index.

Two reviewers independently selected studies for inclusion in the review. Disagreements were resolved by discussion.

Assessment of study quality
Randomisation, blinding and dropouts were assessed according to the Jadad criteria. The maximum score was 5 points; studies that scored at least 3 points were considered high quality.

The authors did not state how many reviewers assessed study quality.

Data extraction
Two reviewers independently extracted odds ratios (OR) for dichotomous outcomes (such as number of improved patients) or mean differences for continuous measures (such as morning stiffness). Authors were contacted for missing information.

Disagreements were resolved by discussion.

Methods of synthesis
The studies were combined in meta-analyses. Pooled OR and weighted mean differences (WMD), and their 95% confidence intervals (CI), were calculated using either a fixed-effect model (if heterogeneity was absent) or a random-
effects model (if significant heterogeneity was present). Heterogeneity was assessed using Cochran's Q test.

Results of the review
Ten trials (n=1,185, range 29 to 303) were included: seven RCTs and three CCTs. Study duration ranged from one to six months. Two studies rated high quality and eight rated low quality.

For patients treated with sinomenine, the number of improved patients was significantly greater when compared with NSAIDs (OR 2.57, 95% CI 1.79 to 3.70; 10 studies) as was the number of rheumatoid-factor-disappeared patients (OR 1.93, 95% CI 1.19 to 3.13; four studies). There was no significant heterogeneity for these comparisons.

Compared with NSAIDs, sinomenine was more effective in amelioration of: morning stiffness (WMD -15.66, 95% CI -19.01 to -12.30; three studies); painful joints (WMD -1.40, 95% CI -2.69 to -0.11; three studies) and erythrocyte sedimentation rate (WMD -2.44, 95% CI -3.39 to -1.49; four studies). Significant heterogeneity was present for the painful joints comparison. No significant differences were observed for the treatment of swollen joints, grip strength and C-reactive protein.

Adverse events occurred less frequently in the digestive system during sinomenine treatment than during NSAID treatment (OR 0.04, 95% CI 0.01 to 0.23; three studies), but occurred more frequently in the dermatomucosal system with sinomenine treatment (OR 3.07, 95% CI 1.14 to 8.22; four studies). There was no significant heterogeneity for these comparisons. Adverse events of the nervous system were similar for both treatments.

Authors' conclusions
Sinomenine may be a valuable remedy to clinically treat rheumatoid arthritis, although current evidence needed to be further verified by more high-quality trials.

CRD commentary
Inclusion and exclusion criteria were clear. The authors searched a large number of sources for publications without language or publication restrictions. Limited population details were reported, so the generalisability of the findings was uncertain. Methods were used to reduce error and bias in the selection of studies and the extraction of data; it was unclear whether this extended to the assessment of study quality. An appropriate assessment of study quality was reported, but the assessment (or summary scores) was not reported for each study and it was unclear which criteria studies did not report; most studies were poor quality. Standard statistical methods were used to pool the data. Heterogeneity was assessed and found to be present for the painful joints comparison, but was absent from all other significant results. Although the findings were limited by a lack of good-quality data, the authors' conclusions were suitably cautious and are likely to be reliable.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors stated that there was a need for trials with a high-quality study design together with both short-term and long-term study data, as well as long-term clinical trials to assess the safety of sinomenine to other functional systems other than the dermatomucosal system. An internationally acknowledged standard should be adopted for measuring outcomes in future clinical trials.

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