Chinese herbal medicine for severe acute respiratory syndrome: a systematic review and meta-analysis

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CRD summary
This review evaluated the efficacy of Chinese herbal medicine for treating severe acute respiratory syndrome. It concluded that Chinese herbal medicine combined with conventional medicine may be beneficial, but the evidence is insufficient. The conservative conclusion is appropriate given the poor quality of the primary studies. However, the lack of detail on the review process should be taken into consideration.

Authors' objectives
To evaluate the effects of Chinese herbal medicine for treating severe acute respiratory syndrome (SARS).

Searching
PubMed, the Cochrane Library, Chinese Biomedical Disc database, Chinese Journals Full-text Database, Chinese Scientific Journal Database, the Cochrane Complementary Medicine Field Trials Registry, and AMED were searched from November 2002 to December 2003; the search terms were reported. The Internet, Chinese newspapers, and reference lists of identified articles and reviews were also searched. Published and unpublished studies were eligible for inclusion, and no language restrictions were applied.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion for the main effectiveness analysis. Non-randomised trials were sought for inclusion in an exploratory analysis to evaluate the impact of study design on the primary outcome.

Specific interventions included in the review
Studies that compared herbal medicine plus conventional drugs with placebo or no intervention plus conventional drugs were eligible for inclusion. A range of herbal medicines and conventional regimens were evaluated in the studies; further details were reported. Most studies used a variety of herbal remedies throughout the course of the disease.

Participants included in the review
Studies of patients that met the World Health Organization criteria for a confirmed or suspected case of SARS were eligible for inclusion. All studies included Chinese patients. Baseline prognostic variables were unbalanced across included studies. Where reported, the age of the included patients ranged from 1 to 78 years and the proportion of males from 29 to 61%.

Outcomes assessed in the review
The primary outcome of interest was death. The secondary outcomes were number of complications, symptoms, quality of life, the use of glucocorticoids, findings on chest radiograph, biochemistry and adverse events.

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

Assessment of study quality
Study quality was assessed in relation to allocation concealment and sequence generation, blinding, withdrawals and drop-outs, the use of an intention-to-treat analysis, sample size calculation and comparability of the studies at baseline. The authors did not state how many reviewers performed the quality assessment.
Data extraction
Two reviewers extracted the data independently, with any disagreements resolved by consensus. Data were extracted to calculate relative risks (RR) with 95% confidence intervals (CIs) for dichotomous outcomes for each study, and a mean difference for continuous outcomes.

Methods of synthesis
How were the studies combined?
Pooled RRs or weighted mean differences (WMDs) and 95% CIs were calculated using both random-effects and fixed-effect meta-analyses for each outcome. Publication bias was investigated using funnel plots.

How were differences between studies investigated?
Heterogeneity was assessed using the chi-squared test and I-squared statistic. An exploratory analysis was conducted where non-randomised trials were included, in order to establish the effect of study design on the results. Differences between the studies were also discussed in the text, and study details were tabulated.

Results of the review
Eight RCTs (n=488) were included in the main analysis of the review. Eight non-randomised trials (n=605) were included in the exploratory analysis.

Quality.
Two of the 8 RCTs described the method to generate the allocation sequence and used random number tables. None of the RCTs provided information on allocation concealment, blinding, withdrawals or drop-outs, intention-to-treat analysis or sample size calculations. Only 4 RCTs provided baseline data on comparability between the treatment groups. Therefore, all RCTs were considered low quality.

Mortality.
There was a statistically significant reduction in the risk of death with combined therapy in comparison with conventional drugs (RR 0.32, 95% CI: 0.12, 0.91, P=0.03), based on 294 patients in 5 RCTs. An exploratory analysis of non-randomised studies also showed a statistically significant benefit of combined therapy compared with conventional drugs (RR 0.27, 95% CI: 0.12, 0.61). No evidence of statistical heterogeneity was observed for either analysis.

Fever and symptoms.
Three RCTs showed a statistically significant reduction in the duration of fever (WMD -0.83, 95% CI: -1.30, -0.35, P=0.0006) with combined therapy compared with conventional drugs, and two showed a shortening of time to fever (WMD -1.23, 95% CI: -2.09, -0.37, P=0.005).

Chest radiography.
Three RCTs showed a statistically significant reduction in the average time to resolution of lung inflammation (WMD -2.27, 95% CI: -3.16, -1.39, P=0.0001) with combined therapy compared with conventional drugs, and two showed a reduction in the number of abnormalities (RR 0.29, 95% CI: 0.15, 0.56, P=0.0002).

Glucocorticoids and secondary fungal infections.
Three studies showed no statistically significant reduction in the total dosage (mg) of glucocorticoids (WMD -770.45, 95% CI: -1,798.47, 257.58, P=0.14) between combined therapy and conventional drugs, and two showed no difference in the daily dose (mg) of methylprednisolone (WMD 54.13, 95% CI: -120.63, 12.38, P=0.11). Two studies showed a statistically significant reduction in the number of secondary fungal infections with combined therapy in patients treated with glucocorticoids (RR 0.35, 95% CI: 0.14, 0.90, P=0.03).

Quality of life.
One study reported no statistically significant difference in quality of life between people receiving combined therapy and conventional drugs (WMD -2.20, 95% CI: -4.93, 0.53, P=0.11).

Adverse events.

No study reported data on adverse events.

Authors' conclusions
Chinese herbal medicine combined with conventional medicines may have a beneficial effect in patients with SARS, but low methodological quality means the evidence is insufficient.

CRD commentary
The review question was clear in terms of the intervention, participants, outcomes and study designs. Several relevant sources were searched, and methods were used to minimise publication and language bias. Relevant criteria were used to assess study quality. Although the data extraction was performed in duplicate, it was not reported whether this procedure was employed during the study selection and quality assessment, therefore error and bias cannot be ruled out. The details provided indicated important differences and poor reporting across the included studies. The pooling of the results from such clinically heterogeneous studies might not have been appropriate, even if statistically significant heterogeneity was not observed. Considering the poor quality (or reporting) of the primary studies, the authors' conservative conclusion may be appropriate. However, the lack of methodological details on the review process should be taken into consideration.

Implications of the review for practice and research
Practice: The authors stated that it is premature to conclude that the combination of herbal medicines and conventional drugs has been proven to be superior to conventional drugs alone for patients with SARS.

Research: The authors stated that there is a need to develop international protocols for further well-designed clinical trials, which can be ready for when a new outbreak occurs. There is also a need to develop new treatment options.

Bibliographic details

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.