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[Intervention Review]

Traditional Chinese herbal products for stable angina

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ABSTRACT

Background

Stable angina pectoris is a common condition, worldwide. Traditional Chinese herbal products (TCHP) are developed for treating stable angina pectoris in China.

Objectives

To assess the effectiveness and safety of TCHP in patients with stable angina.

Search methods

We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* Issue 4, 2006), MEDLINE (1995 to June 2008), EMBASE (1995 to June 2008), the Chinese Biomedical Database (CBM) (1995 to June 2008), Chinese Science and Technique Journals Database (VIP) (1994 to June 2008) and Chinese National Knowledge Infrastructure (CNKI) (1995 to June 2008). We handsearched the relevant Chinese journals. We also contacted researchers in the field and authors of studies evaluated in this review for more information. No language restrictions were applied.

Selection criteria

Randomised controlled trials comparing TCHP with placebo, various other TCHP preparations, or with other regimes commonly used currently in the treatment of stable angina.

Data collection and analysis

Quality of studies was assessed independently by two authors. Data were extracted by one author and checked by the other one.

Main results

Three studies each with the number of participants ranging from 60 to 80, and a total of 216 participants, were included in this review. The interventions used in the included studies were different from one another. One study compared TCHP with nitrates and was of good methodological quality whereas the remaining two trials compared one preparation with another preparation and one was of poor methodological quality. As such, we were unable to perform a summary meta-analysis. Only one trial with small patient numbers showed positive results favouring TCHP treatment compared with nitrates, in improved angina symptoms. Two of the trials stated that adverse reactions occurred but detailed data could not be obtained.

Authors' conclusions

There is currently insufficient evidence for effectively treating stable angina pectoris with any of the examined TCHP in this review, due to the small number of included studies and participants. Therefore, TCHP should be used with caution. High quality randomised trials with similar interventions are required to strengthen the evidence for the effectiveness and safety of Chinese medicinal herbs in angina pectoris.

PLAIN LANGUAGE SUMMARY

This review did not find strong evidence to demonstrate the effect of traditional Chinese herbal products in the treatment of stable angina

Traditional Chinese herbal products (TCHP) are often used to treat patients with stable angina but there is not sufficient evidence to show that TCHP are effective. The authors of this review undertook a systematic review of the potential benefits and safety of TCHP in patients with stable angina. Three randomised controlled studies with a total of 216 patients were identified. Only one small trial was able to detect benefits of using TCHP compared with nitrates in improving angina symptoms. The remaining two trials were inconclusive. Due to the very small number of included studies and participants in the studies, TCHP should be used with caution. We recommend that larger-scale high quality randomised controlled trials of TCHP are required to strengthen the evidence for the efficacy and safety of certain TCHP in treating angina.

BACKGROUND

Angina pectoris is the most common clinical manifestation of myocardial ischaemia, caused by an imbalance between myocardial blood supply and oxygen demand. Angina is a common presenting symptom, typically chest pain, among patients with coronary artery disease (Bernard 1979; Kau 1996). Myocardial ischaemia develops when the coronary blood flow becomes inadequate to meet myocardial oxygen demand. This causes myocardial cells to switch from aerobic to anaerobic metabolism with progressive impairment of metabolic as well as mechanical and electrical function (Bernard 1979). Angina is a sign of increased risk of heart attack, cardiac arrest and sudden cardiac death (Bernard 1979; Kau 1996).

Stable angina is chest pain or discomfort that typically occurs with activity or stress. It persists for more than four months and occurs more than five times a week. The pain usually begins slowly and gets worse over the next few minutes. It disappears rapidly with rest or with sublingual nitroglycerin (Bernard 1979). The stable angina attack (or chronic stable angina) is usually predictable, if the patient feels chest discomfort, pressure, or a squeezing sensation. Less commonly sensations of burning, sticking, or sharp pain may occur (Pope 2000).

As a symptom of cardiac ischaemia stable angina occurs because the flow of blood is being restricted, by any of (1) clogged arteries, which are often a sign of coronary artery disease; (2) problems in the aortic valve (one of the four heart valves), such as regurgitation (leaking) or stenosis (narrowing); (3) problems in the heart muscle (e.g. hypertrophic subaortic stenosis) (Hamby 2001). Ischaemic heart disease is the most common cause of death in Western countries, where it amounts to almost 33% of overall mortality (Braunwald 1992). The 'first clinical sign' in over half of patients is angina pectoris. In recent years, there has been an increasing tendency for ischaemic heart disease incidence to rise in developing countries, in conjunction with their economic development. For example in Beijing, China, mortality from this disease has increased from 21.7/100,000 in 1970 to 62.0/100,000 in 1980 (Chen 2000).

Although angina attacks usually pass with little long-term damage to the heart the episodes of cardiac ischaemia that trigger the angina attacks can lead to dangerous problems if left untreated. They can cause abnormal heart rhythms (arrhythmias), which can lead to either syncope (fainting) or sudden cardiac death; heart disease patients whose episodes are triggered by stress (for example frustration) are more likely to die from their heart condition; severe or lengthy episodes can trigger a heart attack; and the small effects of minor episodes can eventually add up and lead to permanent weakening of the heart muscle (cardiomyopathy). So people with new, worsening, or persistent chest discomfort should be monitored carefully (Hamby 2001).

Antiplatelet agents consist of aspirin, ticlopidine, clopidogrel, and dipyridamole (ACC/AHA 1999). These medications prevent thrombus formation by inhibition of platelet aggregation (Alaeddini 2002). The Swedish Angina Pectoris Trial (SAPAT 1992) randomised 2935 patients with a history of at least one month of exertional angina to receive 75 mg aspirin daily in addition to beta-blockers. The intervention resulted in a 34% reduction in primary outcomes (non-fatal myocardial infarction (MI), fatal MI, or sudden death) and a 32% decrease in secondary vascular events after 72

months. Absolute risk reduction was 4% (95% confidence interval 1% to 7%) (SAPAT 1992).

Beta blockers inhibit the activation of beta-receptors, which is associated with a reduction in cardiac inotropic state and sinus rate and slowing of atrioventricular (AV) conduction. The decreases in resting and exercise heart rate, cardiac contractility and arterial blood pressure with beta blockers are associated with decreased myocardial oxygen demand. A reduction in heart rate also increases diastolic perfusion time, which may enhance left ventricular (LV) perfusion (Frishman 1991; Narahara 1990). Patients who require regular, symptomatic treatment should be treated initially with a beta blocker (unless specifically contraindicated) (SIGN 2001). The Beta-Blocker Pooling Project reported a highly significant reduction in mortality in this subgroup and it seems reasonable to assume that beta blockers have the potential to prevent death, especially sudden death, and also the development of myocardial infarction (MI) even when there has been no prior infarction (ESC 1997).

Calcium antagonists reduce the transmembrane flux of calcium via the calcium channels. They can reduce smooth muscle tension in the peripheral vascular bed. This is associated with vasodilation, and can decrease coronary vascular resistance and increase coronary blood flow. All of these agents cause dilation of the epicardial conduit vessels and the arteriolar resistance vessels. Calcium antagonists improve exercise time to onset of angina or ischaemia (ACC/AHA 1999). Long-acting and slow-release calcium antagonists are effective in relieving symptoms in patients with chronic stable angina (ACC/AHA 1999) and are specifically indicated for vasospastic angina (ESC 1997).

For nitroglycerin and nitrates, nitrates can reduce the myocardial oxygen requirement by reducing LV volume and preload, and also by improved nitroglycerin-induced central arterial compliance. Nitrates can improve myocardial perfusion by dilating large epicardial coronary arteries and collateral vessels. Nitroglycerin also exerts antithrombotic and antiplatelet effects in patients with stable angina (ACC/AHA 1999). Sublingual (under the tongue) nitroglycerin tablets or nitroglycerin spray are used for the immediate relief of angina. However, these have not been shown to decrease death or the incidence of heart attacks (Caremark 2003). Both isosorbide dinitrate and mononitrate have been shown in controlled trials to be superior to placebo in controlling symptomatic angina (Chrysant 1993; Thadani 1992).

Angiotensin converting enzyme (ACE) inhibitors, which lower blood pressure and have other effects on blood vessels, could save lives and prevent heart attacks and strokes among certain patients with chronic stable angina (ACC 2002). The Heart Outcomes Prevention Evaluation (HOPE) trial, which compared the ACE inhibitor ramipril against placebo in more than 9000 patients with vascular disease including more than 3500 patients with diabetes, suggests that the use of an ACE inhibitor reduces the rates of death, MI or heart attack, stroke and revascularization procedures (ACC 2002).

Lipid lowering agents, including statins, help lower lipid levels in blood. Recent clinical trials have documented that low density lipoprotein (LDL) lowering agents can decrease the risk of adverse ischaemic events in patients with established coronary artery disease (CAD) (ACC/AHA 1999). The Scandinavian Simvastatin Survival Study showed that a statin given to patients with angina pectoris, and a total cholesterol level between 5.5 and 8.0 mmol/L (212 and 308 mg/dL), substantially reduce the risk of myocardial

infarction, death, and the need for coronary bypass surgery by 30% to 35% (4S 1994). In patients with established CAD, including chronic stable angina, lipid-lowering therapy should be recommended even in the presence of mild to moderate elevations of LDL cholesterol (ACC/AHA 1999).

Chinese herbal medicine in the treatment of stable angina

Traditional Chinese Medicine (TCM) is a 3000-year old holistic system combining the use of medicinal herbs, acupuncture, food therapy, massage and therapeutic exercise for both treatment and prevention of disease (Fulder 1996). TCM has its unique theories for concepts of etiology, systems of diagnosis and treatment which are vital to its practice. TCM treatment consists typically of complex prescriptions of a combination of different components. The combination is based on the Chinese diagnostic patterns (that is inspection, listening, smelling, inquiry, and palpation) and follows a completely different rationale than many Western drug treatments (Liu 2000).

Some researchers have provided evidence on the rationale for use of traditional Chinese herbal medicines for angina. Rationales include (1) relieving myocardial ischaemia as some herbal medicines can dilate coronary arteries and increase coronary blood flow, for example *Flos carthami*, *Radix puerariae*, *Rhizoma ligustici chuanxiong*, *Radix astragali seu hedysari*, *Radix notoginseng* and *Radix salviae miltiorrhizae* (Ou 1992); (2) reducing myocardial oxygen consumption as some herbal medicines can reduce myocardial oxygen consumption, for example *Radix angelicae sinensis* and *Radix notoginseng* (Ou 1992); (3) antiplatelet and anticoagulant activity as some herbal medicines act on various blood-clotting factors, increase the level of cAMP in thrombocytes, inhibit the rheological state of blood to impede the formation of thrombi, for example *Radix salviae miltiorrhizae* and *Hirudo*; some can lower the level of blood lipids and counter the development of atheroma, for example *Radix angelicae sinensis* (Ou 1992); (4) relieving pain as some herbal medicines can reduce the symptoms of chest pain and radiation pain, for example *Radix angelicae sinensis*, *Radix notoginseng* and *Radix astragali seu hedysari* (Ou 1992).

In addition, when using TCM two or more herbs are always used in the one prescription. In this way, the herbs used correctly interact. They may support each other to increase their effects or counteract each other to reduce or remove toxicity or side effects (Ou 1992).

The term 'Traditional Chinese herbal product' (TCHP) refers to an industrially manufactured drug which contains effective extracts of some herbal medicines according to the TCM prescription. The TCHP can be in various forms, for example as a capsule, injection, granule or tablet. Thus the TCHP can be used very conveniently for clinical purposes.

The effectiveness and safety of such treatments need to be reviewed systematically and appraised critically to inform current practice and direct the continued search for new treatment regimens.

OBJECTIVES

To assess the effects (benefits and harms) of traditional Chinese herbal products (TCHP) for stable angina.

METHODS

Criteria for considering studies for this review

Types of studies

We included randomised controlled trials (RCTs) where the randomisation procedure could be authenticated.

Types of participants

Participants were male or female of any age or ethnic origin with stable angina. Participants were excluded if they had acute myocardial infarction, heart failure, hepatic failure or renal failure.

Types of interventions

TCHP compared with a current standard treatment regime or another anti-anginal drug, placebo or no intervention, as well as comparisons between different doses or routes of administration of TCHP.

We decided to exclude studies that used the author's self-prepared decoctions of herbs because these decoctions are limited and have not undergone quality control. We intend to include and analyse those drugs if in the future they become industrial products and enter the market.

Current standard regimes include the following preparations: antiplatelet agents, beta blockers, calcium antagonists, nitroglycerin and nitrates, ACE inhibitors and lipid lowering agents.

Types of outcome measures

We considered the following outcome measures.

Primary outcome measures

Death or acute myocardial infarction

Secondary outcome measures

- Resolution of anginal symptoms
- Frequency of anginal symptoms
- Consumption of short-acting nitroglycerine
- Quality of life
- Readmission to hospital
- Revascularisation

Adverse event outcome measures

As a result of treatment:

- mortality;
- life threatening events;
- toxic responses, for example gastrointestinal reaction;
- anaphylaxis;
- discontinuation of treatment.

Search methods for identification of studies

Comprehensive and exhaustive search strategies were formulated in an attempt to identify all relevant studies regardless of language or publication status (published, unpublished, in press and in progress).

Electronic searches

The following electronic databases were searched:

1. The Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* Issue 4, 2006);
2. MEDLINE (1995 to June 2008);
3. EMBASE (1995 to June 2008);
4. CBM (Chinese biomedical database, 1995 to June 2008);
5. VIP Chinese Science and Technique Journals Database (1994 to June 2008);

6. Chinese National Knowledge Infrastructure (CNKI) (1995 to June 2008).

See [Appendix 1](#) for a general search strategy which was changed for different databases.

The Chinese databases were searched by Chinese characters. See [Figure 1](#) for the Chinese search strategies.

We checked the references of published studies to identify additional trials. We contacted ongoing trial authors to identify unpublished papers, but could not contact pharmaceutical companies who produced relevant products. Authors of identified studies were contacted for additional information.

Figure 1. Search strategy in the Chinese databases

CNKI (包括中国期刊全文数据库, 中国期刊全文数据库_世纪期刊, 中国博士学位论文全文数据库, 中国优秀硕士学位论文全文数据库) (1978~10 July,

- 1 稳定性心绞痛 AND 中药 ti. (0)
- 2 稳定性心绞痛 AND 中药 ab. (22)
- 3 稳定性心绞痛 AND 中药 tx. (181)
- 4 稳定型心绞痛 AND 中药 ti. (8)
- 5 稳定型心绞痛 AND 中药 ab. (51)
- 6 稳定型心绞痛 AND 中药 tx. (457)
- 7 稳定性心绞痛 AND 中成药 ti. (1)
- 8 稳定性心绞痛 AND 中成药 ab. (2)
- 9 稳定性心绞痛 AND 中成药 tx. (24)
- 10 稳定型心绞痛 AND 中成药 ti. (0)
- 11 稳定型心绞痛 AND 中成药 ab. (1)
- 12 稳定型心绞痛 AND 中成药 tx. (54)
- 13 稳定性心绞痛 AND 中西医结合 ti. (26)
- 14 稳定性心绞痛 AND 中西医结合 ab. (11)
- 15 稳定性心绞痛 AND 中西医结合 tx. (26)
- 16 稳定型心绞痛 AND 中西医结合 ti. (13)
- 17 稳定型心绞痛 AND 中西医结合 ab. (9)
- 18 稳定型心绞痛 AND 中西医结合 tx. (127)

VIP (1988~10 July, 2008)

- 1 稳定性心绞痛 AND 中药 ti. (1)
- 2 稳定性心绞痛 AND 中药 ab. (30)
- 3 稳定性心绞痛 AND 中药 tx. (36)
- 4 稳定型心绞痛 AND 中药 ti. (11)
- 5 稳定型心绞痛 AND 中药 ab. (84)
- 6 稳定型心绞痛 AND 中药 tx. (115)
- 7 稳定性心绞痛 AND 中成药 ti. (1)
- 8 稳定性心绞痛 AND 中成药 ab. (4)
- 9 稳定性心绞痛 AND 中成药 tx. (5)
- 10 稳定型心绞痛 AND 中成药 ti. (0)
- 11 稳定型心绞痛 AND 中成药 ab. (7)
- 12 稳定型心绞痛 AND 中成药 tx. (7)
- 13 稳定性心绞痛 AND 中西医结合 ti. (31)
- 14 稳定性心绞痛 AND 中西医结合 ab. (16)
- 15 稳定性心绞痛 AND 中西医结合 tx. (54)
- 16 稳定型心绞痛 AND 中西医结合 ti. (90)
- 17 稳定型心绞痛 AND 中西医结合 ab. (67)
- 18 稳定型心绞痛 AND 中西医结合 tx. (178)

万方 (包括中国学位论文全文数据库, 中国会议论文全文数据库, 数字化期刊全文数据库) (1993~10 July, 2008)

- 1 稳定性心绞痛 AND 中药 ti. (2)
- 2 稳定性心绞痛 AND 中药 ab. (61)
- 3 稳定性心绞痛 AND 中药 tx. (78)
- 4 稳定型心绞痛 AND 中药 ti. (14)
- 5 稳定型心绞痛 AND 中药 ab. (137)
- 6 稳定型心绞痛 AND 中药 tx. (202)
- 7 稳定性心绞痛 AND 中成药 ti. (11)
- 8 稳定性心绞痛 AND 中成药 ab. (5)
- 9 稳定性心绞痛 AND 中成药 tx. (11)
- 10 稳定型心绞痛 AND 中成药 ti. (1)
- 11 稳定型心绞痛 AND 中成药 ab. (19)
- 12 稳定型心绞痛 AND 中成药 tx. (37)
- 13 稳定性心绞痛 AND 中西医结合 ti. (142)
- 14 稳定性心绞痛 AND 中西医结合 ab. (33)
- 15 稳定性心绞痛 AND 中西医结合 tx. (142)
- 16 稳定型心绞痛 AND 中西医结合 ti. (74)
- 17 稳定型心绞痛 AND 中西医结合 ab. (79)
- 18 稳定型心绞痛 AND 中西医结合 tx. (527)

Searches for ongoing studies

We searched five World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) (<http://apps.who.int/trialsearch/>) primary registers for ongoing trials (up to 30 June 2008), which include trials registered in:

- Australia and New Zealand Clinical Trial Registry (www.anzctr.org.au/),
- Chinese Clinical Trial Register (www.chictr.org/),
- ISRCTN (www.controlled-trials.com/isrctn/),
- National Institute of Health Clinical Trials Database (www.clinicaltrials.gov/),
- Clinical Trials Registry-India (www.ctri.in:8080/Clinicaltrials/index.jsp).

Data collection and analysis

Study selection

Three authors (ZQ, YZY, CHX) searched the databases. To determine which studies were to be assessed further, the authors independently scanned the titles, abstracts and keywords of every record retrieved. Full articles were retrieved for further assessment. We contacted the original authors of these studies to clarify the methods used in the process of randomisation. If the author could not be reached, the article was added to those 'awaiting assessment'. Differences in opinion were mostly resolved by discussion. There was no disagreement in the selection of studies.

Assessment of risk of bias of included studies

Risks of bias were assessed independently by at least two authors using the criteria that are described in the Cochrane Handbook for Systematic Reviews of Interventions 5.0.0 (Higgins 2008) and (Wu 2007).

Randomisation process: assessment for selection bias

Adequate sequence generation was reported using one of the following approaches: random number tables or computer-generated random numbers, coin tossing, or shuffling for generating the allocation sequence before recruiting the participants; trial was eligible and had a low risk of selection bias.

A study that did not specify one of the adequate methods outlined above but only mentioned 'random' was considered to have a moderate risk of selection bias.

Studies that used other methods of allocation, for example quasi-randomisation, and appeared to have a high risk of bias and were excluded.

Allocation concealment process: assessment of selection bias

Adequate measures to conceal allocation meant that the person who generated the allocation sequence did not attend recruitment of the participants. The allocation sequence was kept secure, for example by using central randomisation, sealed opaque envelopes or a locked computer, or another description that contained convincing elements of concealment. These were considered to have a low risk of selection bias.

Trials in which the report mentioned 'concealed allocation' but did not report on the approach were considered as 'unclear', with moderate risk of selection bias.

Trials in which the report described an inadequate method to conceal allocation or did not conceal allocation were considered as having high risk of selection bias.

Level of blinding: assessment for performance bias and detection bias

Double blinding, by masking participants and results assessors, was considered to have a low risk of both performance and detection bias. In particular, the use of a placebo or simulant was considered as being the most effective approach for blinding.

Single blinding of the results assessor was considered to have a moderate risk of both performance and detection bias. If single blinding of the participants was carried out, and not the results assessor, the study was considered to have a high risk of detection bias.

No blinding was considered to have a high risk of both performance and detection bias.

We did not consider that blinding was needed for reporting mortality.

Incomplete data bias

- < 5% of participants dropped out or lost to follow up: low risk of bias
- 5% to 15% of participants dropped out or lost to follow up: moderate risk of bias even if intention-to-treat analysis was used
- ≥ 15% of participants dropped out or lost to follow up, or wide differences in exclusions between groups: high risk of bias

Selective reporting bias

If all outcomes were reported in detail, a trial was recognised as having low risk of reporting bias.

If at least one of the outcomes was reported on, but not in detail, the trial was recognised as having moderate risk of reporting bias.

If one or more outcomes were not reported on, the trial was considered as having high risk of reporting bias.

Data extraction

Each trial was assessed independently by two authors (ZQ, YY). Information on trial design, study population, interventions and outcomes were extracted independently by two authors (ZQ, YY) using a data extraction form specifically designed for this review. The data extraction form included the following items.

1. General information: published or unpublished, title, authors, reference or source, contact address, country, urban or rural etc., language of publication, year of publication, duplicate publications, sponsor and setting.
2. Trial characteristics: design, duration of follow up, method of randomisation, allocation concealment, blinding (patients, people administering treatment, outcome assessors).

3. Intervention(s): intervention(s) (dose, route and timing), comparison intervention(s) (dose, route and timing), and co-medication (dose, route and timing).
4. Patients: exclusion criteria, total number and number in each comparison group, age (adults), baseline characteristics, diagnostic criteria, similarity of groups at baseline (including any co-morbidities), assessment of compliance, withdrawals and losses to follow up (reasons, description) and subgroups.
5. Outcomes: as specified above, any other outcomes assessed, other events, length of follow up, quality of reporting of outcomes.
6. Results: for outcomes and times of assessment (including a measure of variation) if necessary converted to the measures of effect specified below, intention-to-treat analysis.

Differences in data extraction were resolved by referring back to the original article and consensus. When necessary, information was sought from the authors of the primary studies.

All data in the included studies were binary outcomes, so the number of events and total number in each group were extracted or imputed.

We extracted herb names in three languages and the formulation contents for the included studies, given in Additional [Table 1](#) and [Table 2](#).

Data analysis

Because of obvious clinical heterogeneity between included studies, we decided against doing a meta-analysis to calculate pooled effect size. Data for each study were analysed and expressed as relative risks. The numbers of dropouts and participants that were lost to follow up for each study, if available, were summarized using an intention-to-treat analysis. When different herbal preparations were used (the TCHP) as the intervention, we considered treatment groups as a whole and compared them to certain chemical drugs in the control groups using qualitative analysis. In summary, data were summarized in a narrative format and different comparisons were analysed separately.

If data are available for meta-analysis in the future, we will proceed as follows. The data will be included in a meta-analysis if similar and of sufficient quality. We expect both event (dichotomous) and continuous data. Dichotomous data will be expressed as odd ratios (OR). The relative risk (RR) may be used as an alternative to the OR as interpretation is easier, especially if the outcome is a negative event. Continuous data will be expressed as weighted

mean differences (WMD). Overall results will be calculated based on the random-effects model. Heterogeneity will be tested for using the χ^2 statistic with significance set at $P < 0.1$. The I^2 statistic will be used to estimate total variation across studies that is due to heterogeneity rather than chance where: 0% to 40% might not be important, 30% to 60%: may represent moderate heterogeneity, 50% to 75% may represent substantial heterogeneity and 75% to 100% considerable heterogeneity ([Higgins 2003](#)). Possible sources of heterogeneity will be assessed by sensitivity and subgroup analysis, as described below. Publication bias will be tested for using the funnel plot or another corrective analytical method, depending on the number of clinical trials included in the systematic review.

We have listed non-randomised controlled studies and the reasons for exclusion of studies in the 'Characteristics of excluded studies' table, but have not discussed them further.

RESULTS

Description of studies

We contacted the original authors by telephone or e-mail to assess the authenticity of the RCT and to retrieve, where applicable, missed information such as about quality issues including allocation concealment.

Studies identified

Initially, we found 242 potentially relevant publications; we eliminated those that did not appear to meet our inclusion criteria. We subsequently retrieved 127 studies classified as RCTs of traditional Chinese medicine in the treatment of stable angina. However, only three of these that were published in Chinese ([Fang 2002](#); [Wang 1999](#); [Wang 2004](#)) could be included. Detailed descriptions of these trials are provided in the table 'Characteristics of included studies'. [Table 2](#) shows the main components of the herbal formulations in the included studies. The remaining RCTs were excluded because:

1. the methodology used did not fulfil those required for an RCT,
2. patients had complicated unstable angina,
3. they were multiple versions of the publication itself,
4. self-prepared formulations were used.

Specific reasons for exclusion of studies are given in [Characteristics of excluded studies](#). The detailed searches and selection of trials for the review are graphically represented in [Figure 2](#), as recommended by the QUOROM consensus guidelines ([Moher 1999](#)).

Figure 2. QUOROM flow chart

Design of included studies

Details of the included studies are shown in the table 'Characteristics of included studies'. All included studies had a randomised controlled parallel study design. All the trials were conducted in China.

Participants of included studies

In one study (Wang 2004) patients with stable angina pectoris were included according to the diagnostic criteria in 'The Guidance of Conducting A Clinical Trial for New Drug of Traditional Chinese Medicine', issued by the Health Ministry of People's Republic of China. The diagnostic criteria in the other two studies were in accordance with the Report of the Joint International Society and Federation of Cardiology and WHO Task Force on Standardization of Clinical Nomenclature.

No included study mentioned exclusion criteria. Patients were adults aged from 40 to 76 years. In one trial the duration of illness on entry was not mentioned (Wang 2004); in the other two trials the mean duration of illness on entry was more than three years.

Interventions used in the included studies

Fang 2002: Yixinmai granule versus compound Danshen tablet
Wang 1999: Baoxinbao tablet versus isosorbide dinitrate
Wang 2004: Linaoxin capsule versus Xinnaokang capsule

In the study using isosorbide dinitrate as control, the dosage was 10 mg three times daily (Wang 1999). The details about drug components, types, routes and dosages are described in the table 'Characteristics of included studies' and 'Additional Table 2'.

Outcome measures of included studies

No study assessed death or acute myocardial infarction. The included three studies reported outcome measures according to the Standard on the Assessment of Curative Effect of Angina and ECG of Coronary Heart Disease, constituted by a Symposium on Integrated Western and Chinese Medicine for the Angina of Coronary Heart Disease in 1979, in China. It specified the following criteria for the measurement of stable angina.

1. Criteria for improvement of angina symptoms in the included studies

- Marked improvement: symptoms disappeared or are reduced by > 80%
- General improvement: severity, frequency and duration of angina attacks reduced by 50% to 80%
- Inefficacy: the severity, frequency and duration of angina attacks similar to before intervention, or reduced by < 50%

2. Criteria for ECG improvement in the included studies

Marked improvement: ECG became normal

General improvement: ST-segment depression improved by > 0.05 mV; the depth of the inverse T wave decreased by > 25% or horizontal T wave turned positive on the main lead of the 12-lead surface ECG

Inefficacy: no improvement of ECG

Two studies (Wang 1999; Wang 2004) reported the number of people with 50% or more decrease in nitroglycerin use per week. One study (Wang 1999) reported heart rate (HR), systolic blood pressure (SBP) and the rate pressure product (HR* SBP) (RPP). Two studies (Wang 1999; Wang 2004) reported on adverse side effects.

None of the studies reported on our other secondary outcomes of quality of life, readmission to hospital or revascularisation.

Risk of bias in included studies

Randomisation

All of the included studies mentioned randomisation but none of the studies described allocation concealment. After confirmation by telephone, we corroborated that the three included studies were authentic RCTs; in two of the studies allocation concealment was 'adequate' (Wang 1999; Wang 2004).

Blinding

By telephone, we verified that two studies (Wang 1999; Wang 2004) used double blinding in which the patients and people administering the treatment were blind to the intervention. One study employed single blinding (Fang 2002), where only the patients were blind to the intervention.

Incomplete data

Only one of the three included studies mentioned withdrawals and reported the reasons (Wang 2004).

Compliance assessment

None of the studies reported on the methods to ensure compliance.

Similarity of comparison groups at baseline

Similarity of comparison groups at baseline was ensured in all studies by stratified randomisations; based on age, sex and disease duration at entry.

Effects of interventions

The data were heterogeneous and of poor quality. Furthermore, no more than two studies used the same intervention. We decided against undertaking a meta-analysis and instead concentrated on a descriptive summary of results. Unfortunately there were no reported data on our selected primary outcomes of death or acute myocardial infarction. We therefore focused on the following outcome measures.

1. Improvement of angina symptoms

This outcome measure synthesized the severity, duration and frequency of angina attacks, and was reported by all three studies.

Data on marked improvement of angina symptoms are shown in [Analysis 1.1](#).

1. TCHP versus nitrate

One study in this subcategory showed positive results favouring the TCHP: Baoxinbao patch compared with isosorbide dinitrite (RR 4.28; 95% CI 1.60 to 11.39) (Wang 1999).

2. One type of TCM versus another (chief active ingredient of the control group: Danshen root)

Two studies (Fang 2002; Wang 2004) compared one type of TCM with another. The main active ingredient was Danshen root, which is regarded by many Chinese physicians as effective (a so-called 'positive effect drug') in treating ischaemic heart diseases.

Of the two studies, Yixinmai granule was more effective than Danshen tablets (RR 2.71; 95% CI 1.34 to 5.48) (Fang 2002). The more recent and better quality trial (Wang 1999) was not able to demonstrate the effectiveness of Linaoxin capsule over Xinnaokang capsule (Wang 2004).

Data on general improvement of angina symptoms are shown in [Analysis 1.2](#).

1. TCHP versus nitrate

The one study in this subcategory showed no statistical significance favouring the TCHP: Baoxinbao patch compared to isosorbide dinitrite (RR 0.96; 95% CI 0.54 to 1.71) (Wang 1999).

2. The other two studies in this category also showed no statistically significant differences (Fang 2002, Wang 2004) between Yixinmai granule and Danshen tablet (Fang 2002) or Linaoxin and Xinnaokang capsule (Wang 2004).

Data on Inefficacy of interventions in improving angina symptoms are shown in [Analysis 1.3](#)

1. TCHP versus nitrate

The one study in this subcategory showed a significant statistical difference suggesting the inefficacy of TCHP: Baoxinbao patch compared to isosorbide dinitrite (RR 0.30; 95% CI 0.13 to 0.67) (Wang 1999).

2. One type of TCM versus another (chief active ingredient of the control group: Danshen root)

No significant differences were observed for the two studies in this subcategory, which compared Yixinmai granule with Danshen tablet (Fang 2002) and Linaoxin with Xinnaokang capsule (Wang 2004).

2. ECG Improvement

See Analysis 2.1 for 'Marked improvement of ECG', Analysis 2.2 for 'General improvement' and Analysis 2.3 for 'Inefficacy of interventions in improving ECG readings'.

The ECG is a valuable diagnostic tool for evaluating myocardial ischaemia and infarction and the effects of cardiac drugs (Surawicz B 2001). The detailed information about this criterion can be found in the 'Description of studies' segment. All three studies reported on ECG improvement but none could demonstrate a marked improvement. Only Wang 1999 could find a general improvement using nitrates, which was of borderline significance (RR 1.80; 95% CI 1.02 to 3.17).

3. Number of people with decreased use of nitroglycerin per week, by 50% or more

See Analysis 3.1 for 'TCHP versus nitrates' and Analysis 3.2 for 'One type of TCHP versus another'.

Two studies reported on the number of people who decreased their use of nitroglycerin by 50% or more per week (Wang 1999; Wang 2004). One demonstrated statistical significance favouring the TCHP Baoxinbao patch compared with isosorbide dinitrite (RR 2.00; 95% CI 1.32 to 3.02) (Wang 1999).

4. Adverse effects

The included studies mentioned adverse effects of TCHP but only in terms of "none obvious" or "low adverse effect". As such, these data were not used.

DISCUSSION

Summary of main results

This systematic review examined and compared the effectiveness of TCHP for patients with stable angina alone or in combination, with nitrates or another TCHP whose main active ingredient was Danshen root. Overall, studies of TCHP for stable angina lack sufficient power to provide reliable estimates of the effects. No study provided data for us to compare the effect of TCHP on our primary outcome measures of death or acute myocardial infarction. The reason for this might be that most patients with chronic stable angina have a relatively low risk of death or major adverse cardiovascular events.

One study in particular was able to provide positive results for our secondary outcome measures, the frequency of angina symptoms and use of nitroglycerin. This is believed to consistently predict mortality and cardiovascular events among outpatients with coronary artery disease. No study measured patient quality of life. One study was able to demonstrate limited benefit of TCHP compared with nitrates in terms of improved angina symptoms. We were unable to determine if TCHP was more effective than the nitrate regimen, mainly because the trial was small with wide confidence intervals and insufficient statistical power. The improvement in ECG was of borderline significance, inferring that

the observed effects were of limited clinical importance. No other positive results were identified, particularly in the two studies comparing one type of TCHP versus another, with Danshen root as the main ingredient. The effectiveness of TCHP in treating stable angina is yet to be established.

Quality of the evidence

The evidence from the included studies was of low quality.

(1) Publication bias may exist because only Chinese language publications were found and included.

(2) Among the 127 papers that we retrieved for further details, the great majority were small clinical trials (around 100 people) which for various reasons could not be included in the systematic review. A large number of the trials claimed to be RCTs but most of them failed to give adequate and convincing information about the methodological quality. When we telephoned the trial authors about the method of randomisation they had used, we found that the majority of the authors described the concept of randomisation incorrectly. In addition, some of the studies were conducted several years ago and the trial authors may have forgotten the details of the methodology they employed, which could lead to bias and end up influencing the veracity of the information provided.

By careful clarification with the authors, we identified only three of the retrieved studies as true RCTs. These had funding sources and only two studies used allocation concealment. The same two studies used double blinding and the third study employed single blinding, which may introduce performance bias. None of the studies mentioned blinding of the outcome assessors, promoting suspicion of detection bias. No analysis was reported based on intention to treat.

(3) None of the three studies used a placebo as control, but 'positive-effect drugs' were selected in two studies (Fang 2002; Wang 2004). Both studies used Danshen preparations as controls, the reason possibly being that the trialists thought that the effect of Danshen was generally accepted in the treatment of ischaemic heart disease. Large sample multicentre RCTs are required.

This may result in false positive findings as a number of interventions are considered effective for stable angina, particularly if trialists know that a 'positive' drug was used in the trial and the purpose of the study was to demonstrate the same effect as the control (so called 'equal effect test' or comparative effectiveness).

(4) We found that the interventions in two of the three studies (Fang 2002; Wang 2004) were prepared by the trial authors themselves or their colleagues in the trial author's hospital. We included these two study because they were funded either by government or a pharmaceutical company and, therefore, had a guarantee of quality. However, the fact that in these two studies the trialists acted as the main players, including formulation designer, trial designer and trialist, may lead to a high possibility of favouring the intervention and introduce conflict of interest.

Although TCHP as a treatment for stable angina and its method of manufacture are widely accepted in China, most of the constituents of the pharmacologically prepared drugs used in the trials cannot be clearly specified. This is in marked contrast to pharmacological agents used in Western medicine, in which

the chemical constituents, their quantities and the percentages of any impurities or contaminants are precisely known; and the variation between different production batches is kept within specified limits. Variations between decoctions and batches of treatments are inevitable consequences of TCHP, though the Chinese Government also specifies the acceptable limits of variation. This variation is a factor that may contribute to heterogeneity between different study results. Furthermore, one must accept that the overall treatment concept for TCHP is different to that used in Western medicine. When a study uses a self-prepared herbal decoction, the quality of herbs and methods of preparation should be stated in detail in order to achieve consistent effects.

(5) One study (Wang 2004) used unequal numbers of participants in each arm of the trial. Wang 2004 used a proportion of 3:1 and only 20 patients were included in the control group (60:20). Considerations for the sample sizes were not reported and so the trial cannot detect differences between the two groups.

(6) None of the studies abided by the criteria laid down in the CONSORT statement (CONSORT 2001). The results for the interventions did not come close to reaching a confirmable conclusion as to the effectiveness of a certain Chinese patent medicine or a herbal preparation compared to another. If more high quality studies on the same interventions had been found, the effectiveness of certain TCMs could have been evaluated more reliably using meta-analysis.

(7) The outcome definitions adopted by this review, and employed by all the studies, were based on a subjective judgement of the extent of improvement of angina symptoms by individual clinicians, making the results somewhat unreliable. Another main outcome measure used was improvement in ECG, which may be a valuable diagnostic tool to evaluate the effects of cardiac drugs (Surawicz B 2001) but it is a surrogate measure. Furthermore, the current ACC/AHA 2002 guideline states that the treatment of chronic stable angina has two complementary objectives. These are to reduce the risk of mortality and morbid events and to reduce symptoms. From the patient's perspective, it is often the latter that is of greater concern. The definition of successful treatment of chronic stable angina, for most patients, should be complete or nearly complete elimination of anginal chest pain and return to normal activities and a functional capacity of CCS class I angina. This goal should be accomplished with minimal side effects of therapy. Unfortunately, neither mortality nor a more precise and objective symptom improvement outcome measure were used. Specific adverse effects were not adequately reported by any of the studies. We intend to adopt changes and improve the next updated version of this review.

(8) It is difficult to compare the outcomes of TCM with standard 'Western' clinical outcomes. TCHP outcomes rely on the subjective interpretation of experienced TCHP physicians in their observations. For example, in the examination of the pulse and tongue (mai xiang and she xiang respectively) outcomes are dependent on the expertise of the physicians and are usually classified in the three main domains of mild, medium and severe. TCM researchers and physicians need to establish a gold standard method for evaluating TCHP outcomes.

Potential biases in the review process

There were 28 studies for which we were unable to contact the authors to authenticate the RCT methodology. Some of these trials may have used adequate RCT methodology and may be included in this review in the future, perhaps leading to different results.

Agreements and disagreements with other studies or reviews

A research team published a meta-analysis (Wang 2006) and a subsequent quality assessment (Fan 2007) on Dan Shen Di Wan (Compound salvia pellet, CSP) versus nitrates for treating stable angina. In that review, 27 articles were included and the quality was assessed using the Jadad scale. They found the following.

1. CSP significantly improved angina, compared with nitrates, in terms of angina symptoms (RR 1.13; 95% CI 1.07 to 1.20), electrocardiogram results (RR 1.39; 95% CI 1.28 to 1.50) and fewer adverse events (2.4% versus 29.7%) (Wang 2006).
2. The methodological quality of clinical trials needs to be improved (Wang 2006) as none of the studies conducted an ethics review or obtained informed consent and thus were not considered to be good enough to provide reliable evidence for clinical practice (Fan 2007).

The review used different criteria for inclusion of studies and as such may have found more favourable results than our systematic review.

AUTHORS' CONCLUSIONS

Implications for practice

There is currently insufficient evidence on the examined Chinese medicinal herbs for treating stable angina pectoris effectively, due to the small number of randomised controlled trials conducted and the paucity of patients enrolled in these trials. In addition, the safety of TCHP is unknown due to the lack of adequate data on adverse reactions. Therefore, TCM should be used with caution. We recommend that stronger evidence is obtained.

Implications for research

It is largely believed in China that TCM is beneficial in the treatment of stable angina pectoris, compared with routine western medicine. However, current clinical studies generally focus on the descriptive analysis of well-known and patented medicines and lack an analysis of TCHP compounds. Most TCHP physicians will choose the component medicinal herb from their own perspective, which makes summary analysis difficult. Finding new and effective agents and sufficient corresponding evidence is therefore difficult. It is necessary to have a clearer description of the medicinal herbal preparations being tested, including information on plant species, geographical origin, harvest season, preparation procedures and quality control measures.

It is of note that most trials are of low methodological quality and with small numbers of participants (mostly 60 to 80). There is a requirement for more studies with high methodological quality, large numbers of participants and good reporting to provide stronger evidence. Hopefully well-designed, randomised and multicentre, instead of sporadic, small-sampled and poorly-designed, clinical trials will be carried out in future. For most

clinicians in China, allocation concealment should be emphasized and the approaches should be reported clearly. Another problem exists in the specific appearance and smell of TCHP, which may make blinding difficult. Drug types and routes should be consistent in both of the comparison groups and capsules may be a good answer to this problem.

Despite the outcome measures laid down according to TCM theory, clinical trials should include endpoints of death and major cardiovascular events and, from the patients' perspective, quality of life. Both require long-term follow up.

Future trials should use a standard risk-stratified population. Standardized monitoring or an effective reporting system should

be adopted to critically estimate adverse events and the safety of specific preparations.

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CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Fang 2002

Methods	Parallel design. The randomisation procedure was not mentioned in the original article, we telephoned the author and confirmed that a random number table was used to generate the allocation sequence. Single blinding was used, for the participants.
Participants	Ethnicity: Chinese Setting: outpatients 60 patients with at least 3 months history of classic angina of effort and at least 3 episodes of attack per week, being relieved by rest or sublingual nitroglycerin, and all in line with Report of the Joint International Society and Federation of Cardiology/World Health Organization Task Force on Standardization of Clinical Nomenclature: 30 in treatment group, M/F 23/7, mean age 56.8 years (46-76), mean disease duration 3.6 years (3 months- 6 years); 30 in control group, M/F 24/6, mean age 57.2 years (5 months- 8 years). Withdrawals and drop-outs: not stated Exclusion criteria: not stated Characteristics of patients at baseline: similar.
Interventions	Treatment group: 10g 'Yi Xin Mai' Granules a time orally t.i.d for 4 weeks (components: Ginseng 5g, Cassia Twig 10g, Snakegourd Fruit 10g, Leech 6g, Indian Buead 15g); Control group: 3 Compound 'Dan Shen' tablets a time orally t.i.d for 4 weeks.
Outcomes	1. Improvement of clinical symptoms: chest pain, palpitation, dyspnea, fatigue etc): using semi-quantitative scale (1-4 points) graded with marked effect (disappearance of clinical symptoms and total score reduced by $\geq 80\%$), general effect (marked improvement of clinical symptoms and total score reduced by 40%-79%), ineffective (no improvement of clinical symptoms and total score reduced by $< 40\%$), aggravation (worsening of clinical symptoms and total score increased by $\geq 10\%$). 2. Therapeutic effect of angina: 1) marked effect: symptoms disappeared or almost disappeared; 2) general effect: marked improvement of the frequency and severity and duration of the disease; 3) ineffective: almost no improvement as before treatment.

Fang 2002 (Continued)

3. Improvement of ECG: 1) marked effect: rest ECG returning to normal, and/or exercise test from positive to negative; 2) general effect: improvement of rest ECG and exercise test, but still not normal; 3) ineffective: ECG remaining almost the same as before treatment.
4. Adverse effect.

Notes	1 It was a local government supported project 2 This was a clinical study for new drug development 3 The formulation of the drug was provided by author's department 4 The drug was made by the author's hospital.
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Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	Not used
Blinding (performance bias and detection bias) All outcomes	Low risk	Single blinding was used for the participants
Incomplete outcome data (attrition bias) All outcomes	High risk	
Other bias	High risk	The formulation of the drug was provided by author's department, and the drug was made by the author's hospital.

Wang 1999

Methods	Parallel design. The randomisation procedure was not mentioned in the original article, we telephoned the author and confirmed that a random number table was used to generate the allocation sequence. Double blinding was used for the participants and drug provider.
Participants	Ethnicity: Chinese Setting: inpatients and outpatients 76 patients with stable angina pectoris, all in line with the Report of the Joint International Society and Federation of Cardiology/World Health Organization Task Force on Standardization of Clinical Nomenclature: 40 in treatment group, M/F 23/17, mean age 61 years(45-70), mean disease duration 35.7 months(2 weeks-10 years); 36 in control group, M/F 21/15, mean age 59.6 years(47-70), mean disease duration 36.8 months(2 weeks-10 years). Exclusion criteria: not stated Withdrawals and drop-outs: not stated Characteristics of patients at baseline: similar.
Interventions	Treatment group: 'Bao Xin Bao' patch (containing dried medicinal herb 16.2g/piece) precordially 2 pieces for the 1st time, then 1 piece each time for 4 days at a time(altogether 6 pieces for 20 days) with or without isosorbide dinitrate therapy in the meantime. Control group: isosorbide dinitrate orally 10mg t.i.d for 20 days.
Outcomes	1. Therapeutic effect of angina: intensity, duration, frequency of attack per week, dosage of isosorbide dinitrate and precipitating factors 2. Clinical symptoms and signs of CHD: chest pain, palpitation, dyspnea, tongue picture and pulse tracings; 3. Resting ECG

Wang 1999 (Continued)

4. Heart Rate (HR), Systolic Blood Pressure (SBP), HR*SBP (RPP)
5. Routine test of blood and urine, liver and kidney function test and adverse effects
6. Level of blood ET and NO.

Notes

In the telephone interview, we completed the following information missed in the article:
1 this was a pharmaceutical company funded topic; the name of company is Hefei Delin Keji Ltd;
2. this was a clinical study for pre-market drug development. The number of the certificate issued by the State Food and Drug Administration was "CZS0006".

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	
Allocation concealment (selection bias)	Low risk	Adequate
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blinding
Other bias	Low risk	

Wang 2004

Methods	Parallel design. Due to that the randomisation procedure was not mentioned in the original article, we telephoned the author and confirmed that a random number table was used to generate the allocation sequence. Double blinding was used for the participants and drug provider.
Participants	Ethnicity: Chinese Setting: inpatients and outpatients 80 patients with at least 2 episodes of attack per week, all in line with The Golden Rule for Clinical Research of New Traditional Chinese Drug (Zhongyao Xinyao Linchuanyanjiu Zhidaoyuanze), mean age 58-65 years; 60 in treatment group and 20 in control group Exclusion criteria: not stated Withdrawals and drop-outs: 3 drop-outs in treatment group Characteristics of patients at baseline: similar.
Interventions	Treatment group: 4 'Li Nao Xin' capsules orally, t.i.d (components: Danshen Root Szechuan Lovage Rhizome, Kudzu vine Root, Earthworm, Red Paeony Root, Safflower, Turmeric Root-tuber, Oriental Waterplantain Rhizome, Tuber Fleeceflower Root, Spina Date Seed, Barbary Wolfberry Fruit, Drug Sweetflag Rhizome, Thinleaf Milkwort Root-bark, Twotooth Achyranthes Root, Liquoric Root). Control group: 4 'Xin Nao Kang' capsules orally t.i.d. (components unidentified).
Outcomes	1. Therapeutic effect of angina: 1) marked effect: symptoms disappeared or almost disappeared; 2) general effect: marked improvement of the frequency and severity and duration of the disease; 3) ineffective: almost no improvement as before treatment. 2. Improvement of ECG: 1) marked effect: rest ECG returning to normal, and/or exercise test from positive to negative; 2) general effect: improvement of rest ECG and exercise test, but still not normal; 3) ineffective: ECG remaining almost the same as before treatment. 3. Dosage changes of nitroglycerin: 1) cease use: complete stopping use of nitroglycerin after treatment; 2) reduced dosage: dosage reduced by at least 50% after treatment; 3) unchanged: dosage reduced by less than 50% after treatment. 4. Adverse effects.

Wang 2004 (Continued)

Notes

- 1 This was a pharmaceutical company funded topic.
- 2 The formulation of the drug was provided by author's department.
- 3 The drug was made by the author's hospital.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	
Allocation concealment (selection bias)	High risk	Adequate
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blinding was used for healthcare provider and the participants.
Incomplete outcome data (attrition bias) All outcomes	High risk	
Other bias	High risk	The study was funded by a pharmaceutical company. The formulation of the drug was provided by the author's department, and the drug was made by the author's hospital.

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Bian 2005	unable to contact authors on methodology used
Cao 2005	unable to contact authors on methodology used
Chang 2005	We consider acupuncture as having no standard method in the therapeutic process and did not intend to discuss it in details.
Chen 2003	Upon contacting the authors, it was identified that the study was not a RCT.
Chen 2004	We telephoned the original author only to identify and find that the trial was actually not a real RCT.
Chen 2005	We telephoned the original author only to identify and find that the trial was actually not a real RCT.
Chen 2006a	We telephoned the original author only to identify and find that the trial was actually not a real RCT.
Chen 2006b	The authors used self-prepared drug, which was manufactured by the authors themselves and did not have standardised formulations.
Chen 2006c	The authors used self-prepared drug, which was manufactured by the authors themselves and did not have standardised formulations.

Study	Reason for exclusion
Cheng 2006	unable to contact authors on methodology used
Deng 2002	unable to contact authors on methodology used
Ding 1999	unable to contact authors on methodology used
Feng 1999	Upon contacting the authors, it was identified that the study was not a RCT.
Feng 2002	unable to contact authors on methodology used
Feng 2003	Upon contacting the authors, it was identified that the study was not a RCT.
Fu 2006	We telephoned the original author only to identify and find that the trial was actually not a real RCT.
Gao 2000	Upon contacting the authors, it was identified that the study was not a RCT
Guo 2006	unable to contact authors on methodology used
Hai 2004	Upon contacting the authors, it was identified that the study was not a RCT.
Han 1999	unable to contact authors on methodology used
He 2003	The author used another unproved TCHP as control which we consider as inappropriate.
Hou 2003	Upon contacting the authors, it was identified that the study was not a RCT.
Hu 1997	The author used another unproved TCHP as control which we consider as inappropriate.
Huang 2002	Upon contacting the authors, it was identified that the study was not a RCT.
Jia 1999	The authors refused to provide any information about their trial.
Jiang 2005	Upon contacting the authors, it was identified that the study was not a RCT.
Jiang 2005a	Upon contacting the authors, it was identified that the study was not a RCT.
Jiang 2005b	Upon contacting the authors, it was identified that the study was not a RCT.
Jiang 2006	We contacted and interviewed the original author only to identify and find that the trial was actually not a real RCT.
Jin 2003	Upon contacting the authors, it was identified that the study was not a randomised trial.
Jing 2006	unable to contact authors on methodology used
Kong 1998	The authors used self-prepared drug, which was manufactured by the authors themselves and did not have standardised formulations.
Li 1998	The authors refused to provide any information about their trial.
Li 1999	Upon contacting the authors, it was identified that the study was not a RCT.
Li 2001	We tried hard to contact and interview the authors but they refused to provide any information about their trials.

Study	Reason for exclusion
Li 2003	Upon contacting the authors, it was identified that the study was not a randomised trial.
Li 2005a	Upon contacting the authors, it was identified that the study was not a RCT.
Li 2005b	Upon contacting the authors, it was identified that the study was not a RCT.
Li 2005c	unable to contact authors on methodology used
Li 2005d	The authors used self-prepared drug, which was manufactured by the authors themselves and did not have standardised formulations.
Li 2005e	The authors used self-prepared drug, which was manufactured by the authors themselves and did not have standardised formulations.
Li 2005f	We contacted and interviewed the original author only to identify and find that the trial was actually not a real RCT.
Li 2005g	We contacted and interviewed the original author only to identify and find that the trial was actually not a real RCT.
Li 2006a	We contacted and interviewed the original author only to identify and find that the trial was actually not a real RCT.
Li 2006b	The authors used self-prepared drug, which was manufactured by the authors themselves and did not have standardised formulations.
Liang 2005	We contacted and interviewed the original author only to identify and find that the trial was actually not a real RCT.
Liao 2005	The authors used self-prepared drug, which was manufactured by the authors themselves and did not have standardised formulations.
Lin 2004	The authors refused to provide any information about their trial.
Liu 1999	The participants included patients with unstable angina, which did not meet our inclusion criteria.
Liu 2004	Upon contacting the authors, it was identified that the study was not a RCT.
Liu 2006a	We contacted and interviewed the original author only to identify and find that the trial was actually not a real RCT.
Liu 2006b	unable to contact authors on methodology used
Lu 2002	We contacted and interviewed the original author only to identify and find that the trial was actually not a real RCT.
Lu 2003	unable to contact authors on methodology used
Lu 2004	The authors used self-prepared drug, which was manufactured by the authors themselves and did not have standardised formulations.
Luo 2003	The authors refused to provide any information about their trial.
Ma 2004	Upon contacting the authors, it was identified that the study was not a RCT.

Study	Reason for exclusion
Mo 2005	We contacted and interviewed the original author only to identify and find that the trial was actually not a real RCT.
Ni 2005	Upon contacting the authors, it was identified that the study was not a RCT
Ou 2002	unable to contact authors on methodology used
Peng 2005	The authors refused to provide any information about their trial.
Qi 2001	The authors refused to provide any information about their trial.
Qian 2002	unable to contact authors on methodology used
Qiao 2004	unable to contact authors on methodology used
Qiao 2006	unable to contact authors on methodology used
Sang 2004	Upon contacting the authors, it was identified that the study was not a RCT.
Shen 2003	Upon contacting the authors, it was identified that the study was not a RCT.
Shen 2004	The authors used self-prepared drug, which was manufactured by the authors themselves and did not have standardised formulations.
Shi 1997	unable to contact authors on methodology used
Shi 2001	Upon contacting the authors, it was identified that the study was not a RCT.
Sun 2002	Upon contacting the authors, it was identified that the study was not a RCT
Tan 2005	The authors used self-prepared drug, which was manufactured by the authors themselves and did not have standardised formulations.
Teng 2005	Upon contacting the authors, it was identified that the study was not a RCT.
Tursun 2006	unable to contact authors on methodology used
Wang 2001a	Upon contacting the authors, it was identified that the study was not a RCT.
Wang 2001b	The authors used self-prepared drug, which was manufactured by the authors themselves and did not have standardised formulations.
Wang 2003	Upon contacting the authors, it was identified that the study was not a RCT
Wang 2004a	The authors used self-prepared drug, which was manufactured by the authors themselves and did not have standardised formulations.
Wang 2005a	Upon contacting the authors, it was identified that the study was not a RCT.
Wang 2005b	Upon contacting the authors, it was identified that the study was not a RCT.
Wang 2005c	We contacted and interviewed the original author only to identify and find that the trial was actually not a real RCT.

Study	Reason for exclusion
Wang 2005d	We contacted and interviewed the original author only to identify and find that the trial was actually not a real RCT.
Wang 2005e	The authors used self-prepared drug, which was manufactured by the authors themselves and did not have standardised formulations.
Wang 2006a	We contacted and interviewed the original author only to identify and find that the trial was actually not a real RCT.
Wang 2006b	unable to contact authors on methodology used
Wang 2006c	We contacted and interviewed the original author only to identify and find that the trial was actually not a real RCT.
Wei 2002	unable to contact authors on methodology used
Wu 2005a	We tried hard to contact and interview the authors but they refused to provide any information about their trials.
Wu 2005b	We contacted and interviewed the original author only to identify and find that the trial was actually not a real RCT.
Xin 2005	We contacted and interviewed the original author only to identify and find that the trial was actually not a real RCT.
Xing 2005	The authors used self-prepared drug, which was manufactured by the authors themselves and did not have standardised formulations.
Xing 2006	The authors used self-prepared drug, which was manufactured by the authors themselves and did not have standardised formulations.
Xu 2001	The authors refused to provide any information about their trial.
Xu 2003	The authors refused to provide any information about their trial.
Xu 2005	We contacted and interviewed the original author only to identify and find that the trial was actually a retrospective study.
Xue 2001	Upon contacting the authors, it was identified that the study was not a RCT.
Yan 2004	unable to contact authors on methodology used
Yan 2006	unable to contact authors on methodology used
Yang 2000	The authors refused to provide any information about their trial.
Yang 2001	Upon contacting the authors, it was identified that the study was not a RCT
Yao 2002a	The authors refused to provide any information about their trial.
Yao 2002b	unable to contact authors on methodology used
Yi 2006	The authors used self-prepared drug, which was manufactured by the authors themselves and did not have standardised formulations.

Study	Reason for exclusion
Yin 2005	We contacted and interviewed the original author only to identify and find that the trial was actually not a real RCT.
Yu 2004	The trial administered different interventions at different phases which did not meet our inclusion criteria.
Zeng 2000	The authors used self-prepared drug, which was manufactured by the authors themselves and did not have standardised formulations.
Zhang 1999	unable to contact authors on methodology used
Zhang 2001	Upon contacting the authors, it was identified that the study was not a RCT
Zhang 2003a	The authors refused to provide any information about their trial.
Zhang 2003b	unable to contact authors on methodology used
Zhang 2003c	unable to contact authors on methodology used
Zhang 2004	The authors used self-prepared drug, which was manufactured by the authors themselves and did not have standardised formulations.
Zhang 2005	Upon contacting the authors, it was identified that the study was not a RCT
Zhang 2005a	The authors refused to provide any information about their trial.
Zhang 2005b	unable to contact authors on methodology used
Zhang 2005c	We contacted and interviewed the original author only to identify and find that the trial was actually not a real RCT.
Zhang 2005d	unable to contact authors on methodology used
Zhang 2005e	The authors used self-prepared drug, which was manufactured by the authors themselves and did not have standardised formulations.
Zhang 2006	We contacted and interviewed the original author only to identify and find that the trial was actually not a real RCT.
Zhong 2004	The authors refused to provide any information about their trial.
Zhou 2001	Upon contacting the authors, it was identified that the study was not a RCT.
Zhou 2005	The authors used self-prepared drug, which was manufactured by the authors themselves and did not have standardised formulations.
Zuo 2007	unable to contact authors on methodology used

DATA AND ANALYSES

Comparison 1. Improvement of angina symptoms

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Marked improvement (symptoms disappeared or reduced by > 80%)	3	213	Risk Ratio (M-H, Fixed, 95% CI)	2.27 [1.42, 3.62]
1.1 TCMs versus Nitrates	1	76	Risk Ratio (M-H, Fixed, 95% CI)	4.28 [1.60, 11.39]
1.2 One type of TCMs versus another (chief ingredient: Danshen Root)	2	137	Risk Ratio (M-H, Fixed, 95% CI)	1.68 [0.98, 2.87]
2 General improvement (severity, frequency and duration of angina attacks markedly decreased by 50-80%)	3	213	Risk Ratio (M-H, Fixed, 95% CI)	0.90 [0.63, 1.29]
2.1 TCMs versus Nitrates	1	76	Risk Ratio (M-H, Fixed, 95% CI)	0.96 [0.54, 1.71]
2.2 One type of TCMs versus another (chief ingredient: Danshen Root)	2	137	Risk Ratio (M-H, Fixed, 95% CI)	0.87 [0.55, 1.37]
3 Inefficacy (severity, frequency and duration of angina attacks remain similar as before intervention, or reduced by < 50%)	3	213	Risk Ratio (M-H, Fixed, 95% CI)	0.49 [0.31, 0.78]
3.1 TCMs versus Nitrates	1	76	Risk Ratio (M-H, Fixed, 95% CI)	0.3 [0.13, 0.67]
3.2 One type of TCMs versus another (chief ingredient: Danshen Root)	2	137	Risk Ratio (M-H, Fixed, 95% CI)	0.68 [0.38, 1.20]

Analysis 1.1. Comparison 1 Improvement of angina symptoms, Outcome 1 Marked improvement (symptoms disappeared or reduced by > 80%).

Analysis 1.2. Comparison 1 Improvement of angina symptoms, Outcome 2 General improvement (severity, frequency and duration of angina attacks markedly decreased by 50-80%).

Analysis 1.3. Comparison 1 Improvement of angina symptoms, Outcome 3 Inefficacy (severity, frequency and duration of angina attacks remain similar as before intervention, or reduced by < 50%).

Comparison 2. ECG improvement

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Marked improvement (ECG resumed to normal ranges)	3	213	Risk Ratio (M-H, Fixed, 95% CI)	1.43 [0.72, 2.87]
1.1 TCMs versus Nitrates	1	76	Risk Ratio (M-H, Fixed, 95% CI)	1.35 [0.24, 7.63]
1.2 One type of TCMs versus another (chief ingredient: Danshen Root)	2	137	Risk Ratio (M-H, Fixed, 95% CI)	1.45 [0.68, 3.10]
2 General improvement (depth of ST-segment depression recovered by >0.05mv; on the main lead out of surface 12-lead ECG, the depth of inversed T wave decreases by >25%, or horizontal T wave turns positive)	3	213	Risk Ratio (M-H, Fixed, 95% CI)	1.43 [0.94, 2.16]
2.1 TCMs versus Nitrates	1	76	Risk Ratio (M-H, Fixed, 95% CI)	1.8 [1.02, 3.17]
2.2 One type of TCMs versus another (chief ingredient: Danshen Root)	2	137	Risk Ratio (M-H, Fixed, 95% CI)	1.13 [0.61, 2.08]
3 Inefficacy (no improvement of ECG readings)	3	213	Risk Ratio (M-H, Fixed, 95% CI)	0.71 [0.53, 0.97]
3.1 TCMs versus Nitrates	1	76	Risk Ratio (M-H, Fixed, 95% CI)	0.59 [0.37, 0.94]
3.2 One type of TCMs versus another (chief ingredient: Danshen Root)	2	137	Risk Ratio (M-H, Fixed, 95% CI)	0.82 [0.55, 1.21]

Analysis 2.1. Comparison 2 ECG improvement, Outcome 1 Marked improvement (ECG resumed to normal ranges).

Analysis 2.2. Comparison 2 ECG improvement, Outcome 2 General improvement (depth of ST-segment depression recovered by >0.05mv; on the main lead out of surface 12-lead ECG, the depth of inversed T wave decreases by >25%, or horizontal T wave turns positive).

Analysis 2.3. Comparison 2 ECG improvement, Outcome 3 Inefficacy (no improvement of ECG readings).

Comparison 3. Number of people with decrease of nitroglycerin use by 50% and above per week

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 TCHPs versus Nitrates	1	76	Risk Ratio (M-H, Fixed, 95% CI)	1.80 [1.18, 2.76]
2 One type of TCHPs versus another (chief ingredient: Danshen Root)	1	30	Risk Ratio (M-H, Fixed, 95% CI)	1.52 [0.79, 2.95]

Analysis 3.1. Comparison 3 Number of people with decrease of nitroglycerin use by 50% and above per week, Outcome 1 TCHPs versus Nitrates.

Analysis 3.2. Comparison 3 Number of people with decrease of nitroglycerin use by 50% and above per week, Outcome 2 One type of TCHPs versus another (chief ingredient: Danshen Root).

ADDITIONAL TABLES

Table 1. Latin-Chinese-English Names for Chinese Herbs

Latin Name	Pin Yin Name	Common Name
Borneolum	Bingpian	Borneol
Cortex et Radix Polygalae	Yuanzhi	Thinleaf Milkwort Root-bark
Flos Carthami	Honghua	Safflower
Fructus Aurantii	Zhiqiao	Bitter Orange
Fructus Lycii	Gouqizi	Barbary Wolfberry Fruit
Rhizoma Chuanxiong	Chuanxiong	Szechuan Lovage Rhizome
Cortex et Radix Polygalae	Yuanzhi	Thinleaf Milkwort Root-bark
Fructus Trichosanthis	Gualou	Snakegourd Fruit
Herba Epimedii	Yinyanghuo	Epimedium Herb
Hirudo	Shuizhi	Leech

Table 1. Latin-Chinese-English Names for Chinese Herbs *(Continued)*

Lumbricus	Dilong	Earthworm
Poria	Fuling	Indian Buead
Radix Achyranthis Bidentatae	Niuxi	Twotooth Achyranthes Root
Radix Angelicae Sinensis	Danggui	Chinese Angelica
Radix Astragali	Huangqi	Membranous Milkvetch Root / Mongolian Milkcatch Root
Radix Bupleuri	Chaihu	Chinese Thorowax Root /Red Thorowax Root
Radix Codonopsis	Dangshen	Pilose Asiabell Root /Moderate Asiabell Root/Szechwon Tangshen Root
Radix Curcumae	Yujin	Turmeric Root-tuber
Radix Ginseng	Renshen	Ginseng
Radix Glycyrrhizae	Gancao	Liquoric Root
Radix Notoginseng	Sanqi	Sanchi
Radix Paeoniae Alba	Baishao	White Paeony Root
Radix Paeoniae Rubra	Chishao	Red Paeony Root
Radix Polygoni Multiflori	Radix Polygoni Multiflori	Tuber Fleeceflower Root
Radix Puerariae	Gegen	Kudzuvine Root
Radix Salviae Miltiorrhizae	Danshen	Danshen Root
Ramulus Cinnamomi	Guizhi	Cassia Twig
Rhizoma Acori Calami	Changpu	Drug Sweetflag Rhizome
Rhizoma Alismatis	Zexie	Oriental Waterplantain Rhizome
Rhizoma Corydalis	Yanhusuo	Yanhusuo
Rhizoma Cyperi	Xiangfu	Nutgrass Galingale Rhizome
Rhizoma Polygonati Odorati	Yuzhu	Fragrant Solomonseal Rhizome
Semen Platycladi	Baiziren	Platycladi Seed
Semen Ziziphi Spinosae	Suanzaoren	Spina Date Seed

Table 2. Contents of the formulations used in included studies

Study ID	Contents	Treatment

Table 2. Contents of the formulations used in included studies (Continued)

Wang 2004	Linaoxin capsule: Danshen Root, Szechuan Lovage Rhizome, Kudzu vine Root, Earthworm, Red Paeony Root, Safflower, Turmeric Root-tuber, Oriental Waterplantain Rhizome, Tuber Fleeceflower Root, Spina Date Seed, Barbary Wolfberry Fruit, Drug Sweetflag Rhizome, Thinleaf Milkwort Root-bark, Twotooth Achyranthes Root, Liquoric Root	4 capsule orally t.i.d
Fang 2004	Yixinmai granule: Ginseng 5g, Cassia Twig 10g, Snakegourd Fruit 10g, Leech 6g, Indian Buead 15g	10g particles a time orally t.i.d for 4 weeks
Wang 1999	Baoxinbao film: not mentioned	Film (containing dried medicinal herb 16.2g/piece) precordially 2 pieces for the 1st time, then 1 piece each time for 4 days at a time (altogether 6 pieces for 20 days)

APPENDICES

Appendix 1. Search strategy

The general search strategy was used and was changed for different databases:

- #1 ANGINA-PECTORIS*:ME
- #2 ANGINA
- #3 CORONARY-DISEASE*:ME
- #4 (CORONARY near DISEASE*)
- #5 (((#1 or #2) or #3) or #4)
- #6 MEDICINE-ORIENTAL-TRADITIONAL*:ME
- #7 DRUGS-CHINESE-HERBAL*:ME
- #8 (CHINESE near MEDICINE*)
- #9 (TRADITIONAL near CHINESE)
- #10 (TRADITIONAL near MEDICINE*)
- #11 (CHINESE next DRUG*)
- #12 KAMPO
- #13 ((((((#6 or #7) or #8) or #9) or #10) or #11) or #12)
- #14 Composite Danshen droplet pills
- #15 Fu Fang Dan Shen Di Wan
- #16 Fu Fang Dan Shen Pian
- #17 Tong xin tang
- #18 Yi Qi Tong Bi Tang
- #19 Svate
- #20 Ci Wu Jia injection
- #21 Yi Qi Huo Xue Hua Yu Fa
- #22 Puerarin
- #23 Ligustrazine
- #24 Mai Luo Ning
- #25 Sheng Mai
- #26 Huang Dan Xin Le pills
- #27 Xin ta hua capsule
- #28 Yi Qi Huo Xue Tang
- #29 Bao Xin Yao Zhen
- #30 (#14~#29)/or
- #31 (#5 and #13 and #30)

WHAT'S NEW

Date	Event	Description
4 March 2013	Review declared as stable	No longer being updated
25 April 2012	Amended	Lead author's details updated.

CONTRIBUTIONS OF AUTHORS

Yong Yuan and Qi Zhuo worked on searches and selection of trials, telephone interviewed the original authors of trials, undertook data extraction, quality assessment and review development.

Henxi Chen contributed to retrieval of articles and data extraction.

WU Taixiang was responsible for organising the team, methodological advice, development of review.

The authors are responsible for the creation and running of all search strategies.

DECLARATIONS OF INTEREST

None

SOURCES OF SUPPORT

Internal sources

- West China Hospital, Sichuan University, China.

Providing salary for the authors.

External sources

- Cochrane Heart Group, UK.

Providing technique support for the author team.

NOTES

No longer being updated.

INDEX TERMS

Medical Subject Headings (MeSH)

Angina Pectoris [*drug therapy]; Drugs, Chinese Herbal [*therapeutic use]; Randomized Controlled Trials as Topic

MeSH check words

Humans