Clinical efficacy of traditional Chinese medicine as a concomitant therapy for nasopharyngeal carcinoma: a systematic review and meta-analysis

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CRD summary
This review evaluated traditional Chinese medicine combined with conventional cancer therapy for nasopharyngeal carcinoma and found traditional Chinese medicine demonstrated significant efficacy in terms of survival, immediate tumour response, quality of life, immuno-stimulation and acute adverse effects. Due to the possibility of bias and unclear comparability of primary studies the reliability of these conclusions is not clear.

Authors' objectives
To evaluate the effectiveness of traditional Chinese medicine in combination with conventional cancer therapy for nasopharyngeal carcinoma.

Searching
AMED, CINAHL, The Cochrane Library, MEDLINE, EMBASE, EBM Review, ACP Journal Club, Cochrane Database of Systematic Reviews, DARE and Cochrane Central Register of Controlled Trials (CENTRAL) and the Chinese database CNKI were searched for studies in English or Chinese (dates spanned 1966 to 2007). Search terms were reported. Reference lists and review papers from the previous six months were searched.

Study selection
Where reported study duration ranges from five days to 33.5 weeks. Follow-up ranged from one to five years. Randomised controlled trials (RCTs) that compared traditional Chinese medicine combined with conventional cancer therapy with a control group of conventional cancer therapy alone and reported overall survival were eligible for inclusion. The following outcomes were also of interest and were included in the meta-analysis: immediate tumour response; performance status (measured using the Karnofsky scale); selected acute adverse events of cancer therapy; and immuno-stimulation.

Included studies reported use of traditional Chinese medicine combined with chemotherapy, radiotherapy, or both. Where reported, study duration ranges from five days to 33.5 weeks. Follow-up ranged from one to five years. A number of Chinese herb combinations were used in the intervention groups and were described within the review.

Studies were selected independently by two reviewers.

Assessment of study quality
Methodological quality was assessed using the Jadad scale to assess quality in terms of randomisation, blinding, allocation concealment and withdrawals and dropouts and give a quality score out of 5.

The authors did not state how many reviewers performed validity assessment.

Data extraction
Descriptive statistics were extracted for outcomes, percentage of patients with each outcome was calculated and odds ratios (ORs) were calculated if possible. In the case of multiple reporting of the same RCT, reports with the most recent and complete data were used to avoid double counting.

Data were extracted independently by one reviewer and reviewed by a second. Disagreements were resolved by consensus.

Methods of synthesis
Fixed-effect meta-analyses was used to obtain pooled standard mean differences (SMDs) for continuous outcomes and odds ratios for dichotomous outcomes, with corresponding 95% confidence intervals (CIs). Statistical heterogeneity was assessed using the $I^2$ test.

**Results of the review**
Eighteen RCTs were included in the review ($n=1,732$). One trial had a Jadad score of 4, four a score of 3 and 13 a score of 2.

Traditional Chinese medicine was associated with significantly improved survival rate greater than one year (OR 2.51, 95% CI 1.74 to 3.60, $p<0.00001$; 12 RCTs) and greater than three years (OR 1.49, 95% CI 1.08 to 2.07, $p=0.02$; seven RCTs) compared with conventional cancer therapy alone. There was no significant effect for survival greater than five years.

Traditional Chinese medicine was associated with significantly greater immediate tumour response (OR 2.04, 95% CI 1.27 to 3.29, $p=0.003$; six RCTs), improved quality of life (OR 4.30, 95% CI 1.85 to 10.00, $p=0.0007$; two RCTs), lower risk of grade 2-4 oral mucositis (OR 0.38, 95% CI 0.24 to 0.59, $p<0.0001$; four RCTs) and grade 2-4 nausea and vomiting (OR 0.22, 95% CI 0.08 to 0.55, $p=0.001$; two RCTs) than conventional cancer therapy alone.

Traditional Chinese medicine had significantly greater positive effects on immuno-stimulation compared with conventional cancer therapy alone: mean T cell CD4 level was greater in the traditional Chinese medicine groups (SMD 1.31, 95% CI 0.99 to 1.63, $p<0.00001$; two RCTs); mean T cell CD4/CD8 ratio was in favour of traditional Chinese medicine (SMD 1.61, 95% CI 1.27 to 1.95, $p<0.00001$; three RCTs); and mean NK cell level was greater with traditional Chinese medicine (SMD 1.38, 95% CI 0.98 to 1.78, $p<0.00001$; two RCTs).

Statistical heterogeneity was not detected in any of the analyses.

**Authors' conclusions**
This review demonstrated significant efficacy of concomitant traditional Chinese medicine in terms of prolonging survival, enhancement of immediate tumour response, improvement of quality of life, immuno-stimulation and alleviation of acute adverse effects.

**CRD commentary**
The review question was supported by inclusion criteria for study design, intervention and outcomes. Criteria for participants were implied (not specifically stated). Published English- and Chinese-language papers were sought, so it was possible that relevant papers could have been missed due to publication and language biases. Study selection and data extraction were performed in duplicate, which reduced the possibility of reviewer bias and error; no similar steps were reported for validity assessment. Study quality was assessed, but it was unclear whether this was taken into account in the analysis. Meta-analysis appeared appropriate as statistical heterogeneity was not detected; however, as few details were available regarding the control groups and the traditional Chinese medicinal herbs used varied, it was unclear how clinically comparable the studies were. Due to the possibility of bias and unclear comparability of primary studies, the reliability of the authors' conclusions is not clear.

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

**Research:** The authors stated that more controlled trials were required to investigate other efficacy measures of potential interest (such as relapse rate and local and distant metastasis) and determine the role of traditional Chinese medicine for efficacy, safety, feasibility and costs.

**Funding**
Not stated.

**Bibliographic details**

PubMedID
19212827

DOI
10.1080/07357900802392683

Original Paper URL
http://informahealthcare.com/doi/abs/10.1080/07357900802392683

Indexing Status
Subject indexing assigned by NLM

MeSH
Combined Modality Therapy; Drugs, Chinese Herbal /therapeutic use; Humans; Medicine, Chinese Traditional; Nasopharyngeal Neoplasms /immunology /pathology /therapy

AccessionNumber
12009105216

Date bibliographic record published
07/10/2009

Date abstract record published
24/03/2010

Record Status
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.