



Chinese herbal medicine for female infertility: An updated meta-analysis



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KEYWORDS

Infertility;
Traditional Chinese
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Meta-analysis

Summary

Objectives: To assess the effect of Traditional Chinese herbal medicine (CHM) in the management of female infertility and on pregnancy rates compared with Western medical (WM) treatment and update previous meta-analyses.

Methods: We searched the Medline and Cochrane databases until December 2013 for randomized controlled trials and meta-analyses investigating Chinese herbal medicine therapy for female infertility and compared clinical pregnancy rates achieved with CHM versus WM drug treatment. **Results:** Forty RCTs involving 4247 women with infertility were included in our systematic review. Meta-analysis suggested a 1.74 higher probability of achieving a pregnancy with CHM therapy than with WM therapy alone (risk ratio 1.74, 95%CI: 1.56–1.94; $p < 0.0001$; odds ratio 3.14; 95%CI: 2.72–3.62; $p < 0.0001$) in women with infertility. Trials included women with PCOS, endometriosis, anovulation, fallopian tube blockage, or unexplained infertility. Mean pregnancy rates in the CHM group were 60% compared with 33% in the WM group.

Conclusions: Our review suggests that management of female infertility with Chinese herbal medicine can improve pregnancy rates 2-fold within a 3–6 month period compared with Western medical fertility drug therapy. In addition, fertility indicators such as ovulation rates, cervical mucus score, biphasic basal body temperature, and appropriate thickness of the endometrial lining were positively influenced by CHM therapy, indicating an ameliorating physiological effect conducive for a viable pregnancy.

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Introduction

Fertility problems are encountered by about 15% of couples in Western countries.¹ Impaired fecundity, or the impaired ability to get pregnant or to carry a baby to term, affected about 6.7 million (10.9%) of women in the USA.¹

While 80% of infertility might be related to conditions such as endometriosis or polycystic ovary syndrome (PCOS), 20% are 'unexplained' in the Western Medicine model.² However, diagnosis of a specific disease/condition and subsequent treatment with surgery, drugs, in vitro-fertilisation (IVF) or other assisted reproductive technologies (ART) does not always result in a viable pregnancy and live birth. In 2011, for example, more than 170,000 ART cycles were recorded in the USA, and of these 29% resulted in live births.³

Moreover, ART treatment is costly for both governments and individuals. In 2011, for one IVF cycle costs

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were between US\$10–15,000, and individual couples' out-of-pocket expenses were on average US\$5300 and up to US\$19,000 for the first IVF cycle, and on average US\$7000 for subsequent cycles.⁴

Holistic approaches to infertility management, such as Traditional Chinese Medicine (TCM) might address some of the needs of women experiencing infertility, not met in the Western medical approach.^{5,6}

In the last decade, herbal medicines including Chinese herbal medicines are being used for fertility by a small proportion of women in Western countries, e.g. 5% of those surveyed at an infertility clinic in South Australia, 10% in the UK, or 18% in the USA.^{7–10}

Our previous meta-analysis of eight randomized controlled trials reported a doubling in the pregnancy rate in subfertile women using Chinese herbal medicine (CHM) within a 4-month treatment period compared with Western medical drug therapy.¹¹

Here we updated our previous meta-analysis on the effect of CHM on female infertility and pregnancy rates.¹¹ In addition, we summarize the effect of CHM therapy on ovulation rates and other fertility indicators. Furthermore we introduce the principles of TCM diagnosis and therapy, and provide examples of herbal formulae used in Traditional Chinese Medicine conducive to improving fertility.

Methods

Search strategy

We searched the Medline and Cochrane databases until December 2013 for randomized controlled trials and meta-analyses investigating Chinese herbal medicine therapy for female infertility using the following search terms: 'medicine, Chinese traditional' AND 'infertility'. In addition, we checked reference lists of relevant articles.

Study selection

We included randomized controlled trials with women of reproductive age with primary or secondary infertility. Infertility may have been associated with PCOS, anovulation, endometriosis, amenorrhea, fallopian tube blockage, or unexplained infertility.

Types of intervention

Chinese herbal medicine (CHM) treatment was defined as treatment with Chinese Herbs according to TCM pattern diagnosis. We included studies which used CHM alone or in combination with Western Medicine (WM) in the form of drugs or surgery. The control group in RCTs received WM treatment only. We excluded studies using acupuncture alone or TCM therapy in combination with assisted reproductive technologies (ART).

Types of outcome measures

The primary outcome was clinical pregnancy. We also summarized reported ovulation rates, basal body temperature

pattern, endometrial thickness, cervical mucus score, pain, adnexal mass reduction in patients with endometriosis, and restoration of tubal patency in women with blocked fallopian tubes. In addition, we report on the effect of CHM therapy on the continuation of pregnancy in women with threatened miscarriage.

Assessment of trial quality

To assess trial quality, the Cochrane Collaboration recommends the use of the risk-of-bias-tool which includes assessment of the adequacy of random sequence generation, allocation concealment, blinding, attrition/follow-up, and evidence of unselective reporting.¹² The quality of trials is then rated as adequate, unclear, or inadequate for these types of bias. The Jadad score is another commonly used assessment tool, including randomization, blinding, and attrition with a maximum score of five.¹³ A score of one is provided for each adequate method reported.

Data abstraction and analysis

Data from trials fitting the inclusion criteria were abstracted independently by two researchers.

Analysis of trials with sufficient quality was conducted using the Cochrane Review methodology and the Review Manager program.¹² A random effects model and the Mantel–Haenzel method were used to calculate the risk ratio between groups while accounting for heterogeneity. For comparison of results reported in some previous meta-analyses, we also calculated the odds ratio using the inverse variance method and a random effects model. Publication bias was assessed by funnel plot.

Results

Characteristics of included studies

In addition to our previous meta-analysis,¹¹ we identified a further three meta-analyses and one trial on the effect of Chinese herbal medicine compared to Western medical drug treatment for infertility, and reporting pregnancy rates (Fig. 1).^{14–16}

In summary, 40 trials involving 4247 women were included in our meta-analysis, comprising 8 trials^{17–24} from the meta-analysis by Ried,¹¹ 13 trials^{25–37} from the meta-analysis by See,¹⁴ 14 different trials^{38–51} from the meta-analysis by Tan,¹⁵ 4 trials^{52–55} from the meta-analysis by Zhang,¹⁶ and one RCT.⁵⁶ Only one trial²⁰ was reported in two reviews,^{14,15} but included only once in our meta-analysis. Characteristics of included trials are summarized in Table 1.

The majority of trials involved women with anovulation ($n=24$) and PCOS ($n=8$), while two trials studied women with endometriosis, one with immunological infertility, and one with blocked fallopian tubes (Table 1). About half of the trials compared CHM only with Western medical treatment ($n=21$), 40% used CHM plus clomiphene (CC) versus CC, and four trials combined CHM with other WM treatment and compared to WM treatment. In the control groups, two-thirds of the trials used CC as the only WM drug therapy, seven

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