

Chinese herbal medicine for premenstrual syndrome (Review)

Jing Z, Yang X, Ismail KMK, Chen X, Wu T



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TABLE OF CONTENTS

HEADER	1
ABSTRACT	1
PLAIN LANGUAGE SUMMARY	2
SUMMARY OF FINDINGS FOR THE MAIN COMPARISON	3
BACKGROUND	3
OBJECTIVES	4
METHODS	4
RESULTS	8
Figure 1.	9
Figure 2.	10
DISCUSSION	12
AUTHORS' CONCLUSIONS	12
ACKNOWLEDGEMENTS	12
REFERENCES	13
CHARACTERISTICS OF STUDIES	15
DATA AND ANALYSES	21
WHAT'S NEW	21
HISTORY	21
CONTRIBUTIONS OF AUTHORS	21
DECLARATIONS OF INTEREST	22
SOURCES OF SUPPORT	22
DIFFERENCES BETWEEN PROTOCOL AND REVIEW	22
NOTES	22

[Intervention Review]

Chinese herbal medicine for premenstrual syndrome

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ABSTRACT

Background

Traditional Chinese herbal medicines are frequently used to treat premenstrual syndrome (PMS) in China. Until now, their efficacy has not been systematically reviewed.

Objectives

To evaluate the effectiveness and safety of traditional Chinese herbal medicines in the treatment of women with premenstrual syndrome.

Search strategy

We searched MEDLINE (January 1950 to December, 2007), EMBASE (January 1980 to December, 2007), Chinese Biomedical Database (CBM) (January 1975 to December, 2007), China National Knowledge Infrastructure (CNKI) (January 1994 to December, 2007), and the VIP Database (January 1989 to December, 2007).

Selection criteria

Randomised controlled trials (RCTs) studying the efficacy of traditional Chinese herbal medicine(s) for treatment of the premenstrual syndrome were included.

Data collection and analysis

Two review authors telephoned the original authors of the RCTs to confirm the randomisation procedure, extracted and analysed data from the trials that met the inclusion criteria.

Main results

Two RCT considering 549 women were included. One trial which was identified to be of higher methodological quality demonstrated the therapeutic effectiveness of Jingqianping granule. The other study was considered of lower quality due to the inherent risk of various biases in it. Two studies showed statistically significant differences in elimination of symptoms in proliferative phase and premenstrual phase by taking Jingqianping granule than taking Xiaoyaowan (RR 3.50, 95% CI 1.74 to 7.06). Women treated by CIPHER decoction had a higher rate of recovery than those taking Co-vitamin B6 capsules (RR 48.99, 95% CI 3.06 to 783.99).

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1

Authors' conclusions

It is rare in PMS management that efficacy claims are substantiated by clinical trials. One of the identified trials was well designed and reported on the effectiveness of Jingqianping in the treatment of premenstrual syndrome Qiao 2002. However, currently there is insufficient evidence to support the use of chinese herbal medicine for PMS and further, well controlled, trials are needed before any final conclusions could be drawn.

PLAIN LANGUAGE SUMMARY

Herbal treatment for premenstrual syndrome

Herbal medicines are sometimes used for treating premenstrual syndrome (PMS). However, the effectiveness of this type of therapy has not be evaluated rigorously.

The authors identified two trials that evaluated herbal medicines in PMS. One of these was a higher quality study that tested a traditional Chinese medicine decoction (Jingqianping granule) and this was shown to increase the rate of recovery from PMS symptoms. However, because the formula for this herbal medicine was provided by the trialists themselves, the authors recommend further trials to ensure that the results are reproducible. Strong evidence in support of other herbal formulae for the treatment of PMS is currently lacking.

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON [Explanation]

New Summary of findings table

Study	Clinical recovery	No improvement
Qiao 2002	56/202 in intervention group; 8/101 in control group	8/202 in intervention group; 18/101 in control group
Zhu 2003	50/166 in intervention group; 0/80 in control group	2/166 in intervention group; 31/80 in control group

BACKGROUND

Description of the condition

Premenstrual syndrome (PMS) is a common cyclic disorder of young and middle-aged women that consistently occur during the luteal phase of the menstrual cycle. It is characterised by emotional and physical symptoms and can manifest with a wide variety of symptoms, including depression, mood lability, abdominal pain, breast tenderness, headache, and fatigue (Dickerson 2003; Tempel 2001). The symptoms of PMS must be sufficiently severe to disrupt women's normal functioning, quality of life and interpersonal relationships. More severe and mainly psychological symptoms such as depression, anxiety and other affective symptoms which recur in the luteal phase of the menstrual cycle are classified as premenstrual dysphoric disorder (PMDD) (Dickerson 2003; Sundstrom 2003).

As many as 75% of women with regular menstrual cycles experience some symptoms of PMS, PMDD affects only 3% to 8% of women in this group (Steiner 2000). In addition, PMS is more prevalent among white women, smokers, obese, and younger women (Masho 2005).

The Diagnostic and Statistical Manual of Mental Disorders, the fourth edition (DSM-IV) (APA 2005) requires at least five specified symptoms to diagnose premenstrual dysphoric disorder (PMDD), while the International Statistical Classification of Diseases, 10th Revision (ICD-10) (WHO 2005) requires only one distressing symptom for a diagnosis of PMS. A diagnosis of PMS consists of determining the timing of the symptoms in relation to menses, meaningful change between post- and premenstrual symptom severity and a clinically significant severity of the symptoms. The current diagnostic standard requires confirmation of subjective symptom reports by prospective daily diaries. Diagnostic criteria for PMS must recognize the broad range of symptoms, the temporal pattern of the symptoms and the critical issue of symptom severity, which differentiates clinically significant PMS from normal menstrual cycle changes (Freeman 2003). The best tool to diagnose PMS is a daily symptoms rating calendar. To have

the diagnosis of PMS, the symptoms must be severe enough to disrupt normal daily activities (Tempel 2001).

The pathogenesis of PMS remains uncertain, research suggests that altered regulation of neurohormones and neurotransmitters is involved (Dickerson 2003). Several biological mechanisms that underlie menstrually related symptoms have been proposed. They focus mostly on gonadal hormones, their metabolites and interactions with neurotransmitters and neurohormonal systems, such as serotonin, GABA, cholecystokinin, and the renin-angiotensin-aldosterone system. Altered responses of these systems to ovarian hormones fluctuations during the menstrual cycle, as well as an increased sensitivity to changes in ovarian hormones may contribute to menstrually related symptoms in vulnerable women. Disrupted homeostasis and deficient adaptation may be core underlying mechanisms (Halbreich 2003). Current research, focusing on the biological background of premenstrual syndrome, suggests that both psychological and physiological factors exert their effect through dysregulation of the serotonergic function. The results of several studies point to a variation in the function of the serotonergic system throughout the menstrual cycle. Ovarian steroids have been found to influence profoundly the activity of the serotonergic system (Eriksson 1994; Gonda 2004; Joffe 1998; Rubinow 1998;). Additionally, reduced Serotonin uptake by platelets and whole blood serotonin levels during the luteal phase has been demonstrated in women with PMS compared to controls (Taylor 1984; Rapkin 1987; Steege 1992).

Hypomagnesaemia (low magnesium levels in blood) has been implicated in the pathogenesis of PMS (Ventskiv'ska 2005). Moreover, high intake of fats and low intake of foods with high concentration of carbohydrate may be associated with premenstrual symptoms (Nagata 2004).

Description of the intervention

Many different treatments have been suggested as possible therapies for PMS due to the uncertainty of its pathogenesis, the wide range of its manifestations and the high placebo effect. As serotonin has been implicated in the pathogenesis of PMS, the ther-

apeutic effectiveness of continuous and luteal phase dosing of selective serotonin reuptake inhibitors (SSRIs) has been evaluated in this disorder (Dimmock 2000). This has emerged as the first-line therapy for PMS (Steiner 2006).

Ovarian function appears to play a fundamental role in PMS, accordingly, treatment strategies designed to suppress ovulation have generally been found to be effective for treatment of menstrually-related syndromes and symptoms. Gonadotrophin-releasing hormone analogues (GnRH_a) appear to be an effective treatment of premenstrual syndrome (Backstrom 2003; Kouri 1998; Wyatt 2004).

In other studies, women with PMS who practiced aerobic exercise reported fewer symptoms than participants in the control group (O'Brien 2000; Steege 1993). Dietary restrictions or supplements may also be useful in women with PMS (Kessel 2000; Moline 2000). Sodium restriction has been proposed to minimize bloating, fluid retention, breast swelling and tenderness. Caffeine restriction is recommended because caffeine intake is related to premenstrual irritability and insomnia. A systematic review of placebo-controlled trials of evening primrose oil suggested lack of benefit in PMS, although mild relief was demonstrated in women with breast tenderness (Budeiri 1996).

A randomised placebo-controlled study reported there were significant improvements in the symptoms of negative feeling, pain, water retention, and total PMS symptoms in women receiving qigong therapy compared to placebo controls (Jang 2004). Qigong consists primarily of meditation, relaxation, physical movement, mind-body integration, and breathing exercises. Practitioners of qigong develop an awareness of qi sensations (energy) in their body and use their mind to guide the qi. When the practitioners achieve a sufficient skill level (master), they can direct or emit external qi for the purpose of healing others.

Some studies also indicate that acupuncture, homeopathy, aromatherapy, reflexology, Gingko biloba, kava kava, black cohosh, and agnus castus can relieve the symptoms of PMS such as anxiety, depression and irritability (Jones 2003; Tesch 2003; Yu 2005).

Other treatments for PMS, for which there is inconclusive evidence, include photic stimulation, cognitive behavioural therapy, relaxation therapy, vitamin B6, L-tryptophan, stress reduction, spironolactone, or a complex carbohydrate drink. Although evidence for relief of PMS symptoms is inconclusive, it is reasonable to recommend these as healthy lifestyle changes which may have overall benefits (Douglas 2002; Girman 2003; Rapkin 2003).

How the intervention might work

Herbal medicines have long been used in traditional healing systems to treat conditions of particular interest to women, such as premenstrual syndrome (PMS) and menopausal symptoms. For a select number of phytomedicine's, including evening primrose oil, black cohosh root extract, dong quai, and chaste tree berry, scientific investigation is revealing the pharmacologically active constituents, mechanism of action, and clinical value. Based on

the available evidence chaste tree berry may be reasonable treatment alternatives for some patients with PMS. Dong quai (in standard pinyin it's called dang gui) may be used to treat PMS when combined with traditional Chinese multiple-herb formulations (Hardy 2000). The current literature supports the use of chaste berry for cyclical breast discomfort and premenstrual syndrome (Roemheld-Hamm 2005).

Why it is important to do this review

Traditional Chinese medicine (TCM) has been used for thousands of years to treat PMS. The rule of TCM for PMS is 'Bian Zheng Lun Zhi': adding or reducing some herbs in a traditional preparation so-called 'demonstrated preparation' depending on the TCM signs 'Zheng' recognised by a TCM physician. At least eight types of 'Zheng' were recognised by TCM physicians, and various formulations can be used to treat the same type of 'Zheng'. Some new preparations for various 'zheng xing' (TCM signs) have been developed, for example, 'gan yu qi ci' type PMS can be treated by using adjusted 'cai hu su gan san' (Lang 1996), 'pi shen yang xu' type PMS by adjusted 'fang ji huang qi tang' combined with 'you gui wan' (Zhu 1995), etc. These formulations or preparations have been described as effective remedies and it has been suggested they could have clinical applications.

There is increasing public interest in, and use of, herbal medicine therapies which lie outside the 'mainstream' or traditional Western medical practice across the globe (HLSC 2000). There is evidence to indicate that not all herbs are risk-free. There are concerns about adverse events, particularly allergic reactions, as well as Chinese herbal nephropathy (CHN), which affects the kidneys (Lampert 2002; Lord 2001; Nortier 2000). Hence, the need to review herbal medicines systematically for their effectiveness and safety.

OBJECTIVES

To evaluate the effectiveness and safety of traditional Chinese herbal medicines in the treatment of women with premenstrual syndrome.

METHODS

Criteria for considering studies for this review

Types of studies

Only randomised controlled trials were included without restriction on language and publication types. Pseudo-RCTs were not be considered.

Types of participants

Women in the reproductive age diagnosed with premenstrual syndrome who suffer with one or more symptoms occurring periodically during 0 to 14 days before menstruation, for three or more menstrual cycles. Women known to have medical problems such as hypothyroidism, hypoglycaemia, psychiatric disorders, had bilateral oophorectomy, or any type of cancer were excluded.

Types of interventions

Any form of herbal medicine was considered, including oral preparations, decoctions, injections, and tablets, etc. Comparisons could be placebo, no intervention, acupuncture, western medication or any other interventions. Comparing of one kind of herbal medicine versus other herbal medicine were also included.

Types of outcome measures

Primary outcomes

Change of overall symptoms. The following tools will be considered:

(1) PMS scoring systems

Any validated objective scoring system used for evaluating premenstrual symptoms, such as the Moos Menstrual Distress Questionnaire or the Daily Symptom Report were considered.

(2) Improvement of overall symptoms (dichotomous data)

If the above two outcome measures were not used in a study, we considered the outcome measures as follows:

records made by participants or doctors by chart or using visual analogue scale;

severity of symptoms reported were judged in accordance with the definitions of numerical scales used in the charts.

Secondary outcomes

1. Quality of life

The Health Related Quality of Life (HRQOL) or other validated scales were considered in this review.

2. Adverse events

Events such as functional injury of liver or kidney, nausea, vomiting, diarrhoea and skin rash were recorded.

Search methods for identification of studies

We attempted to identify all relevant studies regardless of language or publication status (published, unpublished, in press, and in progress) (Appendix 1).

We searched:

(1) the Trials Registers of the Cochrane Menstrual Disorders and Subfertility Group and the Cochrane Complementary Medicine Field;

(2) the Cochrane Central Register of Controlled Trials (CENTRAL) in The Cochrane Library (Issue 4, 2007) Appendix 2.

(3) MEDLINE (January 1966 to December 2007), EMBASE (January 1980 to December 2007) Appendix 4, CISCOM (to December 2007), Chinese Biomedical Database (CBM) (January 1975 to December 2007), China National Knowledge Infrastructure (CNKI) (January 1979 to December 2007), and the VIP Database (January 1989 to December 2007) AMED Appendix 4.

(4) ongoing trials in the Meta-register of Controlled Trials, which includes the Medical Research Council Clinical Trials Directory and the National Research Register, Chinese Clinical Trial Register, as well as other registers for ongoing trials;

(5) reference lists of relevant trials and reviews identified;

(6) unpublished and on-going trials through correspondence with authors;

(7) major herbal treatment and obstetrics and gynaecology conferences proceedings and poster abstracts about this disease over the last five years for further eligible studies;

(8) for side-effect studies and contacted various adverse reaction reporting bodies.

Data collection and analysis

The study selection and data analysis were undertaken by two authors (ZJ and WTX).

Selection of studies

ZJ and YXZ scanned the search results abstracts and relevant records were identified. Full articles for all potentially relevant trials were retrieved. Since all the publications were in Chinese, WTX and ZJ were able independently to interview by telephone the original authors to identify what method was used to generate the allocation sequence. WTX selected the trials for inclusion. All identified reports were scrutinised to check for multiple publications of the same trials.

Data extraction and management

Using a piloted data extraction form, we extracted data on study characteristics including methods, participants, interventions and outcomes. There were no disagreements.

We extracted the formulation contents of included studies and herb names in three languages (Table 1 and Table 2).

Table 1. Herbs names in different language

Pinying name	Latin name	English name
Baishao	Radix Paeoniae Alba	White Peony Root
Baishu	Atractylodes macrocephala Koidz.	Largehead Atractylodes Rhizome
Bohe	Herba Menthae	Field mint/ peppermint
Chaihu	Radix Bupleuri	Chinese Thorowax Root /Red Thorowax Root
Chaozaoren	Stir-baked Semen Ziziphi Spinosae	Stir-baked Semen Ziziphi Spinosae
Chuanlianzi	Fructus Toosendan	Szechwan chinaberry fruit
Chuanxiong	Rhizoma Chuanxiong	Szechwan Lovage Rhizome
Cuchaihu	Stir-baked Radix Bupleuri with vinegar	Stir-baked Radix Bupleuri with vinegar
Danggui	Radix Angelicae Sinensis	Angelica; angelica root
Fuling	Poria	Indian Bread/ Poria cocos/ Poria cocos Wolf
Hehuanpi	Cortex Albizziae	Silktree albizzia bark
Juye	Citrus reticulata Blanco var. erythorosa H.H.Hu	Tangerine leaf
Shenglongchi	Dens Draconis	Dragon'sTeeth
Sigualuo	Retinervus Luffae Fructus	Retinerus Luffae Fructus
Xiangfu	Rhizoma Cyperi	Nutgrass Galingale Rhizome
Yujin	Radix Curcumae	Aromatic Turmeric Root-tuber
Zhigancao	Radix Glycyrrhizae Preparata	Prepared Radix Glycyrrhizae
Zhike	Fructus Aurantii	Bitter Orange

Table 2. Contents of the formulae in included studies

Study ID	Contents
Qiao 2002	Did not provide any information about the contents of interventions, but the drugs were the same as Wei 2006a, including the types and drug manufactory. Jingqianping granule: baishao, xiangfu, chuanxiong, zhike, chuanlianzi, etc; Xiaoyaowan: chaihu, danggui, baishao, baishu, fuling, zhigancao, bohe.
Wei 2006a	Jingqianping granule: baishao, xiangfu, chuanxiong, zhike, chuanlianzi, etc; it did not provide any information about the contents of xiaoyaowan (the control). We had indexed and found the contents of xiaoyaowan: chaihu, danggui, baishao, baishu, fuling, zhigancao, bohe.
Zhu 2003	Cipher Fang decoction: cuchaihu, baishao, yujin, juye, sigualuo, chaozaoren, hehuanpi, fuling, shenglongchi, etc. Vitamin B6 capsule: vitamin B6 20mg, vitamin B1 10mg, oryzanol 10mg.

Assessment of risk of bias in included studies

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

The following characteristics were assessed.

Randomisation process: assessment for selection bias

A - adequate sequence generation is reported using one of following approaches: random number tables or computer-generated random numbers. Coin tossing, or shuffling was used for generating the allocation sequence before the trial launching was considered eligible and with a low risk of selection bias.

B - does not specify one of the adequate methods outlined in (A) but only mentioned 'random' and will be considered with a moderate risk of selection bias.

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

Allocation concealment process: assessment of selection bias

A - adequate measures to conceal allocation defined as that the person who generated an allocation sequence but did not attend to recruitment of the participants, and the allocation sequence was sealed in opaque envelopes or conserved in locked computer, or another description that contains convincing elements of concealment, were considered to have a low risk of selection bias.

B - unclear: concealed trials in which the author does not report an approach of allocation concealment at all and were considered as having a moderate risk of selection bias.

C - inadequately-concealed allocation that reports an approach that does not fall into one of the categories in (A).

D - does not conceal allocation.

C and D were considered as having a high risk of selection bias.

Level of blinding: assessment for performance bias and detection bias

A - double blinding: participants and outcome assessor were masked and were considered as having a low risk of both performance and detection bias.

B - single blinding of the outcome assessor was considered to have a moderate risk of both performance and detection bias. If subjects were blind to group allocation but not the outcome assessor, the study was considered to have a high risk of detection bias.

C - non-blinding was considered to have a high risk of both performance and detection bias.

Measures of treatment effect

We have analysed the data using Review Manager (Version 5.0). We compared outcome measures for continuous data using the mean difference with 95% confidence interval. For binary data, we used relative risks with 95% confidence interval.

Dealing with missing data

The risk of bias of missing data was estimated according to following method (Higgins 2008):

A - low risk of bias: trials where few drop-out/losses to follow up are noted and an intention-to-treat analysis is possible.

B - moderate risk of bias: trials which reported the rate of exclusions was about 10% whatever intention-to-treat analysis was used.

C - high risk of bias: the rate of exclusion was at least 15%, or wide differences in exclusions between groups whatever the intention-to-treat was used.

Assessment of heterogeneity

We will analyse the clinical and methodological heterogeneity if the included studies similar enough in the future. We will assess

heterogeneity amongst trials to decide whether the data could be pooled or not by using the chi-square test. $I^2 < 25\%$, it means low heterogeneity, I^2 between 25% and 50% is considered moderate heterogeneity, and $I^2 > 50\%$ means notable heterogeneity. We will combine data using random-effects model. If $I^2 > 75\%$ which means substantive heterogeneity was existed, the data will not be combined (Higgins 2008).

Assessment of reporting biases

The risk of reporting bias was assessed refer to the description of Cochrane Handbook of Systematic Reviews of Interventions 5.0.0 (Higgins 2008)

No - low risk of reporting bias: all of outcomes were reported in detail.

Probably yes - moderate risk of reporting bias: at least one of outcomes were mentioned but not in detail.

Yes - high risk of reporting bias: at least one of outcomes were not reported.

Data synthesis

We had not performed combination analysis due to different formulae of TCM therapy and comparators were used in included studies.

Potential publication bias was not tested because there were only two studies in this review.

Subgroup analysis and investigation of heterogeneity

We performed subgroup analysis based on the different formulae of traditional Chinese herbal medicine.

Sensitivity analysis

We did not conduct the sensitivity analysis due to the combine analysis had not been performed.

RESULTS

Description of studies

See: [Characteristics of included studies](#); [Characteristics of excluded studies](#); [Characteristics of studies awaiting assessment](#).

A total of 17 trials, that claimed to be randomised, were identified. We successfully contacted 7 trial authors of these claimed RCTs by telephone. Of these studies, 4 were excluded, because the trial authors misunderstood the random allocation and they were not real randomised controlled trials. The two remaining studies were identified as true RCTs (Qiao 2002; Zhu 2003).

Excluded studies

See [Characteristics of excluded studies](#)

Of the 17 published articles initially identified, 9 articles were excluded as they were not randomised controlled comparisons (Li 2003; Pei 2005; Sun 2003; Wang 1997; Wang 2004; Yin 1999; Yue 2005; Zhang 2000; Zhang 2003). Outcome measures in Wei 2006 were not according to the review. Excluded studied and the reason of exclusion are listed in the 'Characteristics of excluded studies' table. We were unable to contact the authors of 5 studies hence listed in "Studies awaiting classification" (Feng 1996; Guo 2004; Li 2002; Xie 1994; Yuan 2004).

Included studies

See [Characteristics of included studies](#)

Two RCTs fulfilled our inclusion criteria (Qiao 2002; Zhu 2003).

Design

Both trials used parallel groups design. One of these studies (Qiao 2002) was a multi-centre, double-dummy, double blind design.

Participants

The two studies recruited participants based on traditional Chinese medicine (TCM) signs. These studies included a total of 549 participants (age range 16-45).

The trials authors reported that the diagnosis of PMS was made according to the "Regulation of clinical study of new TCM for PMS" in both studies, however, there was no detailed description of the regulation.

Interventions

Qiao 2002 compared Jingqianping granule and Xiaoyaowan.

Zhu 2003 compared Cipher Fang decoction and Vitamin B6 capsule

Outcomes

The two studies (Qiao 2002; Zhu 2003) did not report outcomes using the tools defined in this review, but reported recovery, marked improvement and no improvement based on TCM signs instead.

Risk of bias in included studies

See [Figure 1](#); [Figure 2](#)

Figure 1. Methodological quality graph: review authors' judgements about each methodological quality item presented as percentages across all included studies.

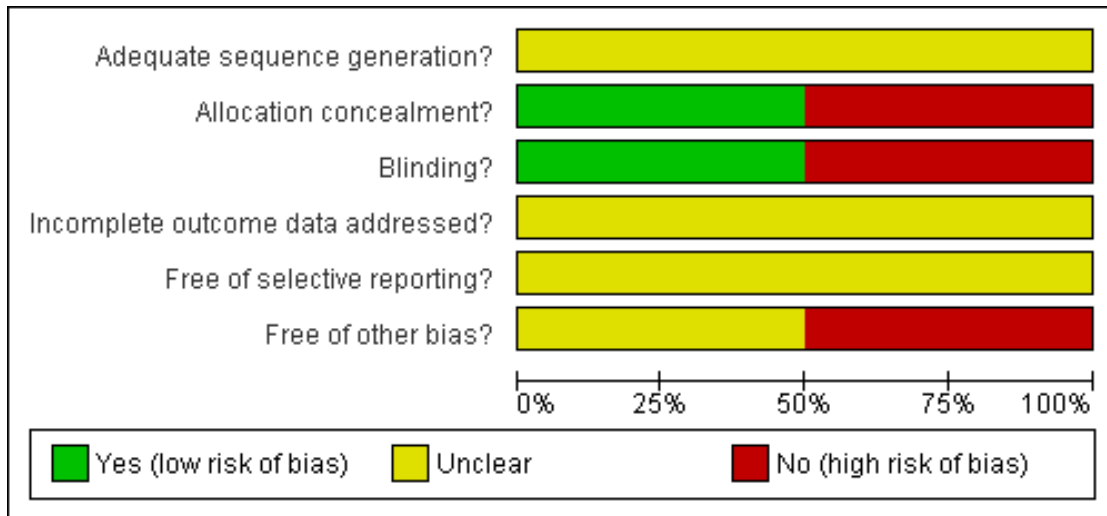


Figure 2. Methodological quality summary: review authors' judgements about each methodological quality item for each included study.

	Adequate sequence generation?	Allocation concealment?	Blinding?	Incomplete outcome data addressed?	Free of selective reporting?	Free of other bias?
Qiao 2002	?	+	+	?	?	-
Zhu 2003	?	-	-	?	?	?

Randomisation

All the included studies were RCTs that used random number tables. This was clearly stated in the study by [Zhu 2003](#), while it was confirmed following contacting the authors of [Qiao 2002](#) study.

Allocation concealment

None of the of the included trials mentioned allocation concealment. However,

Following contacting the studies authors, concealment was considered adequate in one of the included trials [Qiao 2002](#) where the random number allocation sequence was generated by a statistician not involved in participants' recruitment.

Blinding

Single blinding was used in one study ([Zhu 2003](#)), while the [Qiao 2002](#) study used a double dummy, double blind methodology, hence the risk of both perform bias and detection bias was deemed very low.

Withdrawal, drop-out and loss to follow up rate, and intention-to-treat

None of the included trials reported withdrawal, drop-out or loss to follow up of participants.

Effects of interventions

See: [Summary of findings for the main comparison](#) [New Summary of findings table](#)

1. The change of symptoms of the premenstrual syndrome.

(1) Rate of recovery (defined as the symptoms disappeared during the trial)

The two studies ([Qiao 2002](#); [Zhu 2003](#)) reported recovery rates and showed statistically significant differences in elimination of symptoms between their intervention and control groups:

- The rates of recovery in the group using Jingqianping granule was 27.7% (56/202), while it was 8% (8/101) in the Xiaoyaowan group (RR 3.50, 95% CI 1.74 to 7.06), suggesting that Jingqianping granule is more effective than Xiaoyaowan in eliminating PMS symptoms ([Qiao 2002](#)).
- Participants who took CIPHER decoction had a recovery rate of 30% (50/166), while there was no reported recoveries in the vitamin B6 capsules group (0/80) (RR 48.99, 95% CI 3.06 to 783.99), suggesting that CIPHER decoction is more effective than vitamin B6 in eliminating PMS symptoms ([Zhu 2003](#)).

(2) Rate of no improvement (defined as symptoms severity remaining unchanged during the trial)

Both studies also reported the rate of 'no improvement' and showed statistically significant differences between the intervention and control groups:

Eight participants reported no improvement (4%, 8/202) in the Jingqianping granule group compared to 18 in the Xiaoyaowan group (18%, 18/101) (Qiao 2002).

Two participants only reported no improvement in TCM signs (1.2%, 2/166) in the Cipher Fang decoction group, while 31 in vitamin B6 group (38.8%, 31/80) (Zhu 2003).

2. Time between commencing treatment and BBT or endocrine returning to normal.

One study (Zhu 2003) reported on changes in prolactin, estradiol and progesterin concentration before and after treatment. However, only a very small number of participants contributed to these data (14/166 in the experiment and 10/80 in the control group), we therefore did not include these results in the analysis of this review.

3. Development of adverse events

Both studies did not report any toxic reactions or adverse events.

DISCUSSION

Only two trials (Qiao 2002; Zhu 2003) fulfilled the inclusion criteria. One study (Qiao 2002) was considered to be of higher methodological quality with regards to study design and trial processing because a double-dummy technique was used. However, due to the potential of selection, detection and attrition biases in Zhu 2003, the study was considered to be of a lower methodological quality. However, the formula of experimental drug (Jingqianping granule) was prepared by the authors themselves and the drug was made by authors' university. Similarly, the experimental drug used in the study by Zhu 2003 was also prepared by authors themselves. Therefore, independent validation of the findings of these trials is advisable.

None of the included trials used a placebo control, however, active controls were used instead. PMS is a condition with substantial placebo response rate, hence it is scientifically important to include a placebo group in trials evaluating the therapeutic effectiveness of new medications. Moreover, it has been suggested that, by making comparisons with external placebo, the need for placebo control groups in new studies on psychotic patients could be minimised assuming that the novel medication will perform the same way in a study with only active controls as it would have in a placebo-controlled trial. However, evidence from 32 RCTs involving 7,264 patients showed that in the degree of improvement was nearly double in active-controlled trials than that seen with the same drugs and dosages in placebo-controlled studies Woods 2005. Therefore, the high RRs identified in this review could be secondary to the lack of use of placebo controls.

None of the trials provided sufficient information about allocation concealment. Further to contacting the authors, it was judged that

Qiao 2002 used adequate methodology to ensure concealment at the time of randomisation.

In addition, none of the studies reported on their justification for the required sample size. Although, the included trials seem to have recruited a large sample size (Qiao 2002 included 303 participants 202:101, and Zhu 2003 included 166:80) it is needed to have formal sample size calculation to ensure that the trial is of sufficient power to identify a difference if one exists.

Surprisingly, several trials claimed to be RCTs, however, following contacting the trial authors to enquire about the method of randomisation used, we found that most of the authors misunderstood the concept of randomisation or have forgotten the details of the methodology they employed, because they conducted the studies several years ago. Therefore, most of the Chinese herbal medicines in the management of premenstrual syndrome (PMS) studies were inadequate to provide reliable therapeutic effect estimates because of poor study design and methodological quality.

Finally, although the diagnostic standard was mentioned in two studies, However, a detailed description of the standard was not provided. In the absence of this key parameter we were unable to judge the validity of the study and how the diagnosis of PMS was made for the studies participants.

AUTHORS' CONCLUSIONS

Implications for practice

Currently, there is insufficient evidence for the efficacy of traditional Chinese medicine in the treatment of PMS.

Implications for research

Further randomised clinical trials of traditional Chinese herbal medicine for the treatment of the premenstrual syndrome are required. Independent validation of the therapeutic effectiveness of Jingqianping Granule is advisable. It is crucial that investigators should give considerable attention to the method of randomisation, blinding, sample size and the use of placebo controlled trials. The information on trial conduction should also be reported in detail according to CONSORT (Moher 2001) and CONSORT for TCM (Wu 2007 CONSORT).

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- * Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Qiao 2002

Methods	Multicentre (6 hospitals) parallel design, double simulation. "Randomly allocated" was mentioned but no detail about the method in original article, so we telephoned the author. A random number table was used to generate the allocation sequence. Double blinding was used.
Participants	Patients with premenstrual syndrome (PMS) with "Gan Qi" invasion. Diagnosed as TCM signs 'premenstrual tension syndrome', aged 18 to 40 years old. 403 cases were divided into the intervention group (n=202), the control group (n=101), and the open treatment group (n=100). Status of disease of the treatment groups: light/moderate/heavy: 22/133/147.

Interventions	Jingqianping granule was used in the intervention group, oral 15 g, t.i.d. and xiaoyaowan simulator 9g, b.i.d, for two menstrual cycles; Xiaoyaowan for the control group, oral 9 g, b.i.d.,and Jingqianping granule simulator 15 g,po, t.i.d. for two menstrual cycles.
Outcomes	<p>Observation for symptoms, menstrual cycle, BBT, body weight, and endocrine.</p> <ol style="list-style-type: none"> 1. Recovery: TCM signs disappeared, BBT or endocrine was normal, and after treatment, it did not relapse in three menstrual cycles, signs scores reduced more than 90%. 2. Marked improvement: TCM signs markedly improved. BBT or endocrine was almost normal, and after treatment, it did not worse in three menstrual cycles, TCM signs scores reduced more than 60% 3. Improvement: Main TCM signs improved, partial TCM signs relapsed after treatment, but better than before the treatment. Signs scores reduced more than 30% but less and 59%. 4. No improvement: TCM signs had no significant change or got even worse, signs scores reduced less than 30% 5. Safety 6. Adverse events
Notes	<ol style="list-style-type: none"> 1. This was a clinical study for new drug development in phase III trial and approved by the State Food and Drug Administration (SFDA) of China. 2. 100 persons were in the open treatment group. But we did not know how this treatment went on. 3. No statement for sample size calculation. 4. The drug was made by the authors' university.

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	Not mentioned the randomisation method.
Allocation concealment?	Yes	The allocation sequence was generated by statistician, and the sequences (four copies) were put in the optic envelopes.
Blinding? All outcomes	Yes	Double simulation technique was used.
Incomplete outcome data addressed? All outcomes	Unclear	Not mentioned
Free of selective reporting?	Unclear	Not mentioned
Free of other bias?	No	There was potential risk of conflict of interest existed because of the Jingqianping granule was made by the authors' university.

Zhu 2003

Methods	Parallel design. In the published article, it had been described that a random number table was used to generate the allocation sequence. The participants were blinded to the drugs.
Participants	246 women with premenstrual tension syndrome, according to the diagnostic criteria (Le Jie, Gynecology and Obstetrics, 4th edition, Beijing: People's Medical Publishing House, 1997:341.) 166 women in intervention group, aged 16 to 42 years old; 80 women in control group, aged 16 to 40 years old.
Interventions	Cipher Fang decoction was used in the intervention group, oral 20g, t.i.d, since the day BBT increased in the menstrual cycle. Oral for 12 days. And the same in the next menstrual cycle. Or before menstruation, oral 20g, t.i.d. for 12 days. Total 3 menstrual cycles. Vitamin B6 capsule was given in the control group: oral 1 pill, t.i.d. The usage same as intervention.
Outcomes	<ol style="list-style-type: none"> 1. Recovery: it did not relapse in three menstrual cycles after the treatment; TCM signs disappeared completely; BBT became normal; one or two of the hormones, xylose test returned to normal. 2. Marked improvement: Main TCM signs disappeared or partial TCM signs improved more than 50%, signs scores reduced from serious to mild; BBT and PRL were marked improved. 3. Improvement: TCM signs were better; signs scores reduced from middle to mild; BBT score increased 1 score or temperature increased 0.1. 4. No improvement. 5. Change of hormones. 6. BBT. 7. Xylose excretory rate. 8. Toxicity and adverse effects: By liver and kidney function tests, no adverse effects were observed.
Notes	<ol style="list-style-type: none"> 1. The formula was prepared by authors themselves 2. The Cipher Fang decoction was made by author's hospital 3. The Cipher Fang decoction contained cuchaihu, baishao, yujin, juye, sigualao, chaozaoren, hehuanpi, fuling, shenglongchi, etc. 4. The control was vitamin B6 capsule(vitamin B6 20mg, vitamin B1 10mg, oryzanol 10mg) 5. There is no evidence about effect of vitamin B6 capsule for premenstrual syndrome (PMS) 6. No statement for sample size calculation.

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	No any description about the method of randomisation.

Zhu 2003 (Continued)

Allocation concealment?	No	No any description about allocation.
Blinding? All outcomes	No	No any description.
Incomplete outcome data addressed? All outcomes	Unclear	Not mentioned.
Free of selective reporting?	Unclear	Not mentioned
Free of other bias?	Unclear	Potential risk of conflict of interest existed.

Characteristics of excluded studies [ordered by study ID]

Li 2003	It was claimed 'RCT'. We telephone interviewed the original author and learned that the method of allocation was according to the order of patients coming the hospital
Pei 2005	It was claimed 'RCT'. We telephone interviewed the original author and learned that the method of allocation was according to the order of patients coming the hospital
Sun 2003	It was claimed 'RCT'. We telephone interviewed the original author and learned that the method of allocation was according to the order of patients coming the hospital
Wang 1997	It was claimed 'RCT'. We telephone interviewed the original author and she said she had forgotten the method.
Wang 2004	It was claimed 'RCT'. We telephone interviewed the original author and learned that the method of allocation was according to the order of patients coming the hospital
Wei 2006	Hormone levels were used as outcomes in the study which have very little relationship to PMS.
Yin 1999	It was claimed 'RCT'. We telephone interviewed the original author and learned that the allocation method was performed optionally
Yue 2005	It was claimed 'RCT'. We telephoned the original author and learned that the patients were allocated according to the order of patients came to hospital
Zhang 2000	We telephoned the original author and learned that the patients were allocated by authors optionally
Zhang 2003	It was claimed 'RCT'. We telephoned the original author and learned that this actually was a retrospective paper for a summary of the author's clinical experience.

Characteristics of studies awaiting assessment *[ordered by study ID]*

Feng 1996

Methods	“Randomly allocated patients to two groups” mentioned.
Participants	
Interventions	
Outcomes	
Notes	The original author cannot be contacted by telephone for conformation of the randomisation method.

Guo 2004

Methods	“Randomly allocated patients to two groups” mentioned.
Participants	
Interventions	
Outcomes	
Notes	The original author cannot be contacted by telephone for conformation of the randomisation method.

Li 2002

Methods	“Randomly allocated patients to two groups” mentioned.
Participants	
Interventions	
Outcomes	
Notes	The original author cannot be contacted by telephone for conformation of the randomisation method.

Xie 1994

Methods	“Randomly allocated patients to two groups” mentioned.
Participants	
Interventions	
Outcomes	

Xie 1994 (Continued)

Notes	The original author cannot be contacted by telephone for conformation of the randomisation method.
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Yuan 2004

Methods	“Randomly allocated patients to two groups” mentioned.
Participants	
Interventions	
Outcomes	
Notes	The original author cannot be contacted by telephone for conformation of the randomisation method.

DATA AND ANALYSES

Comparison 1. Jinqianping granule versus Xiaoyao wan tablet

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Recovery	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
2 No improvement	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only

Comparison 2. CIPHER decoction versus covitamine B

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Recovery	1	246	Risk Ratio (M-H, Fixed, 95% CI)	48.99 [3.06, 783.99]
2 No improvement	1	246	Risk Ratio (M-H, Fixed, 95% CI)	0.03 [0.01, 0.13]

WHAT'S NEW

Last assessed as up-to-date: 27 May 2008.

30 April 2008	New search has been performed	Converted to new review format.
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HISTORY

Protocol first published: Issue 1, 2007

Review first published: Issue 1, 2009

8 September 2006	New citation required and major changes	Substantive amendment
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CONTRIBUTIONS OF AUTHORS

Xiaoyan Chen, Taixiang Wu and Khaled MK Ismail contributed to develop the protocol, Zheng Jing, Xunzhe Yang, Taixiang Wu and Khaled MK Ismail contributed to develop the review.

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

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

External sources

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

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

1. The outcomes measures were revised;
2. The standard of “assessment of quality of included studies” had changed according to the new version of Cochrane Handbook of Systematic Reviews of Interventions 5.0.0.

NOTES

Approved by all of the authors.