Traditional Chinese medicinal herbs in the treatment of patients with esophageal cancer: a systematic review

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CRD summary
The authors concluded that current studies provided some evidence that traditional Chinese medicine combined with radiotherapy or chemotherapy may be superior to conventional treatment alone for oesophageal cancer, but that these studies had a high risk of bias. Although the authors acknowledged the poor quality of the evidence, their conclusions appear over-optimistic and should be interpreted with caution.

Authors' objectives
To determine the effectiveness and safety of traditional Chinese medicine as an adjunct to chemotherapy or radiotherapy for treating oesophageal cancer.

Searching
Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, the Chinese Biomedical Literature Database, the China National Knowledge Infrastructure, VIP and Wanfang Data were searched to September 2008. Search terms were reported.

Study selection
Randomised controlled trials (RCTs) of any form of traditional Chinese medicine for treating any type or stage of oesophageal cancer were eligible for inclusion, provided the traditional Chinese medicine was given as an adjunct to active cancer therapy such as radiotherapy or chemotherapy. The comparator could be either active therapy without traditional Chinese medicine, or placebo. Outcomes of interest were mortality, time to progression, quality of life (including control of treatment side effects), treatment response, immune function (measured by T-cell counts) and adverse events.

The participants in the included studies were patients with oesophageal cancer (squamous epithelioma, where stated), either following surgery or with advanced disease. Different formulae of traditional Chinese medicine were used, including Sijunzi Tang and Liuwei Dihuang Wan herbal decoctions. All studies used oral decoctions prepared by study researchers, started before or during conventional treatment, and given for four weeks or until conventional treatment was completed (where stated). The included studies compared patients receiving chemotherapy and/or radiotherapy with adjunctive traditional Chinese medicine versus a group receiving conventional treatment only. One study also included a study arm receiving traditional Chinese medicine only. Included studies reported a wide range of outcomes. All were conducted in China.

Two reviewers selected studies for inclusion, without disagreement.

Assessment of study quality
The following components of study validity were assessed: randomisation, allocation concealment, blinding, completeness of outcome data and risk of selective reporting. Authors of potentially eligible studies were contacted (if possible) for details of randomisation methods and to check other quality issues. The authors did not state how many reviewers this involved.

Data extraction
Relative risks (RRs) were calculated for dichotomous outcomes and mean differences (MDs) were calculated for continuous outcomes, with 95% confidence intervals (CIs).

The authors did not state how the data were extracted for the review or how many reviewers performed the data extraction.
Methods of synthesis
Studies were combined in a narrative synthesis, grouped by outcomes.

Results of the review
Five studies, described as RCTs, were included in the review (n=406 patients, range 54 to 128). None of the authors of these studies could be contacted to check randomisation methods, and the review authors noted that some were probably non-randomised. None of the studies reported their method of randomisation or allocation concealment. One study apparently blinded outcomes assessment, but otherwise no blinding was used.

TCM plus conventional treatment versus conventional treatment only

Mortality/survival (two studies): One study reported significantly lower mortality in the intervention group for up to five years (RR at five years 0.14, 95% CI 0.03 to 0.65). The other study reported significantly higher survival rates in the intervention group for up to two years (RR at two years 2.0, 95% CI 1.15 to 3.46), but found no statistically significant difference between the groups at three years.

Quality of life (three studies): Two studies suggested a reduction in the number and severity of radio-chemotherapy side-effects in the intervention group.

Treatment response (two studies): One study reported a significantly lower rate of relapse or metastasis in the intervention group (RR 0.35, 95% CI 0.14 to 0.88).

Immune response (three studies): All studies reported statistically significant improvements in the intervention group in at least one measure of immune function: effect sizes were reported in the review.

Adverse events: No studies reported any adverse events associated with traditional Chinese medicine.

Authors' conclusions
Current studies provided some evidence that traditional Chinese medicine combined with radiotherapy or chemotherapy may be superior to conventional treatment alone for oesophageal cancer. However, these studies have a high risk of bias.

CRD commentary
The objectives and inclusion criteria of the review were clear and relevant sources were searched for studies. It was not stated whether there was any restriction by language or publication status. Steps were apparently taken to minimise reviewer bias and error by having more than one reviewer independently involved in study selection, but it was unclear whether similar steps were taken in the processes of data extraction and validity assessment. The decision to combine the studies by narrative synthesis was appropriate, in view of the marked clinical heterogeneity between studies. Suitable criteria were used to assess study validity; vigorous efforts were made to check the methodological quality of primary studies by contacting their authors for details. However, since all 119 studies whose authors could be contacted were reported to be non-randomised, it appeared unlikely that the five studies whose authors could not be contacted (i.e. the included studies) were properly randomised. The included studies were small, and as the review authors noted, they had a high potential for bias and conflict of interest. Although the authors acknowledged the poor quality of the evidence, their conclusions appear over-optimistic and should be interpreted with caution.

Implications of the review for practice and research

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

Research: The authors stated that RCTs of traditional Chinese medicine should be conducted worldwide by independent researchers.

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