![Cochrane Library logo]

Cochrane Database of Systematic Reviews

Chinese herbal medicines for treating pre-eclampsia (Review)

Li W, Tang L, Wu T, Zhang J, Liu GJ, Zhou L

www.cochranelibrary.com

WILEY

TABLE OF CONTENTS

[Intervention Review]

Chinese herbal medicines for treating pre-eclampsia

Wenjuan Li[1], Liulin Tang[1], Taixiang Wu[2], Jing Zhang[3], Guan J Liu[2], Lingling Zhou[1]

[1]Department of Obstetrics and Gynecology, West China Second University Hospital, Sichuan University, Chengdu, China. [2]Chinese Cochrane Centre, Chinese EBM Centre, West China Hospital, Sichuan University, Chengdu, China. [3]Reproductive Endocrinology, Department of Obstetrics and Gynecology, West China Second University Hospital, Sichuan University, Chengdu, China

Contact: Taixiang Wu, Chinese Cochrane Centre, Chinese EBM Centre, West China Hospital, Sichuan University, No. 37, Guo Xue Xiang, Chengdu, Sichuan, 610041, China. txwutx@hotmail.com.

ABSTRACT

Background

Traditional Chinese medicine (TCM) considers that, when a woman is pregnant, most of the blood of the mother is directed to the placenta to provide the baby with the required nutrition, As a consequence, other maternal organs may be vulnerable to damage. These organs include the liver, the spleen and the kidneys. The use of Chinese herbal medicines is often individualised and based on the presence of TCM symptoms. The general effects of Chinese herbal medicines may be valuable in pre-eclampsia by encouraging vasodilatation, increasing blood flow and decreasing platelet aggregation.

Objectives

To assess the efficacy and safety of Chinese herbal medicines for treating pre-eclampsia and compare it with that of placebo, no treatment, Western medicine or other Chinese herbal medicines.

Search methods

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (June 2009), the Cochrane Central Register of Controlled Trials (*The Cochrane Library* 2009, Issue 2), MEDLINE (1950 to June 2009) and Chinese National Knowledge Infrastructure (1979 to June 2009).

Selection criteria

Randomised controlled trials in which Chinese herbal medicines were used for treating pre-eclampsia.

Data collection and analysis

Three review authors searched studies and assessed full texts independently. Another author also assessed the studies if there was any doubt about whether or not to include the trial. We did not perform analysis as there were no trials included in this review.

Main results

No trials were suitable for inclusion in this review.

Authors' conclusions

The efficacy and safety of Chinese herbal medicines for treating pre-eclampsia remains unclear. There are no randomised controlled trials in this field. High-quality randomised controlled trials are urgently required.

PLAIN LANGUAGE SUMMARY

Chinese herbal medicines for the treatment of pre-eclampsia

Pre-eclampsia is a condition in pregnancy involving high blood pressure and protein in the urine (proteinuria) after 20 weeks of pregnancy. Most women with mild pre-eclampsia give birth without problems. However, severe pre-eclampsia can cause major problems with the liver, blood clotting etc, and some women go on to have fits (eclampsia). This can lead very occasionally to serious complications, and possibly to a life-threatening situation for both the mother and her baby. Chinese herbal medicines might help to protect vulnerable organs like the liver and kidneys, and so these remedies may help with pre-eclampsia. Traditional Chinese medicine (TCM) incorporates concepts of cause, diagnosis and treatment. Typical treatment in TCM is Chinese herbal remedies based on one or several herbs that come from natural plants. Their selection is often based on the individual and presence of TCM symptoms. The prescribed herbs are combined by a distinctive method to form the prescription. In recent decades, TCM has sometimes been integrated with Western medicine to incorporate its therapeutic concepts. Not all Chinese herbal medicines are free of risk, and there are concerns regarding adverse events; for example, allergic reaction and Chinese herbal nephropathy (kidney damage).

The authors searched for controlled trials that randomly assigned women with pre-eclampsia, toxaemia or pregnancy-induced hypertension to treatment with Chinese herbal medicines (or integrated Western medicine with Chinese herbal medicines) or a control treatment. The control treatment could be a placebo, no treatment or a Western medicine. The authors identified no trials that were suitable for inclusion and so the efficacy and safety of Chinese herbal medicines for treating pre-eclampsia remains unclear. Although the authors identified 45 studies, none of the trials reported adequate methodology to be classified as randomised controlled trials.

BACKGROUND

Pre-eclampsia has classically been defined as the triad of hypertension, proteinuria and oedema occurring after 20 weeks' gestation in a previously normotensive woman (Anonymous 1996). Recently, pre-eclampsia (toxaemia) is defined as hypertension accompanied by proteinuria (protein in the urine) (Meher 2005; NHBPEP 2000). Pre-eclampsia is a common disorder that complicates 6% to 8% of pregnancies and can progress to a life-threatening situation for both the mother and the fetus. A number of medications have been used in an attempt to prevent and treat pre-eclampsia. Given the gaps in understanding the underlying pathophysiology of pre-eclampsia, the mechanisms by which many of these agents are reputed to act are theoretical at best. Anticonvulsants (agents that can inhibit a blood vessel from spasm) are used in the belief that they help treating eclamptic fits and subsequent poor outcomes for mother and infant. If an anticonvulsant is used for pre-eclampsia, magnesium sulphate appears to be the best choice but with side effects, especially flushing (Duley 2003). Antihypertensive drugs are often used for severe hypertensive pregnant women in the belief that lowering blood pressure will inhibit progression to more severe disease, and thereby improve outcomes, but which antihypertensive drug is the best is still unclear (Duley 2006). However, it remains unclear whether antihypertensive drug therapy for mild to moderate hypertension during pregnancy is worthwhile (Abalos 2007). Antiplatelet agents, low-dose aspirin in particular, might delay the development of pre-eclampsia (Duley 2007). Dopamine (a catecholamine neurotransmitter in the brain and the precursor to norepinephrine and epinephrine) which help to increase urine output may theoretically help with the low urine output for severe pre-eclampsia (Steyn 2007).

In recent years there have been a number of definitions of pre-eclampsia in China. Prior to 2004, women were considered as having pre-eclampsia if they had mild, moderate or severe pregnancy-induced hypertension (PIH). Since 2004, the international criteria for pre-eclampsia have been applied in China (Gou 2004). Pre-eclampsia is classified as mild or severe. Mild pre-eclampsia is defined as hypertension occurring after 20 weeks' gestation (blood pressure is equal to or more than 140/90 mmHg), proteinuria (equal to or more than 300 mg/24 h or (1+)), with or without symptoms, such as headache. There is no widely accepted definition of severe pre-eclampsia. Nevertheless, the following are generally regarded as features of severe disease: severe hypertension (blood pressure at least 160 mmHg systolic, or 110 mmHg diastolic), severe proteinuria (usually at least 3 g (range 2 g to 5 g) protein in 24 hours, or 3+ on dipstick), reduced urinary volume (less than 400 ml to 500 ml in 24 hours), neurological disturbances such as headache, visual disturbances, and exaggerated tendon reflexes, upper abdominal pain, pulmonary oedema (fluid in the lungs), impaired liver function tests, high serum creatinine, low platelets, intrauterine growth restriction or reduced liquor volume (ACOG 1996; Brown 2000; Brown 2001; Meher 2005).

Chinese herbal medicines in the treatment of pre-eclampsia

Traditional Chinese medicine (TCM) is a theoretical and methodological system that incorporates concepts of cause, diagnosis and treatment. Chinese herbal medicines (CHM) are taken, or made, from natural plants. They are used as medication in the TCM system. TCM herbal formulas are primarily given according to the syndrome/pattern identified from the disease. In recent decades, TCM has sometimes been integrated with Western medicine to incorporate its diagnostic, etiological and therapeutic concepts.

In TCM before the middle of the 1990s, PIH was thought to have been caused by damage to the Pi (the spleen). According to TCM, the function of the spleen is to digest, absorb and transport nutrients, and control blood pressure. CHM were used in order to protect and improve the function of the spleen. However, these medicines were later found to be ineffective. After the middle of the 1990s, further advances were made regarding the pathophysiologic mechanism of PIH. Spasms in the arterioles were identified as being the main mechanism. Medicines which are thought to encourage vasodilation and increase the blood flow are now widely used in treating women with PIH. These CHM include Chuan Xiong Qin (Ligustrazine, extracted from rhizome of Sichuan lovage). Their pharmacological functions were suggested by experimental research. For example, Dan Shen (Salvia Miltiorrhiza) may reduce whole blood viscosity and dilate small arteries (Liu 1998); Fu Ling (Sclerotium Poriae Cocos) may increase urinary output in women with oedema (Sun 1998); Chuan Xiong (rhizome of Sichuan lovage) may produce a marked and sustained reduction in blood pressure (Wang 1998a); Dang Gui (angelica) may relax uterine smooth muscle and inhibit platelet adhesion (Huang 1998); Yi Mu Cao (Herba Leonuri) may reduce whole blood viscosity and inhibit platelet adhesion (Ran 2003). All the above CHM, except Chuan Xiong Qin, are usually used as a composition of mixed CHM prescription. Chuan Xiong Qin may be used as either a single CHM (Zhang 1993) or as the composition of prescription (Wei 2002).

TCM considers that, when a woman is pregnant, most of the blood of the mother is directed to the placenta to provide the baby with the required nutrition. Maternal liver, spleen and kidneys may in consequence be vulnerable to damage. CHM that can protect these organs in pre-eclampsia by encouraging vasodilatation, increasing blood flow and decreasing platelet aggregation, such as Dan Shen, Yi Mu Cao, and Chuan Xiong are of potentially great value. The use of CHM is often based on the individual situation and presence of TCM symptoms. For example, Dan Shen, Chuan Xiong Qin may be prescribed as basic drugs for pre-eclamptic women, while Fu Ling is prescribed as an assistant drug only for women with edema. Therefore, different women with different symptoms might use different assistant drugs.

Increasing the quantity of blood flow provided to the placenta is the purpose of TCM in treating pre-eclampsia. Many CHM improving blood microcirculation, preventing vessel spasm, decreasing blood pressure, are used in treating pre-eclampsia. Ligustrazine and Salvia Miltiorrhizae are the main basic medicines. Ligustrazine extracted from rhizome of Sichuan lovage is a kind of alkaloid. It can increase the level of prostaglandin I2 (PGI2) secreted by vascular endotheliocyte (Tao 1987). The major composition of Salvia Miltiorrhizae is salvia miltiorrhiza ketone-A and sulfonic natrium. Salvia miltiorrhiza ketone-A and sulfonic natrium can significantly inhibit the action of Mg-ATP enzyme activated by platelet actin, depress activity of platelet contractive protein and decrease the level of plasma thromboxane2 (TXA2) (Zhang 1988). Both Ligustrazine and Dan Shen can clear oxygen-derived free radicals, improving function of endotheliocyte, expand the smooth muscle of blood vessel and bronchia, increase the blood

flow of heart and brain, expand arteriolar vessel, improving microcirculation, inhibit platelet congregating and depress platelet activity (Industry 1977; Li 1992; Yang 1990). Other CHM have different effects. For example, angelica can decrease the level of plasma endothelin (ET) (Huang 1998b); puerarin can inhibit excessive release of ET and increase the level of PGI2 (Zhao 2005); taurine can inhibit the increase of ET and calitonin gene related peptide in central nerve system (Qu 2003); flavone of ginkgo leaf can decrease the level of nitric oxide and the activity of ET (Geng 2002); motherwort can inhibit congregating of red blood cells and platelets (Ran 2003); and tuckahoe can increase the blood flow of kidney and increase the quantity of urine (Sun 1998).

Many non-randomised controlled trials on TCM in treating pre-eclampsia have been published. Most of the conclusions of these studies are positive.

Rationale for undertaking this review

In China, the use of CHM is very popular. CHM, either with or without Western medicine, has been reported to be effective for the treatment of pre-eclampsia (Hu 2004; Liao 2004; Liu 1994). Increasing numbers of doctors believe that using CHM with Western medicines has a beneficial effect. Evaluating methods for the treatment of pre-eclampsia has resulted in a number of publications comparing the benefits of CHM with Western medicines. For example, three trials including 346 participants have been conducted to investigate the use of Chuan Xiong, Dan Shen, etc, in the treatment of pre-eclampsia (Wang 1997; Zhang 1993; Zhang 1997). These showed apparent benefits, but the quality and the effects of these trials have not been assessed and systematically reviewed. Therefore, it is important to review available evidence exploring the exact effect that CHM has on the treatment of women with pre-eclampsia.

Interest is not confined to China; CHM are widely used elsewhere: "We are now experiencing a rapid increase in the use of Chinese herbal medicines across the Western world" (HLSC 2004). There is increasing public interest in, and use of, a range of therapies, which lie outside the 'mainstream' of traditional medical practice.

However, there is evidence to indicate that not all CHM are free of risk. There are concerns regarding adverse events: for example, allergic reaction, and Chinese herbal nephropathy (Lampert 2002; Lord 2001; Nortier 2000). However, very few studies have reported the side effects of these herbal medicines when used by pregnant women.

This review aimed to summarise the existing evidence on the comparative effectiveness and safety of CHM for treating pre-eclampsia.

OBJECTIVES

To assess the efficacy and safety of Chinese herbal medicines (CHM) for treating pre-eclampsia. We were interested in comparing the effects and adverse events of CHM (or integrated Western medicine with CHM) with that of placebo, no treatment, or Western medicine in the treatment of pre-eclampsia.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials. We excluded quasi-randomised trials, such as alternation and odd/even admission sequence. It is important to note that Chinese authors often describe trials as 'randomised controlled trials' and participants as 'randomised' when they are not randomised at all "because of a lack of adequate understanding on the part of the authors of rigorous clinical trial design" (Wu 2009).

Types of participants

Women with pre-eclampsia. Diagnostic criteria such as the definition of the National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy (NHBPEP 2000) were acceptable. The terms ' toxaemia', 'gestational proteinuric hypertension' and 'pre-eclampsia' were also acceptable although it should be noted that the term 'pre-eclampsia' was usually used when there was proteinuria. We included women irrespective of age, gestational week and whether the pregnancy was singleton or multiple. In order to identify all relevant trials, our search strategy included women with pregnancy-induced hypertension as well as pre-eclampsia.

Types of interventions

The treatment group's intervention was CHM therapy including single herb preparation and mixture preparations (for example, the injection of Chuan Xiong, Da Huang (Radix et Rhizoma Rhei), the mixture injection of Chuan Xiong and Dan Shen, herbal preparations, integrated CHM with Western medicine). The control group's interventions were placebo, no treatment, Western medicine (for example, nifedipine, magnesium sulphate) or a different CHM from treatment group but with definite efficacy for pre-eclampsia.

Types of outcome measures

Primary outcomes

Maternal

1. Death.
2. Serious events related to pre-eclampsia: eclampsia (fitting), stroke (brain damage), renal failure (kidney failure), liver failure, HELLP (haemolysis, elevated liver enzymes and low platelets) syndrome, pulmonary oedema (fluid in the lungs), cardiac arrest.

Neonatal

1. Stillbirth or neonatal death.

Secondary outcomes

Maternal

1. The need for invasive monitoring, such as central venous catheterisation (intravenous lines into the great veins around the heart);
2. caesarean section;
3. use of health service resources, including need for intensive or high-dependency care/observation.

Neonatal

1. Low Apgar score less than seven at five minutes;
2. neonatal seizures;
3. intraventricular haemorrhage (bleeding in the brain);
4. hyaline membrane disease (stiff lungs);
5. pneumothorax (air leaks from the lungs);
6. necrotising enterocolitis (bleeding into the bowel wall) and ventilation for more than seven days;
7. measures of long-term growth and development, such as important impairment and cerebral palsy;
8. use of health service resources, including length of stay in neonatal intensive care, ventilation or surfactant.

Search methods for identification of studies

Electronic searches

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register by contacting the Trials Search Co-ordinator (June 2009).

The Cochrane Pregnancy and Childbirth Group's Trials Register is maintained by the Trials Search Co-ordinator and contains trials identified from:

1. quarterly searches of the Cochrane Central Register of Controlled Trials (CENTRAL);
2. weekly searches of MEDLINE;
3. handsearches of 30 journals and the proceedings of major conferences;
4. weekly current awareness alerts for a further 44 journals plus monthly BioMed Central email alerts.

Details of the search strategies for CENTRAL and MEDLINE, the list of handsearched journals and conference proceedings, and the list of journals reviewed via the current awareness service can be found in the 'Specialized Register' section within the editorial information about the Cochrane Pregnancy and Childbirth Group.

Trials identified through the searching activities described above are each assigned to a review topic (or topics). The Trials Search Co-ordinator searches the register for each review using the topic list rather than keywords.

In addition, we searched the CENTRAL (*The Cochrane Library* 2009*, Issue 2*), MEDLINE (1950 to June 2009) and Chinese National Knowledge Infrastructure (CNKI, 1979 to June 2009, including Chinese journal full-text database (CJFD), Chinese selected doctoral dissertations and master's theses full-text databases (CDMD), Chinese important conference dissertations full-text database), using the search strategies detailed in Appendix 1.

Searching other resources

References from published studies

We searched the reference lists of relevant trials and reviews to identify additional trials.

Unpublished literature

We identified unpublished and ongoing trials by correspondence with authors and by contacting the pharmaceutical companies who produce relevant products.

Other search strategies

We contacted organisations, individual researchers working in the field, and medicinal herbs manufacturers in order to obtain additional references.

We did not apply any language restrictions.

Data collection and analysis

(1) Selection of trials

To determine the studies to be assessed further, three review authors (Zhang, Zhou, Tang) independently scanned the titles, abstract sections and keywords of every record. We retrieved full articles for further assessment if the information given suggested that the study:

1. included participants with pre-eclampsia;
2. compared CHM with any other active or placebo intervention;
3. assessed one or more relevant clinical outcome measure;
4. used random or pseudo-random allocation to the comparison groups.

If there was any doubt regarding these criteria from the information given in the title and abstract, we also retrieved the full article for clarification. We included only randomised controlled trials, which we trained investigators to identify. We resolved differences in opinion by discussion (Zhang, Wu). If we could not reach agreement, we added the article to those 'awaiting assessment' and contacted the trial authors for clarification by phone or e-mail. We contacted the first author of the article but, if the first author was unavailable, we contacted another of the named authors. We investigated the methodological quality of the article starting with the method of randomisation. If the randomisation was adequate, we then investigated blinding, allocation concealment, etc. If the randomisation was inadequate, we recorded detailed methods of allocation and excluded the studies. If we could not contact any of the authors and we could not confirm that the studies were truly randomised controlled trials, we excluded them. We will continue to try to contact the authors for clarification.

(2) Quality assessment of trials

We assessed trials as described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2008) and the methodological guidelines prepared by the Pregnancy and Childbirth Group's statistician (Gates 2005).

We planned to address three areas:
(a) randomisation (method of sequence generation and concealment of allocation);
(b) blinding (blinding of participants, caregivers administering treatment and outcome assessors);
(c) loss to follow up (presence of dropouts and withdrawals, and the analysis of these).

We evaluated the following components for each study:

- randomisation (sequence generation) - adequate when the allocation sequence protected against biased allocation to the comparison groups;
- randomisation (allocation concealment) - adequate when any sequence where the assignment could not be foreseen;
- blinding - adequate when the participants, caregivers administering treatment and outcome assessor were unaware of the allocation;
- loss to follow up - adequate when more than 80% of participants were followed up, then analysed in the groups to which they were originally randomised (intention-to-treat).

In addition, had there been trials identified for inclusion, we planned to assess the following:

- the severity degree of disease in the trials (if the trials included different degree of severity, we would have performed subgroup analysis);
- baseline comparison for general condition of participants in the trial, such as the gestational age, etc.

Had we identified trials for inclusion, we would have supplied a description of the quality of each study based on a summary of these components.

(3) Data extraction

We have included no trials in this review. If we find suitable trials in the future, we will undertake the following.

Two review authors (Zhang, Wu) will independently extract data concerning details of study population, intervention and outcomes using a data extraction form. We will design a data extraction form specifically for this review. We will include the following items in the data extraction form:

1. general information: published/unpublished, title, authors, reference/source, contact address, country, urban/rural etc., language of publication, year of publication, duplicate publications, sponsor, setting;
2. trial characteristics: design (parallel, individual randomised with or without being blocked), duration of follow up, method of randomisation, allocation concealment, blinding (participants, people administering treatment, outcome assessors);
3. intervention(s): intervention(s) (dose, route, timing), comparison intervention(s) (dose, route, timing), co-medication(s) (dose, route, timing);
4. participants: exclusion criteria, total number and number in comparison groups, age, baseline characteristics, diagnostic criteria, similarity of groups at baseline (including any co-morbidity), assessment of compliance, withdrawals/losses to follow up (reasons/description), subgroups;
5. outcomes: outcomes specified above, any other outcomes assessed, other events, length of follow up, quality of reporting of outcomes (whether the outcome follows the CONSORT principles);
6. results: for outcomes and times of assessment (including a measure of variation), if necessary converted to measures of effect specified below, intention-to-treat analysis.

We will resolve differences in data extraction by consensus, referring back to the original article, wherever necessary, in consultation with a third review author (Liu). If necessary, we will request information from the trial authors of the primary studies.

For binary outcomes, we will extract the number of events and total numbers in each group. For continuous outcomes, we will extract the mean, standard deviation and sample size of each group.

(4) Data analysis

If we find suitable trials in the future, we will perform the following analysis.

We will include data in the meta-analysis if they are of sufficient quality and are sufficiently similar. We will perform overall analysis to generally explore the efficacy and safety of CHM in pre-eclampsia. However, we will also perform subgroup analysis according to the different CHM and control interventions. We will allocate only studies with the same CHM and control intervention to a subgroup. We will include both dichotomous and continuous data. We will express dichotomous data as risk ratio, and continuous data as mean difference. We will test heterogeneity using the Chi^2 statistic (with significance being set at P < 0.1) and the I^2 statistic. We will treat an I^2 value above 50% as substantial heterogeneity. We will assess possible sources of heterogeneity by sensitivity and subgroup analysis as described below. We will test potential bias using the funnel plot or other corrective analytical methods depending on the number of clinical trials included in the systematic review (Egger 1997).

(5) Subgroup analysis

If we find suitable trials in the future, we will perform the following subgroup analyses in order to explore the effect size differences:

1. contents of herbal medicine preparations used in the intervention group (for example, whether Chuan Xiong was used in the group);
2. the intervention method used in the experimental group (only CHM or integrated Western medication with CHM);
3. the degree of severity of disease (mild or severe);
4. the combination of interventions used in the experimental group.

We will use interaction tests in the subgroup analysis for comparing subgroup results.

(6) Sensitivity analyses

If we find suitable trials in the future, we will perform the following sensitivity analyses in order to explore the influence of the following factors on effect size:

1. repeating the analysis taking account of study quality, as specified above;
2. repeating the analysis excluding studies using the filter of source of funding (industry versus other).

We will also repeat the analysis using different measures of effects size (risk difference, odds ratio, etc) and different statistical models (fixed- and random-effects models), if needed.

R E S U L T S

Description of studies

We identified 116 references through the electronic and hand searches. We retrieved full texts for all for clarification. We identified 62 references to be inconsistent with the inclusion criteria, and excluded these from the present review.

We have identified 48 different studies that claimed to be randomised controlled trials. We attempted to contact the authors of these trials by phone or e-mail to confirm the study design. We were unable to contact the authors of two trials (Sun 1991; Zhao 2005). Five studies proved to be case reports (Hong 2002; Li 2003; Wei 2004; Zhang 2005; Zhu 2002). Three studies (Huang 1996; Huang 1998c; Zhang 2006) did not provide relevant usable data, and we have not been able to communicate with the trialists to identify the validity of the randomisation. The remaining 38 studies were in fact quasi-randomised, with participants optionally allocated by the doctors or themselves. For studies published before 2005, the previous authors of this review provided details of communication with authors and clarification regarding the types of study (Figure 1).

Figure 1. Articles identified through electronic and hand searches.
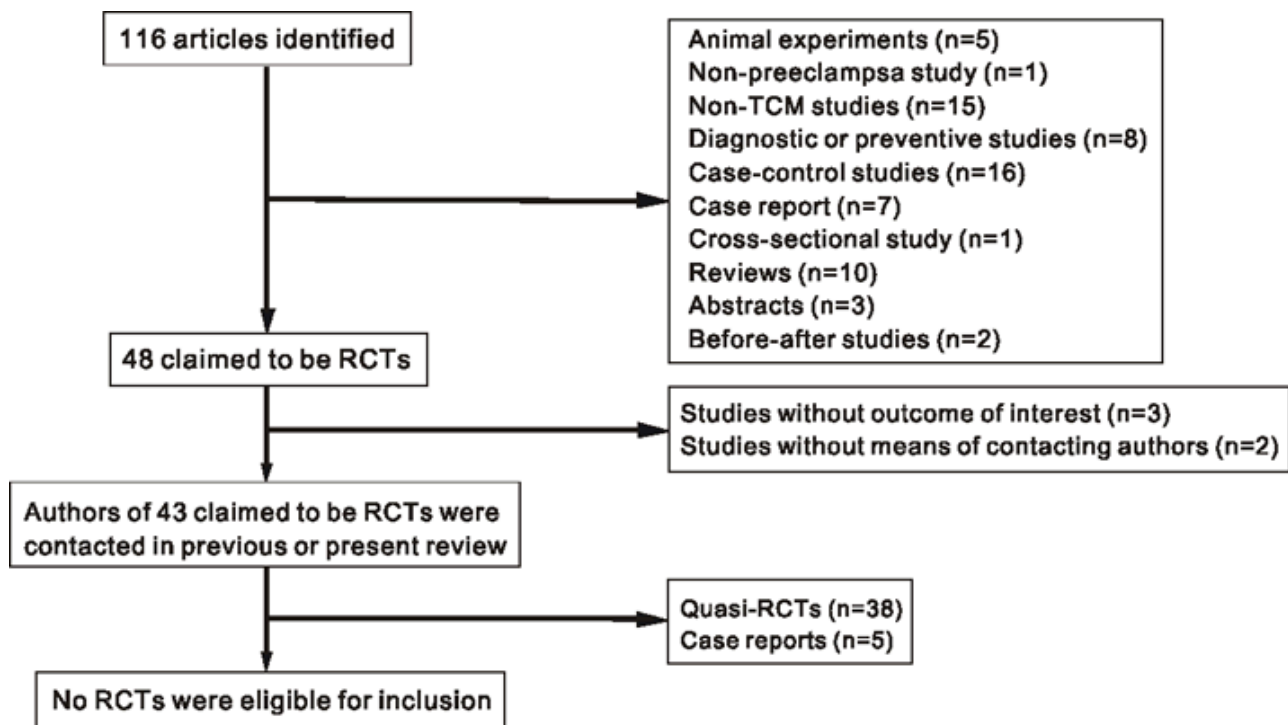
Risk of bias in included studies

No trials were suitable for inclusion in this review.

Effects of interventions

No trials were suitable for inclusion in this review.

D I S C U S S I O N

We identified many potentially relevant trials, but we found all to be non-randomised controlled trials. None of the trials reported adequate methodology in their original publications, and we have no way of verifying the information we obtained from personal communication with the authors. Some studies were conducted several years ago and may be influenced by recall bias.

Studies which stated 'randomisation' were either observational, case reports, case-control studies, before-after studies or quasi-randomised trials. Most authors thought 'casual allocation' was 'random allocation' and none of them knew what 'allocation concealment' was, even in the college-affiliated hospitals.

Of the 36 quasi-randomised controlled trials, allocation methods were based on admission sequence for 18 studies (even in one and odd in the other), admission date for two studies (even in one and odd in the other) and doctors' alternation for 16 studies. Only one study included women with pre-eclampsia according to present international criteria (Yang 2006); others included PIH women according to previous criteria. Eighteen studies included all PIH women; one, women with mild PIH (Man 2004); three, women with moderate PIH (Chen 2003b; Fu 2008; Liu 2004); one, women with severe PIH (Shen 1984); three, women with mild and moderate PIH (Guo 1986; Kuang 2005; Wang 2004); seven, women with moderate and severe PIH; two, women with PIH and fetal growth restriction (Wei 2000; Zhong 2002). All studies were conducted in east China. The baseline of participants was unclear in nine studies; age was unclear in five and gestational weeks in eleven. The number of participants ranged from 38 to 401. Thirteen studies did not report treatment durations, and reported durations were different for the other studies; they ranged from three days to 'up to delivery'. One CHM decoction (Zicaojueming decoction) was compared to the other (Tianmagouteng decoction) in one study (Wang 1998b), and one CHM capsule was compared with no treatment (You 1999). The

others were compared with Western medicines, including different CHM mixed prescriptions in eight studies, salvia miltiorrhiza in seven, ligustrazine in ten, salvia miltiorrhiza plus ligustrazine in one (Meng 2003), mailuoning injection in two (Luan 1995; Yang 2001), milkvetch in three (Cao 2002; Fang 2006; Man 2004), rhubarb in two (Su 2002; Wang 1999), and angelica and paeonia powder in one (Guo 1986). CHM combined with Western medicines were applied in the intervention group for most studies. Magnesium sulphate, nifedipine, diazepam were the most common Western medicines.

The authors' conclusions about TCM for PIH were mainly positive. We have listed characteristics of quasi-RCTs in Table 1 and Table 2.

AUTHORS' CONCLUSIONS

Implications for practice

There are currently no good quality randomised controlled trials evaluating the efficacy and safety of CHM for the treatment of pre-eclampsia. Although CHM is widely used throughout the world, there is insufficient evidence from randomised controlled trials to show whether it is an effective treatment for pre-eclampsia.

Implications for research

Well-conducted randomised controlled trials assessing the effectiveness and the safety of CHM for women with pre-eclampsia are required. The trials should use true randomisation, not quasi-randomisation (for example, computer randomisation or random-number table) and have adequate allocation concealment (for example, by utilising sequentially numbered, sealed, opaque envelopes prepared remotely); only treatments which have a demonstrated effect for pre-eclampsia should be used as the control; participating researchers and outcome assessors should be blinded; and trials should be large enough to assess pre-eclampsia and serious maternal and infant long-term morbidities. The power calculation for sample size should be reported and the trial methodology should be reported in detail according to the CONSORT statement (Moher 2001).

In China, women eligible to be recruited to such trials should be those diagnosed with pre-eclampsia using the international definition. Trialists should be adequately trained in order to carry out and report such trials. Chinese doctors and researchers urgently need to be trained about clinical epidemiologic knowledge of research design, especially in rural areas.

REFERENCES

References to studies excluded from this review

Cao 2002 *{published data only}*

Cao W, Yuan M, Zhu A. Observation on effect of milkvetch injection in treating 401 patients with PIH. *Shangdong Medical Journal* 2002;**42**(20):50.

Chen 2002 *{published data only}*

Chen S. Clinical observation on integrated treatment of Ligustrazin injection and western medicine for PIH. *Fujian Journal of TCM* 2002;**33**(5):11-2.

Chen 2003 *{published data only}*

Chen D, Zhao Y, She R, Wen L, Su C, Huang Y, et al. Comparative study on effect of ligustrazine and magnesium sulfate on patients with pregnancy induced hypertension syndrome. *Chinese Journal of Integrated Traditional and Western Medicine* 2003;**23**(3):185-7.

* Chen D, Zhao Y, She R, Wen L, Su C, Huang Y, et al. Effect of salvia miltiorrhiza, ligustrazine and magnesium sulfate on outcomes of patients with pregnancy-induced hypertension. *Chinese Journal of Perinatal Medicine* 2003;**6**(5):259-62.

Chen 2003b *{published data only}*

Chen D, Zhao Y, She R, Wen L, Su C, Huang Y, et al. Mechanism investigation and primary observation on clinical effect of Salvia miltiorrhiza in treating PIH. *China Journal of Modern Medicine* 2003;**13**(18):114-5.

Fang 2006 *{published data only}*

Fang J. Integrated treatment of TCM and western medicine for HSP and variety of plasma Hcy and NO. *Journal of Heman Medical College for Staff and Workers* 2006;**18**(4):308-10.

Fu 2008 *{published data only}*

Fu H. Analysis of clinical efficacy of Salvia Miltiorrhizae on PIH. *Zhejiang Journal of Clinical Medicine* 2008;**10**(1):76.

Guo 1986 *{published data only}*

Guo TL, Liu C, Liu P. Clinical observation on treatment of gestational hypertension syndrome with angelica and paeonia powder. *Chinese Journal of Integrated Traditional and Western Medicine* 1986;**6**(12):14-6.

Hong 2002 *{published data only}*

Hong M. Observation on effect of Danshen in treating PIH. *Henan Journal of Practical Nervous Diseases* 2002;**5**(2):66.

Hou 2002 *{published data only}*

Hou W, Zhang X, Zheng G, Li H. Clinical observation on Ligustrazin in treating PIH. *Chinese Journal of Integrated Traditional and Western Medicine* 2002;**22**(8):617.

Hu 2004 *{published data only}*

Hu Z, Fang M, Wu L, Wang Y, Chen L, Li J. Study of ligustrazine combined with bitter salt on pregnancy induced hypertension syndrome. *Modern Journal of Integrated Traditional Chinese and Western Medicine* 2004;**13**(11):1409-12.

Huang 1996 *{published data only}*

Huang Y, Ye D, Ma T. The effects of 3,4-dihydroxyacetophynone on the activity of nitric oxide synthenase in placental vascular endothelial cells and smooth muscle cells and on the level of endothelin-1in plasma from pregnancy-induced hypertension patients. *Chinese Journal of Obstetrics and Gynecology* 1996;**31**(11):667-9.

Huang 1998c *{published data only}*

Huang Y, Ye D, Ma T, Wu X. The influence of 3,4-dihydroxyacetophynone on the levels of atrial natriuretic polypeptide, cGMP and cAMP in maternal and fetal plasma from PIH-patients. *Acta Universitatis Medicines Tongji* 1998;**27**(6):470-3.

Kuang 2005 *{published data only}*

Kuang B. Clinical observation on the treatment of 37 cases of gravidic HBP syndrome with combination of traditional Chinese and Western medicine. *Guiding Journal of TCM* 2005;**11**(7):34-5;49.

Li 2003 *{published data only}*

Li Z. Clinical analysis of pregnant hypertension treated by integration of Chinese and western medicine. *Chinese Journal of Integrative Medicine on Cardio-/Cerebrovascular Disease* 2003;**1**(7):399-401.

Liao 2004 *{published data only}*

Liao YT, Wu XQ, Peng J. Effective observation on Ligustrazine in treating 65 cases with PIH. *Journal of Qiaihar Medical College* 2004;**25**(4):379-80.

Liu 2000 *{published data only}*

Liu L, Zhang Y, Ma B. Clinical research on TCM in treating PIH. *Chinese Journal of Information on Traditional Chinese Medicine* 2000;**17**(2):48-9.

Liu 2004 *{published data only}*

Liu Z, Wu C. Effect of Salvia Miltiorrhizae in treating moderate PIH. *Occupation and Health* 2004;**20**(6):139-40.

Luan 1995 *{published data only}*

Luan F, Yin H, Dong P. Clinical observation on Mailuoning in treating 46 patients with PIH. *Chinese Journal of Integrated Traditional and Western Medicine* 1995;**15**(3):153-5.

Man 2004 *{published data only}*

Man D, Feng B, Jiang G. Cohort study of Milkvetch Root combined with vitamin E in treating mild PIH. *Lishizhen Medicine and Materia Medica Research* 2004;**15**(4):231-1.

Meng 2003 *{published data only}*

Meng H, Guo J, Wang X, Yang L, Liang F. Clinical observation on effect of salvia miltiorrhiza injection combined with ligustrazine in treating 50 patients with moderate or severe pregnancy-induced hypertension syndrome. *Hebei Journal of Traditional Chinese Medicine* 2003;**25**(6):409-10.

Qian 1991 {published data only}

Qian X, Huang Y, Wu S. Clinical analysis of ligustrazine in treating PIH. *Chinese Journal of Integrated Traditional and Western Medicine* 1991;**11**(9):533-4.

Shen 1984 {published data only}

Shen D, Lin Q, Zhou H, Jia S, Pan J, Guo Q. Huoxuehuayujiejin preparation to treat PIH. *Shangdong Medical Journal* 1984;**7**(9):552-3.

Su 2002 {published data only}

Su C, Wang D. Research on effect of little dose of rhubarb in treating PIH. *Clinical Journal of Anhui Traditional Chinese Medicine* 2002;**14**(2):86-7.

Sun 1991 {published data only}

Sun Y, Ma T, Wu X. Primary research on effect and mechanism of 3,4-dihydroxyacetophynone in treating PIH. *Journal of Practical Obstetrics and Gynecology* 1991;**7**(3):141-3.

Tan 2000 {published data only}

Tan Z, Li K, Wang Y. Clinical observation of integrated treatment of TCM and western medicine for hypertensive syndrome of pregnancy. *Hunan Guiding Journal of Traditional Chinese Medicine Pharmacology* 2000;**6**(2):21-2.

Tang 1998 {published data only}

Tang S, Liu Z, Liu Y, Ge C. Clinical observation on ligustrazine in treating 38 patients with PIH. *Lishizhen Medicine and Materia Medica Research* 1998;**9**(5):393-4.

Wang 1997 {published data only}

Wang B, Luo X, Wu R. Effect analysis of the Quyu soup in treating PIH. *New Journal of Traditional Chinese Medicine* 1997;**29**(8):15-7.

Wang 1998b {published data only}

Wang L. The soup of Zicaojueming to treat 60 patients with PIH. *Zhejiang Journal of Traditional Chinese Medicine* 1998;**33**(7):303.

Wang 1999 {published data only}

* Wang Z, Song H. Clinical observation on therapeutical effect of prepared rhubarb in treating pregnancy induced hypertension. *Chinese Journal of Integrated Traditional and Western Medicine* 1999;**19**(12):725-7.

Wang Z, Song H. Primary observation on effect of rhubarb in treating PIH. *China Journal of Traditional Chinese Medicine and Pharmacy* 2000;**15**(2):69-70.

Wang 2004 {published data only}

Wang S, Wei S. Protective effect of Salvia Miltiorrhizae injection on renal function in PIH patients. *Journal of Sun Yatsen University (Medical Sciences)* 2004;**25**(3S):136-8.

Wang 2004b {published data only}

Wang W, Qing A. Effective observation of TCM combined with western medicine in treating PIH. *Lishizhen Medicine and Materia Medica Research* 2004;**15**(9):626.

Wang 2005 {published data only}

Wang Z, Shao C, Song H. Influence of prepared rhubarb on TH1 and TH2 cytokine in PIH patients. *Shangdong Journal of Traditional Chinese Medicine* 2005;**24**(10):619-21.

Wang 2006 {published data only}

Wang Q, Shen Z, Zhou C, Xiao H, Liu S, Hu Y, et al. Clinical research and investigation of Danshen pill in treating PIH. *Chinese Traditional Patent Medicine* 2006;**28**(2):212-4.

Wei 2000 {published data only}

Wei Y, Shi X, Wang C. Clinical observation of intrauterine growth retardation of fetus treated mainly by 'Granule for pregnancy hypertension'. *Shanghai Journal of Traditional Chinese* 2000;**34**(5):36-7.

Wei 2002 {published data only}

Wei S, Hu S, Tian N. Clinical observation on therapeutic effect of the soup of decreasing viscosity and eliminating thromboembolism in treating PIH. *Chinese Journal of Information on Traditional Chinese Medicine* 2002;**9**(7):56.

Wei 2004 {published data only}

Wei L. Clinical application of Danshen injection in treating PIH. *Chinese Community doctors* 2004;**20**(258):36.

Wu 1993 {published data only}

Wu S, Qian X, Huang Y, Huang Q. Effect investigation of ligustrazine in treating PIH -monitoring of bulbar conjunctiva microcirculation. *Journal of Chinese Microcirculation* 1993;**1**(4):193-4.

Xu 1984 {published data only}

Xu M, Qian Z. Clinical analysis of integrated treatment of TCM and western medicine for 63 patients with PIH. *Shanghai Journal of Traditional Chinese Medicine* 1984;**18**(3):14-7.

Yang 2001 {published data only}

Yang Z, Jiao Z, Nou H, Xu C. Clinical observation on integrated treatment of Mailuoning injection and western medicine for PIH. *Chinese Journal of Integrated Traditional and Western Medicine* 2001;**21**(7):536-7.

Yang 2006 {published data only}

Yang HL. Aspirin combined with ligustrazine in treating 42 patients with PIH. *Shangdong Medical Journal* 2006;**46**(14):34.

You 1999 {published data only}

Wang R, You Z, Fu L. Research on effect of Buqihuoxue method for the level of TXB2 and 6-K-PGF1 in patients with PIH. *Chinese Journal of Traditional Medical Science and Technology* 1999;**6**(4):250-1.

Wang R, You Z, Fu L. Research on the effect of Buqihuoxue method for ability of changing shape of RBC in patients with PIH. *Chinese Journal of Traditional Medical Science and Technology* 1999;**6**(4):251-2.

* You Z, Wang R, Fu L. Research on effect of Buqihuoxue method for the level of ET in the patients with PIH. *Chinese*

Journal of Traditional Medical Science and Technology 1999;**6**(4):247-9.

You Z, Wang R, Fu L. Research on effect of Buqihuoxue method for the level of NO in PIH. *Chinese Journal of Traditional Medical Science and Technology* 1999;**6**(4):249-50.

Zhang 1993 *{published data only}*

Zhang C, Yu L, Lv S, Guan S. Clinical research of ligustrazine in treating patients with PIH. *Chinese Journal of Obstetrics and Gynecology* 1993;**28**(4):232-3.

Zhang 2002 *{published data only}*

Zhang H. Integrated treatment of TCM and western medicine in treating PIH. *Chinese Journal of Rural Medicine and Pharmacy* 2002;**9**(9):18-9.

Zhang 2005 *{published data only}*

Zhang X, Li J. Clinical observation of TCM combined with western medicine in treating PIH. *Chinese Community Doctors* 2005;**7**(114):59-60.

Zhang 2006 *{published data only}*

Zhang Y, You Z, Wu Z, Wei H, Luo J. Research of Yiqihuayu intervention on serum IGT-1, IGFBP-1 of PIH patients. *Journal of Emergency in Traditional Chinese Medicine* 2007;**16**(6):652-3.

* Zhang Y, You Z, Wu Z, Zhang W. Influence of Yiqihuayu intervention on placenta tissue HIF-1a of PIH patients. *Journal of Emergency in Traditional Chinese Medicine* 2006;**15**(5):485-6.

Zhao 2005 *{published data only}*

Zhao Y, Wen J, Zhao S, Lai Y. Study of puerarin on outcomes of patients with hypertensive disorder complicating pregnancy. *Chinese Journal of Practical Gynecology and Obstetrics* 2005;**21**(3):158-60.

Zhong 2002 *{published data only}*

Zhong S, Yuan Y. Clinical research on Dangui mixture in treating patients with PIH and IUGR. *Shangdong Journal of Traditional Chinese Medicine* 2002;**21**(3):141-2.

Zhu 2002 *{published data only}*

Zhu Y. Clinical research on Ligustrazin in treating PIH. *Lishizhen Medicine and Materia Medica Research* 2002;**13**(5):293-4.

Additional references

Abalos 2007

Abalos E, Duley L, Steyn DW, Henderson-Smart DJ. Antihypertensive drug therapy for mild to moderate hypertension during pregnancy. *Cochrane Database of Systematic Reviews* 2007, Issue 1. [DOI: 10.1002/14651858.CD002252.pub2]

ACOG 1996

American College of Obstetricians and Gynecologists. Hypertension in pregnancy. *ACOG Technical Bulletin* 1996;**219**:1-8.

Anonymous 1996

Anonymous. Hypertension in pregnancy. American College of Obstetricians and Gynecologists Technical Bulletin. Washington, DC: American College of Obstetricians and Gynecologists, 1996.

Brown 2000

Brown MA, Hague WM, Higgins J, Lowe S, McCowan L, Oats J, et al. The detection, investigation, and management of hypertension in pregnancy: full consensus statement. *Australian and New Zealand Journal of Obstetrics and Gynaecology* 2000;**40**(2):139-55.

Brown 2001

Brown MA, Lindheimer MD, De Swiet M, Van Assche A, Moutquin J. The classification and diagnosis of the hypertensive disorders of pregnancy: statement from the international society for the study of hypertension in pregnancy (ISSHP). *Hypertension in Pregnancy* 2001;**20**(1):ix-xiv.

Duley 2003

Duley L, Gülmezoglu AM, Henderson-Smart DJ. Magnesium sulphate and other anticonvulsants for women with pre-eclampsia. *Cochrane Database of Systematic Reviews* 2003, Issue 2. [DOI: 10.1002/14651858.CD000025]

Duley 2006

Duley L, Henderson-Smart DJ, Meher S. Drugs for treatment of very high blood pressure during pregnancy. *Cochrane Database of Systematic Reviews* 2006, Issue 3. [DOI: 10.1002/14651858.CD001449.pub2]

Duley 2007

Duley L, Henderson-Smart DL, Meher S, King JF. Antiplatelet agents for preventing pre-eclampsia and its complications. *Cochrane Database of Systematic Reviews* 2007, Issue 2. [DOI: 10.1002/14651858.CD000492.pub2]

Egger 1997

Egger M, Smith GD, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997;**315**:629-34.

Gates 2005

Gates S. Methodological guidelines. In: The Editorial Team. Pregnancy and Childbirth Group. About The Cochrane Collaboration (Collaborative Review Groups (CRGs)) 2005, Issue 2.

Geng 2002

Geng XF, Sun XL, Wang HG, Xu LZ, Zhang NS, Li GZ. Experimental and clinical research on flavone of ginkgo leaf in decreasing blood pressure. *China Journal of Chinese Materia Medica* 2002;**27**(8):606-8.

Gou 2004

Gou W, Fang J. The prediction and progress of hypertension in pregnancy. *Chinese Journal of Practical Gynecology and Obstetrics* 2004;**20**(10):581-3.

Higgins 2008

Higgins JPT, Green S, editors. Cochrane Handbook for Systematic Reviews of Interventions Version 5.0.1 [updated

September 2008]. The Cochrane Collaboration, 2008. Available from www.cochrane-handbook.org.

HLSC 2004

House of Lords Select Committee. Science and Technology - Sixth Report: complementary and alternative medicine. http://www.publications.parliament.uk/pa/ld199900/ldselect/ldsctech/123/12303.htm#a3 (accessed 2004).

Huang 1998

Huang B, Wang X, Liu G. Danggui. In: Wang Y, Deng W, Xue C editor(s). Pharmacology and applications of Chinese materia medica. 2nd Edition. Beijing: People's Medical Publishing House, 1998:439-49.

Huang 1998b

Huang WZ, Zhang BY, Wang XJ. The effect of Danggui on plasma ET in hypertension patients. *Journal of Mathematical Medicine* 1998;**11**(4):367-8.

Industry 1977

Industry institution of Beijing pharmacy. Research on effective composition of Ligustrazine. *Chinese Medical Journal* 1977;**57**:420-3.

Lampert 2002

Lampert N, Xu Y. Chinese herbal nephropathy. *Lancet* 2002;**359**(9308):796-7.

Li 1992

Li YK, Jiang MY. Pharmacology of Chinese traditional medicine. Beijing: Chinese CTM press, 1992.

Liu 1994

Liu SY, Xu YY, Zhu JY. The effects of Salvia miltiorrhizae Bge and Ligustrazine on thromboxane A2 and prostacyclin in pregnancy induced hypertension. *Chinese Journal of Obstetrics and Gynecology* 1994;**29**(11):648-50, 697.

Liu 1998

Liu C. Danshen. In: Wang Y, Deng W, Xue C editor(s). Pharmacology and applications of Chinese materia medica. 2nd Edition. Beijing: People's Medical Publishing House, 1998:190-218.

Lord 2001

Lord GM, Cook T, Arlt VM, Schmeiser HH, Williams G, Pusey CD. Urothelial malignant disease and Chinese herbal nephropathy. *Lancet* 2001;**358**(9292):1515-6.

Meher 2005

Meher S, Duley L, Prevention of Pre-eclampsia Cochrane Review authors. Interventions for preventing pre-eclampsia and its consequences: generic protocol. *Cochrane Database of Systematic Reviews* 2005, Issue 2. [DOI: 10.1002/14651858.CD005301]

Moher 2001

Moher D, Schulz KF, Altman DG. The CONSORT statement: revised recommendations for improving the quality of reports

of parallel group randomized trials. *Annals of Internal Medicine* 2001;**134**(8):657-62.

NHBPEP 2000

Anonymous. Report of the National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy. *American Journal of Obstetrics and Gynecology* 2000;**183**(1):1-22.

Nortier 2000

Nortier JL, Martinez MC, Schmeiser HH, Arlt VM, Bieler CA, Petein M, et al. Urothelial carcinoma associated with the use of a Chinese herb (Aristolochia fangchi). *New England Journal of Medicine* 2000;**342**(23):1686-92.

Qu 2003

Qu YH, Li SL, Xu W. Effects of taurine on brain ET and CGRP in spontaneously hypertensive rats. *Journal of Zhengzhou University (Medical Sciences)* 2003;**38**(4):541-2.

Ran 2003

Ran JL, Du JR, Zeng QZ, Qian ZM. Advance in studies on chemical components, pharmacological effect and clinical application of Leonurus japonicus. *Chinese Traditional and Herbal Durgs* 2003;**34**(11):15-9.

Steyn 2007

Steyn DW, Steyn P. Low-dose dopamine for women with severe pre-eclampsia. *Cochrane Database of Systematic Reviews* 2007, Issue 1. [DOI: 10.1002/14651858.CD003515.pub2]

Sun 1998

Sun X. Fuling. In: Wang Y, Deng W, Xue C editor(s). Pharmacology and applications of Chinese materia medica. 2nd Edition. Beijing: People's Medical Publishing House, 1998:803-7.

Tao 1987

Tao JX, Shao WZ, Zhang Y. The effect of Ligustrazine and glonoin on prostacyclin secreted by human vascular endotheliocyte in vitro. *Chinese Journal of Neurosurgery* 1987;**3**:223.

Wang 1998a

Wang J. Chuan Xiong. Pharmacology and applications of Chinese materia medica. Beijing: People's Medical Publishing House, 1998:112-9.

Wu 2009

Wu T, Li Y, Bian Z, Liu G, Moher D. Randomized trials published in some Chinese journals: how many are randomized. *Trials* 2009;**10**:46. [DOI: 10.1186/1745-6215-10-46]

Yang 1990

Yang WD, Zhu HL, Zhao BL. The effect of Danshen on clearance of oxygen-derived free radicals. *Chinese Pharmacological Bulletin* 1990;**5**(2):118-20.

Zhang 1988

Zhang HM, Zhuang QQ, Li CZ. The effect of Salvia miltiorrhiza ketone and sulfonic natrium on the activity of Mg-ATP enzyme activated by platelet actin. *Journal of FuDan University (Medical Science)* 1988;**15**:289.

Zhang 1997

Zhang C, Ma G, Yv L, Guan S. The research of the complex of Danshen and Vit E for the prevention of the PIH. *Chinese Journal of Obstetrics and Gynecology* 1997;**9**:356-8.

* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Cao 2002	Quasi-randomised controlled trial. Participants were allocated based on admission sequence.
Chen 2002	Quasi-randomised controlled trial. Participants were allocated based on admission sequence.
Chen 2003	Quasi-randomised controlled trial. Participants were allocated based on admission sequence.
Chen 2003b	Quasi-randomised controlled trial. Participants were allocated based on admission sequence.
Fang 2006	Quasi-randomised controlled trial. Participants were allocated based on admission sequence.
Fu 2008	Quasi-randomised controlled trial. Participants were allocated based on admission sequence.
Guo 1986	Quasi-randomised controlled trial. Participants were allocated based on admission sequence, odd or even.
Hong 2002	Case report.
Hou 2002	Quasi-randomised controlled trial. Participants were allocated based on admission sequence, odd or even.
Hu 2004	Described as quasi-randomised controlled trial but no systematic approach to allocation. Participants were casually allocated by authors.
Huang 1996	Outcomes of relevance not reported.
Huang 1998c	Outcomes of relevance not reported.
Kuang 2005	Quasi-randomised controlled trial. Participants were allocated based on admission sequence.
Li 2003	Case report.
Liao 2004	Quasi-randomised controlled trial. Participants were allocated based on admission sequence.
Liu 2000	Quasi-randomised controlled trial. Participants were allocated based on admission sequence, odd in one group and even in the other.
Liu 2004	Described as quasi-randomised controlled trial but no systematic approach to allocation. Participants were casually allocated by authors.
Luan 1995	Described as quasi-randomised controlled trial but no systematic approach to allocation. Participants were casually allocated by authors.
Man 2004	Described as quasi-randomised controlled trial but no systematic approach to allocation. Participants were casually allocated by authors.

Study	Reason for exclusion
Meng 2003	Quasi-randomised controlled trial. Participants were allocated based on admission sequence, odd in one group and even in the other.
Qian 1991	Described as quasi-randomised controlled trial but no systematic approach to allocation. Participants were casually allocated by authors.
Shen 1984	Quasi-randomised controlled trial. Participants were allocated based on admission sequence, odd in one group and even in the other.
Su 2002	Quasi-randomised controlled trial. Participants were allocated based on admission sequence, odd in one group and even in the other.
Sun 1991	We were unable to contact the authors and therefore cannot confirm if this is a randomised controlled trial.
Tan 2000	Quasi-randomised controlled trial. Participants were allocated based on admission sequence, odd or even.
Tang 1998	Quasi-randomised controlled trial. Participants were allocated based on order of case history, even or odd.
Wang 1997	Quasi-randomised controlled trial. Participants were allocated based on admission sequence, odd in one group and even in the other.
Wang 1998b	Described as quasi-randomised controlled trial but no systematic approach to allocation. Participants were casually allocated by authors.
Wang 1999	Quasi-randomised controlled trial. Participants were allocated based on admission date, odd in one group and even in the other.
Wang 2004	Described as quasi-randomised controlled trial but no systematic approach to allocation. Participants were casually allocated by authors.
Wang 2004b	Described as quasi-randomised controlled trial but no systematic approach to allocation. Participants were casually allocated by authors.
Wang 2005	Quasi-randomised controlled trial. Participants were allocated based on admission date, odd in one group and even in the other.
Wang 2006	Described as quasi-randomised controlled trial but no systematic approach to allocation. Participants were casually allocated by authors.
Wei 2000	Described as quasi-randomised controlled trial but no systematic approach to allocation. Participants were casually allocated by authors.
Wei 2002	Quasi-randomised controlled trial. Participants were allocated basing on admission date, odd in one group and even in the other.
Wei 2004	Case report.
Wu 1993	Described as quasi-randomised controlled trial but no systematic approach to allocation. Participants were casually allocated by authors.
Xu 1984	Described as quasi-randomised controlled trial but no systematic approach to allocation. Participants were casually allocated by authors.

Study	Reason for exclusion
Yang 2001	Described as quasi-randomised controlled trial but no systematic approach to allocation. Participants were casually allocated by authors.
Yang 2006	Described as quasi-randomised controlled trial but no systematic approach to allocation. Participants were casually allocated by authors.
You 1999	Quasi-randomised controlled trial. Participants were casually allocated based on admission sequence.
Zhang 1993	Quasi-randomised controlled trial. Participants were allocated based on admission sequence, odd in one group and even in the other.
Zhang 2002	Participants were casually allocated by authors.
Zhang 2005	Case report.
Zhang 2006	Outcomes of relevance not reported.
Zhao 2005	Authors were contacted by e-mail but we did not receive a reply. We have therefore been unable to confirm if this is a randomised controlled trial.
Zhong 2002	Described as quasi-randomised controlled trial but no systematic approach to allocation. Participants were casually allocated by authors.
Zhu 2002	Case report.

Studies	quasi-random method of allocation	Participants					No.		
		Inclusion Criteria	Province	Baseline	Age	Gestational weeks	Total	intervention group (IG)	control group (CG)
Cao 2002	admission order	PIH (moderate and severe)	Shandong	comparable	unclear	unclear	401	205	196
Chen 2002	admission order	PIH	Fujian	comparable	IG: 22-35; CG: 23-35	IG: 32.1+/-4.81; CG: 32.3+/-4.6	150	80	70
Chen 2003b	admission order	PIH (moderate)	Guangdong	comparable	IG1: 28.8+/-1.6; IG2: 25.8+/-1.8; CG: 27.6+/-1.8	IG1: 35.5+/-0.8; IG2: 34.2+/-0.6; CG: 34.8+/-0.9	225	IG1: 75; IG2: 75	75
Fang 2006	admission order	PIH (moderate and severe)	Henan	comparable	28.55+/-5.12	unclear	62	42	20
Fu 2008	admission order	PIH (moderate)	Zhejiang	unclear	IG: 23-38; CG: 21-37	IG: 35.1+/-0.78; CG: 34.8+/-0.83	129	63	66
Guo 1986	admission order	PIH (mild and moderate)	Shanghai	unclear	IG: 22-32; CG: 22-40	unclear	92	46	46
Hou 2002	admission order	PIH	Liaoning	comparable	IG: 22-33; CG: 23-35	IG: 32.2+/-3.19; CG: 31.9+/-4.71	100	50	50
Hu 2004	alternation	PIH	Zhejiang	comparable	IG: 21-38; CG: 22-39	IG: 35.88+/-1.67; CG: 36.02+/-1.98	66	32	34
Kuang 2005	admission order	PIH (mild and moderate)	Hunan	unclear	IG: 21-40; CG: 21-40	unclear	72	37	35
Liao 2004	admission order	PIH	Guangdong	comparable	IG: 22-35; CG: 23-35	IG: 32.2+/-3.3; CG: 31.8+/-4.3	126	65	61
Liu 2000	admission order	PIH	Heilongjiang	unclear	20-35	32-40	60	30	30

Table 1.   Characteristics of quasi-RCTs (1) *(Continued)*

Liu 2004	alternation	PIH (moderate)	Shandong	comparable	28.5+/-1.7	26-34	126	60	66
Luan 1995	alternation	PIH	Henan	comparable	IG: 23-34; CG: 22-35	IG: 31.6+/-4.92; CG: 32.1+/-3.34	86	46	40
Man 2004	alternation	PIH (mild)	Hubei	comparable	IG: 26.6+/-3.3; CG: 25.9+/-2.6	IG: 31.1+/-4.1; CG: 31.6+/-6.5	96	50	46
Meng 2003	admission order	PIH (moderate and severe)	Shandong	comparable	IG: 23-36; CG: 22-36	IG: 34.5+/-1.8; CG: 35.1+/-2.7	100	50	50
Qian 1991	alternation	PIH (moderate and severe)	Hubei	unclear	22-30	35-40	75	41	34
Shen 1984	admission order	PIH (severe)	Shanghai	comparable	unclear	unclear	50	25	25
Su 2002	admission order	PIH	Shandong	comparable	IG: 25-32; CG: 25-31	IG: 32+/-2; CG: 32+/-2	100	50	50
Tan 2000	admission order	PIH (moderate and severe)	Hunan	comparable	27.55+/-6.09	unclear	60	40	20
Tang 1998	admission order	PIH	Anhui	comparable	IG: 23-32; CG: 22-34	IG: 32.6; CG: 33.6	68	38	30
Wang 1997	admission order	PIH	Guang-dong	unclear	20-42	unclear	124	62	62
Wang 1998b	alternation	PIH	Zhejiang	comparable	23-35	unclear	90	60	30
Wang 1999	admission date	PIH	Shandong	comparable	IG: 22-35; CG: 23-37	IG: 31.8+/-3.7; CG: 31.2+/-4.1	95	46	49
Wang 2004	alternation	PIH (moderate and severe)	Guang-dong	comparable	21-36	36-42	60	IG1: 20; IG2: 20	20
Wang 2004b	alternation	PIH (mild and moderate)	Hubei	comparable	23-39	28-39	44	22	22
Wang 2006	alternation	PIH	Anhui	comparable	IG: 26.31+/-3.35; CG: 26.53+/-2.97	IG: 26.28+/-2.73; CG: 27.02+/-2.66	98	50	48

Table 1. Characteristics of quasi-RCTs (1) *(Continued)*

Wei 2000	alternation	PIH with fetal growth restriction	Shandong	unclear	24-38	24-34	173	93	80
Wei 2002	admission date	PIH	Henan	comparable	IG: 23-50; CG: 25-35	IG: 31.6+/-4.92; CG: 31.1+/-3.34	200	100	100
Wu 1993	alternation	PIH (moderate and severe)	Hubei	unclear	IG: 21-37; CG: 22-35	IG: 38; CG: 38	38	20	18
Xu 1984	alternation	PIH	Shanghai	unclear	unclear	unclear	118	63	55
Yang 2001	alternation	PIH	Henan	comparable	IG: 23-35; CG: 25-35	IG: 31.6+/-4.92; CG: 31.1+/-3.34	300	160	140
Yang 2006	alternation	pre-eclampsia	Henan	comparable	32	29+/-5	84	42	42
You 1999	admission order	PIH	Hunan	comparable	22-30	20-39	66	36	30
Zhang 1993	admission order	PIH	Shandong	comparable	unclear	unclear	102	52	50
Zhang 2002	alternation	PIH	Henan	comparable	unclear	unclear	108	68	40
Zhong 2002	alternation	PIH with fetal growth restriction	Shandong	comparable	24-37	25.21+/-1.23	140	80	60

Table 2.   Characteristics of quasi-RCTs (2)

Studies	Intervention				Outcome indexes	Conclusion
	Duration	Intervention Group (IG)	Control Group (CG)	Co-medications		
Cao 2002	10 days	milkvetch injection	/	routine western medicine	blood pressure; protein in urine; blood viscosity; S/D ratio in umbilicus blood	milkvetch combined with western medicine is better than western medicine only
Chen 2002	7 days	ligustrazine injection	magnesium sulphate	routine western medicine, such as nifedipine, diazepam and nicorol	score of clinical performance; delivery method; cesarean section; delivery time; bleeding volume after baby birth; Apgar score	ligustrazine is more effective and much safer than magnesium sulphate
Chen 2003b	7-10 days	IG1: salvia miltiorrhiza injection; IG2: ligustrazine injection	magnesium sulphate	/	mean arteria pressure; fetal distress; neonatal asphyxia; postpartum hemorrhage; cesarean section; secrete function of blood endothelial cell; side effect	salvia miltiorrhiza and ligustrazine are as effective as magnesium sulphate but with fewer side effects
Fang 2006	6 days	milkvetch injection	/	magnesium sulphate	score of clinical performance; plasma homocysteine and nitric oxide	milkvetch combined with magnesium sulphate is better than magnesium sulphate only
Fu 2008	7 days	salvia miltiorrhiza injection	magnesium sulphate	other western medicine will be applied if disease deteriorate such as nifedipine	score of clinical performance; fetal distress; neonatal asphyxia; postpartum hemorrhage	salvia miltiorrhiza injection is less effective but much safer than magnesium sulphate
Guo 1986	up to delivery	angelica and paeonia powder	hydrazine	/	blood pressure; delivery method and time; bleeding volume; fetal death; fetal distress; neonatal birth; blood viscosity	angelica and paeonia powder is as effective as hydrazine
Hou 2002	unclear	ligustrazine injection	magnesium sulphate	/	mean arterial pressure; calcium level in plasma and red blood cell	ligustrazine is better than magnesium sulphate
Hu 2004	3 days	ligustrazine injection	/	magnesium sulphate and sedatives	score of clinical performance; renal function; dystocia; postpartum hemorrhage; Apgar score	ligustrazine combined with western medicine is much better than western medicine only
Kuang 2005	up to delivery	CHM compound prescription	/	western medicine such as	score of clinical performance; side effects	TCM combined with western medicine

Table 2. Characteristics of quasi-RCTs (2) *(Continued)*

			magne-sium sul-phate and nifedipine			is much better than western medicine only
Liao 2004	unclear	ligustrazine injection	magnesium sulphate	/	score of clinical performance; postpartum hemorrhage; fetal distress; neonatal asphyxia; side effects	ligustrazine is better than magnesium sul-phate
Liu 2000	unclear	CHM com-pound pre-scription	nicorol, magne-sium sul-phate and hypoten-sive drugs	/	estradiol, progesterone	TCM is as effective as western medicine
Liu 2004	5-20 days	salvia milti-orrhiza in-jection	/	routine western medicine	delivery method; fetal growth restriction; neonatal weight; Ap-gar score; perinatal death	salvia miltiorrhiza combined with west-ern medicine is bet-ter than western med-icine only
Luan 1995	unclear	Mailuoning injection	magnesium sulphate	diazepam	score of clinical performance; mean arterial pressure; hemo-dynamics; proteinuria; delivery method; postpartum haemor-rhage; Apgar score	mailuoning injection is as effective as magne-sium sulphate
Man 2004	up to 36 weeks' ges-tation	milkvetch decoction; vitamin E	/	rest	incidence of severe PIH; cesare-an section; mean arterial pres-sure; neonatal weight; Apgar score	milkvetch combined with vitamin E are ef-fective for mild PIH
Meng 2003	5-7 days	salvia milti-orrhiza in-jection plus ligustrazine injection	magnesium sulphate	/	mean arterial pressure; fetal distress; neonatal asphyxia; postpartum hemorrhage; side effects	salvia miltiorrhiza combined with ligus-trazine are as effective as magnesium sul-phate but with fewer side effects
Qian 1991	unclear	ligustrazine injection	magnesium sulphate	diazepam	score of clinical performance; mean arterial pressure; hemo-dynamics; proteinuria; delivery method and time; postpartum hemorrhage; Apgar score	ligustrazine is more ef-fective and much safer than magnesium sul-phate
Shen 1984	unclear	salvia milti-orrhiza in-jection	/	magnesium sulphate; dextran; heparin	mean arterial pressure; hemo-dynamics; proteinuria	salvia miltiorrhiza combined with west-ern medicine is bet-ter than western med-icine only
Su 2002	42-56 days	prepared rhubarb	/	nifedipine	Apgar score; neonatal weight; blood fat; neonatal death; bleeding volume after baby birth	rhubarb combined with nifedipine is bet-ter than nifedipine on-ly

Table 2. Characteristics of quasi-RCTs (2) *(Continued)*

Tan 2000	6 days	salvia milti-orrhiza in-jection	/	magnesium sulphate	score of clinical performance; blood viscosity	salvia miltiorrhiza combined with mag-nesium sulphate is as effective as magne-sium sulphate only
Tang 1998	unclear	ligustrazine injection	magnesium sulphate	diazepam	score of clinical performance; mean arterial pressure; hemo-dynamics; protein uria; delivery method; Apgar score; postpar-tum hemorrhage	ligustrazine is more ef-fective and much safer than magnesium sul-phate
Wang 1997	unclear	CHM com-pound pre-scription	/	magnesium sulphate; hypoten-sive drugs; nicorol	neonatal weight; fetal growth restriction; fetal distress; neonatal death; mean arterial pressure	TCM combined with western medicine is much better than western medicine only
Wang 1998b	14 days	CHM (Zi-caojueming decoction)	CHM (Tian-magouteng decoction)	/	score of clinical performance	Zicaojueming is much better than Tian-magouteng
Wang 1999	42-56 days	prepared rhubarb	/	nifedipine; magnesium sulfate and diuretic	renal function; blood fat; Apgar score; neonatal weight; neona-tal death; bleeding volume after baby birth	rhubarb combined with western medicine is much better than western medicine only
Wang 2004	5 days	IG1: salvia miltiorrhiza injection; IG2: salvia miltiorrhiza injection plus mag-nesium sul-phate	magnesium sulphate	/	renal function	Compound therapy is much better than sin-gle medicine
Wang 2004b	14 days	Tian-magouteng decoction	/	nifedipine	score of clinical performance; side effects	TCM combined with nifedipine is much better than nifedipine only
Wang 2006	up to deliv-ery	salvia mil-tiorrhiza tablet	vitamin C; vitamin E	hypoten-sive drug; diuretic	mean arterial pressure; protein-uria; fetal distress; Apgar score; perinatal death; hemodynam-ics; side effects	salvia miltiorrhiza tablet is much better than vitamin
Wei 2000	14 days	CHM com-pound pre-scription	/	western medicine such as magne-sium sul-phate and nifedipine	score of clinical performance; neonatal weight; neonatal death; infection; neonatal in-tracranial hemorrhage	TCM combined with western medicine is much better than western medicine only
Wei 2002	7 days	CHM com-pound pre-scription	magnesium sulphate	sedative; hypoten-sive drug	neonatal weight; neonatal in-tracranial hemorrhage; bleed-	TCM is better than magnesium sulphate

Table 2. Characteristics of quasi-RCTs (2) *(Continued)*

					ing volume after baby birth; score of clinical performance	
Wu 1993	unclear	ligustrazine injection	magnesium sulphate	diazepam; hypotensive drug	microcirculation of bulbar conjunctiva; score of clinical performance	ligustrazine is better than magnesium sulphate
Xu 1984	unclear	CHM compound prescription	/	magnesium sulphate; diazepam; hypotensive drug	score of clinical performance; perinatal death; neonatal weight; neonatal distress; delivery method	TCM combined with western medicine is better than western medicine only
Yang 2001	7 days	Mailuoning injection	magnesium sulphate	sedative; nifedipine; diuretic	score of clinical performance; delivery method; cesarean section; delivery time; bleeding volume after baby birth; Apgar score;	mailuoning injection is better than magnesium sulphate
Yang 2006	unclear	ligustrazine injection; aspirin	/	magnesium sulphate	score of clinical performance; blood viscosity; proteinuria; S/D	Compound therapy is much better than single medicine
You 1999	unclear	CHM capsule	/	/	score of clinical performance; mean arterial pressure	TCM capsule is effective
Zhang 1993	5 days	ligustrazine injection	magnesium sulphate	sedative	score of clinical performance; mean arterial pressure; proteinuria; hemodynamics; delivery method; postpartum hemorrhage; Apgar score	ligustrazine is better than magnesium sulphate
Zhang 2002	unclear	CHM compound prescription	/	western medicine such as magnesium sulfate and nifedipine	score of clinical performance; delivery method; neonatal asphyxia	compound therapy is much better than western medicine only
Zhong 2002	28 days	CHM compound prescription	/	western medicine such as magnesium sulphate and nifedipine	score of clinical performance;	compound therapy is much better than western medicine only

APPENDICES

Appendix 1. Search Strategies

Review authors carried out the following searches

A. Search strategy for CENTRAL(Ovid)
a) Search strategy to locate RCTs
#1 randomized controlled trial
#2 random allocation

#3 random* allocat*
#4 random*
#5 RCT*
#6 #1~#5/or
b) Search strategy to locate pre-eclampsia
#7 preeclamp*
#8 pre-eclamp*
#9 pregnancy induced hypertension
#10 pregnancy toxemias
#11 pregnanc* hypertens*
#12 PIH
#13 hypertens* disorders in pregnanc*
#14 #7~#13/or
c) Search strategy to locate Chinese herbal medicine
#15 traditional Chinese herbal medicine
#16 Chinese traditional medicine
#17 traditional Chinese medic*
#18 Chinese traditional medic*
#19 herbal medicine
#20 herb* medic*
#21 medic* herb*
#22 Chinese herbal medicine
#23 Chinese herb* medic*
#24 Chinese medic* herb*
#25 herbal
#26 herb*
#27 complementary
#28 alternative medicine
#29 comp*
#30 alterna* medic*
#31 #15~#30/or
#32 #6 and #14 and #31

B. Search strategy for MEDLINE(Ovid)
a) Search strategy to locate RCTs
#1 randomized controlled trial
#2 random allocation
#3 random* allocat*
#4 random*
#5 RCT*
#6 #1~#5/or
b) Search strategy to locate pre-eclampsia
#7 preeclamp*
#8 pre-eclamp*
#9 pregnancy induced hypertension
#10 pregnancy toxemias
#11 pregnanc* hypertens*
#12 PIH
#13 hypertens* disorders in pregnanc*
#14 #7~#13/or
c) Search strategy to locate Chinese herbal medicine
#15 traditional Chinese herbal medicine
#16 Chinese traditional medicine
#17 traditional Chinese medic*
#18 Chinese traditional medic*
#19 herbal medicine
#20 herb* medic*
#21 medic* herb*
#22 Chinese herbal medicine
#23 Chinese herb* medic*
#24 Chinese medic* herb*
#25 herbal

#26 herb*
#27 complementary
#28 alternative medicine
#29 comp*
#30 alterna* medic*
#31 #15~#30/or
#32 #6 and #14 and #31

C. A similar strategy for CNKI
#1 pre-eclampsia
#2 pregnancy induced hypertension syndrome
#3 PIH
#4 pregnancy toxemias
#5 hypertensive disorders in pregnancy
#6 traditional Chinese herbal medicine
#7 Chinese herbal medicine
#8 herbal medicine
#9 traditional Chinese medicine
#10 traditional medicine
#11 Chinese medicine
#12 random
#13 #1~#5/or
#14 #6~#11/or
#15 #13 and #14 and #15

All of the search terms were translated to Chinese terms when we conducted the searches in CNKI databases.

WHAT'S NEW

Date	Event	Description
22 July 2009	New search has been performed	Search updated; 21 new reports identified but all excluded.

HISTORY

Protocol first published: Issue 1, 2005
Review first published: Issue 2, 2006

Date	Event	Description
30 April 2008	Amended	Converted to new review format.

CONTRIBUTIONS OF AUTHORS

Wenjuan Li: updated the review.
Taixiang Wu: commented on and revised the drafts, and updated the review.
Lingling Zhou: handsearched and evaluated new studies for this update.
Liuling Tang: handsearched and evaluated new studies for this update.
Jing Zhang: wrote the review.
Guanjian Liu: carried out data analysis.

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- Chinese Cochrane Center, China.
- West China Hospital of Sichuan University, China.
- West China Second University Hospital, Sichuan University, China.

External sources

- Chinese Medical Board of New York (CMB), USA.

INDEX TERMS

Medical Subject Headings (MeSH)

Drugs, Chinese Herbal [*therapeutic use]; Phytotherapy [*methods]; Pre-Eclampsia [*drug therapy]

MeSH check words

Female; Humans; Pregnancy