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Review

Traditional Chinese Medicine for Diminished Ovarian Reserve: A Systematic Review and Meta-analysis

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ABSTRACT

Objective To assess the effectiveness and safety of traditional Chinese medicine (TCM) for women with diminished ovarian reserve (DOR). **Methods** A literature search was conducted in eight electronic databases for randomized controlled trials. **Results** Seventeen randomized controlled trials involving 1174 patients were included. Meta-analysis indicated that TCM was superior to Western medicine (WM) in reducing basal serum FSH level [MD = −1.70, 95% CI (−2.63, −0.77); P = 0.0004] and FSH/LH (MD = −0.43, 95% CI [−0.56, −0.30]; P = 0.0001), and the effect was more obvious two months after the last treatment (MD = −4.60, 95% CI [−6.26, −2.90], P < 0.000 01 and MD = −0.56, 95% CI [−0.85, −0.28], P = 0.0001), and increasing antral follicle count (AFC) (MD = 0.44, 95% CI [0.04-0.83]; P = 0.03). The review also revealed the positive role of CMM as an adjuvant to IVF-ET in improving pregnancy rate (PR = 1.75, 95% CI [1.25, 2.46]; P = 0.001). **Conclusion** TCM, with its unique way of replenishing the kidney, may provide an effective and safe alternative therapy to patients with DOR.

Key words

meta-analysis; ovarian disease; randomized controlled trial; systematic review; traditional Chinese medicine

1. Introduction

Diminished ovarian reserve (DOR) refers to the condition of poor fertility which is characterized by limited numbers of remaining primordial follicles in the ovary and possibly impaired preantral oocyte development or recruitment (Wikipedia, 2012).

Global prevalence of DOR is not studied largely because thus far the standard and agreed diagnostic criteria for it have not been defined. But it had been reported that merely 5% of women with evidence of DOR would achieve pregnancy, despite using of ovulation inducing agents (Scott et al, 1995).

The exact causes for DOR have only been inadequately understood. The most common reason is advanced reproductive age (Gleicher et al, 2011), and others include congenital (Skiadas et al, 2012; Pastore et al, 2012; Livshyts et al, 2013), surgical (Biacchiardi et al, 2011), medical causes (Clowse et al, 2011), psychosocial stress (Pal et al, 2010), and

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alcohol intake (Li et al, 2013). Women confirmed of DOR diagnosis might present with infrequent menstruation, scanty periods, infertility, absence of menstrual bleeding, short follicular phase, or poor ovarian response to exogenous gonadotrophin at reproductive age (Loutradis et al, 2007).

The current treatment strategies to address DOR have primarily focused on hormone replacement therapy to adjust the endocrine system and restore hormone balance. A few clinical studies showed some beneficial effects of dehydroepiandrosterone (DHEA) on DOR (Barad et al, 2007; Gleicher et al, 2009; Gleicher and Barad, 2011). However, its extensive use was not well-grounded and should be discouraged (Urman and Yakin, 2012). Traditional Chinese medicine (TCM) might provide a holistic approach and less harmful therapy to address the conditions of menstrual disorder or infertility affecting DOR patients.

The efficacy of TCM on patients with DOR has been tested in a few preliminary clinical studies with positive outcomes (Xu, 2007). Moreover, both acupuncture and electro-acupuncture therapies have been reported to regulate the endocrine system (Cui et al, 2007), stimulate ovulation (Yan and Huang, 1997), and improve ovarian blood flow (Stener-Victorin et al, 2004) in women with DOR. Based on the current evidence, we conducted a systematic review and meta-analysis to examine the role of TCM in DOR, with special attention on TCM as an adjuvant to *in vitro* fertilization and embryo transfer (IVF-ET) in patients with DOR.

2. Methods

2.1 Inclusion criteria

2.1.1 Type of studies

Published randomized controlled trials (RCTs) examing the role of various forms of TCM in treating women with DOR were eligible for inclusion.

2.1.2 Type of participants

Women of reproductive age with a serum level of follicle stimulating hormone (FSH) above 10 and below 40 IU/L.

2.1.3 Type of interventions

Intervention treatment with TCM therapeutic tools includes herbal medicine (HM), acupuncture (ACU), electro-acupuncture (EACU), moxibustion etc, and by alone or in the combination with Western medicine (WM) or IVF-ET or with them both as well. Treatment in the control group included placebo, no treatment, WM, IVF-ET, or combination of them.

2.1.4 Type of outcome measures

The primary outcomes were changes in basal serum FSH level and pregnancy rate (PR). The secondary outcomes were total effectiveness rate (TER), improvement in basal FSH/LH (luteinizing hormone) ratio, adverse events, and changes in basal serum E2 level, antral follicle count (AFC), and basal serum anti-Müllerian hormone level (AMH). We also compared the short-term (immediately after a 3-month treatment) and long-term (2 or 3 months after the last treatment) effects for one primary outcome and two secondary outcomes, namely changes in basal serum FSH level, improvement in FSH/LH ratio, and TER. Special attention was also paid to the role of TCM therapies as an adjuvant to IVF-ET.

2.2 Exclusion criteria

We excluded studies in which DOR was induced by unilateral or bilateral ovary removal surgery or participants included were diagnosed with premature ovarian failure (POF). Studies with unclear diagnostic criteria or without full texts were also considered ineligible for this review.

2.3 Search strategies

A comprehensive literature search was conducted in January 2013 in three English and five Chinese electronic databases including the Cochrane Central Register of Controlled Trials (CENTRAL, Issue 12, 2012), EMBASE (1974.1–2013.1), PubMed (1966.1–2013.1), China National Knowledge Infrastructure (1956.1–2013.1), WanFang Database (1982.1–2013.1), VIP Database (1989.1–2013.1), Chinese Biomedical Database (CBM, 1978.1–2013.1), and Chinese Clinical Trial Register (ChiCTR). The search strategy was formulated using MeSH terms in combination with free text words. The following is the search strategy developed for PubMed:

1. ovarian (text word, tw)
2. complementary medicine [Mesh terms]
3. acupuncture therapy [Mesh terms]
4. acupuncture [tw]
5. electroacupuncture [tw]
6. moxibustion [tw]
7. traditional Chinese medicine [Mesh terms]
8. Chinese medicine [tw]
9. herbal drug [tw]
10. herbal formula [tw]
11. herbal preparation [tw]
12. herbal medicine [tw]
13. Chinese patent drug [tw]
14. Chinese patent medicine [tw]
15. 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14
16. 1 and 15

We also checked the reference lists of included studies and relevant review articles for possible identification of eligible trials. Conference proceedings on ovarian diseases and women infertility were manually retrieved and screened.

2.4 Study selections

Two reviewers independently undertook the afore-mentioned search. Studies identified from electronic