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Study Protocol

Complementary therapy for female infertility: protocol for an overview of systematic reviews

Jang Won Lee [a], Min Kyung Hyun [a,*], Lin Ang [b]

[a] Department of Preventive Medicine, College of Korean Medicine, Gyeongju, Dongguk University, Republic of Korea
[b] Clinical Medicine Division, Korea Institute of Oriental Medicine, Daejeon, Republic of Korea

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ABSTRACT

Background: There are numerous reports worldwide on the use of complementary therapy for female infertility. This paper presents an overview of the available systematic reviews (SRs) on the outcomes of complementary therapy for female infertility.
Methods: Electronic databases, including Pubmed, the Cochrane Central Register of Controlled Trials (CENTRAL) and Google scholar, and six Korean medical databases (KoreaMed, KMBASE, OASIS, NDSL, KCI, and RISS) will be searched from their date of inception. Eligible SRs will be independently selected by two authors, according to the defined inclusion criteria. Methodological quality of the final selected SRs will then be evaluated using the 'Assessment of multiple systematic reviews 2 (AMSTAR2)'. Finally, we will report on the characteristics and outcomes of efficacy and safety of each individual SR.
Discussion: This overview will apprise the overall quality and evidence of the outcomes of SRs of complementary therapy for female infertility.

1. Introduction

An estimated 48.5 million couples worldwide were established with infertility in 2010.[1] The most common causes of female infertility are ovulation disorders, obstruction of the fallopian tube, and about 20% unexplained infertility.[2] in vitro fertilization (IVF) is the most common treatment for infertility.[3] Female infertility of unspecified origin is known to be administered complementary medicine (CM) prior to or concurrently with ongoing medical treatment.[4,5]

Recent systematic reviews (SRs) and meta-analysis have compared the effect of CM, such as acupuncture or Chinese herbal medicine, on infertility, but there were significant differences in outcomes of acupuncture. One meta-analysis reported significant increase in pregnancy rate and live birth rate, and a significant decrease in miscarriage at the time of embryo transfer.[6] Another review reported different results, depending on the scheduling of acupuncture at the time of embryo transfer.[7] However, recent randomized clinical trial (RCT) studies have reported that acupuncture performed before and after embryo transfer has no benefit, when compared to sham-acupuncture.[8] In addition, systematic reviews on the effectiveness of Chinese herbal medicine in patients with infertility and polycystic ovary syndrome (PCOS) also report contradictory results. One review reported insufficient evidence for Chinese herbal medicine to benefit patients with infertility and PCOS.[9] However, another review stated that Chinese herbal medicine significantly improves pregnancy rates in subjects with infertility and PCOS.[10]

Considering the conflicting reports in literature, we have undertaken to conduct an overview of SRs on the outcomes and methodological quality of CM for female infertility.

2. Methods

2.1. Study registration

This overview of systematic review was registered in the registry study database (https://www.researchregistry.com/) on 19 November 2019 (reviewregistry769).

2.2. Eligibility criteria

2.2.1. Type of study

This article will cover systematic reviews of RCTs, with each SR describing a systematic search method. All systematic reviews, with or without meta-analysis, will be included. Although language

* Corresponding author.
E-mail addresses: a20190438@dongguk.ac.kr (J.W. Lee), mk3three@dongguk.ac.kr (M.K. Hyun), anglin2808@kiom.re.kr (L. Ang).

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restrictions will not be applied to the search process, the study selection will be limited to literature written in Korean and English. Articles without full text will be excluded.

2.2.2. Type of participant

Women diagnosed with primary infertility or secondary infertility should be included in all SRs. There is no restriction age, period of infertility, or cause of infertility.

2.2.3. Type of intervention

Women undergoing IVF and concurrently taking CM will be included. Exclusion of subjects will depend on CM therapies enrolled in control group.

2.2.4. Types of outcomes

Reviews will be included if the CM outcomes are beneficial in improving pregnancy rate, decreasing anxiety of the infertile patient, or reducing the pain of assisted reproductive technology (ART).

2.2.4.1. Primary outcomes.

1) Clinical pregnancy rate: Evidence of a gestational sac with fetal heart movement measured between 7 and 8 weeks, and confirmed by ultrasound.
2) Ongoing pregnancy rate: Evidence of a gestational sac with fetal heart movement for 12 weeks to 18 weeks, and confirmed by ultrasound.
3) Live birth: Birth of a live fetus after 20 weeks of pregnancy.

2.2.4.2. Secondary outcomes.

1) Anxiety level: Spielberger's State-Trait Anxiety Inventory (STAI), shortened version of the 20-item STAI, Hamilton Anxiety Scale (HAS), and the Chinese version of STAI questionnaire.
2) Pain level: VAS, McGill Pain Questionnaire.
3) Adverse Events: miscarriage, ovarian hyperstimulation syndrome.

2.3. Search strategy

International and Korean electronic databases, including the Cochrane Central Register of Controlled Trials (CENTRAL), PubMed, Google Scholar, Koreamed (www.koreamed.org), KMBASE (kmbase.medric.or.kr), NDSL (www.ndsl.kr), KCI (www.kci.go.kr), RISS (www.riss.kr), and OASIS (oasis.kiom.re.kr) will be searched from their inception till June 2019. There will be limitation on language of the articles included (English, Korean). However, there will be no limitation on the year of publication. The search strategy is presented in Supplementary material.

2.4. Data collection and analysis

2.4.1. Selection of studies

A standardized selection form will be generated and applied by two independent authors to select appropriate studies. Each study selection process will be described and summarized in the PRISMA flowchart, and reasons for exclusion will be provided.

2.4.2. Data extraction

Two independent authors will extract the data using a predefined data extraction form. Following information will be collected: author, year of publication, affiliation of main authors, numbers of included studies, participants, intervention, and outcomes.

2.5. Methodological quality assessment

Two independent authors will evaluate the methodological quality of the included studies using the 'Assessment of multiple systematic reviews 2' (AMSTAR2) tool consisting of 16 items.[11]

2.6. Data analysis

A narrative description of the included reviews will be performed. We will report and summarize all included review characteristics, methodological quality assessment results, and major outcomes. Furthermore, the RCTs included in each review will be compared and reported.

3. Discussion

The success rate of IVF clinics ranges from 10 to 40%.[12] In order to alleviate the burden of medical expenses for patients and reduce anxiety regarding their infertility treatments, various approaches (including CM) are required to increase the success rates. The primary aim of this study is a qualitative integration of SRs and meta-analyses, to assess the study evidence of outcomes related to CM for female infertility. This will be a comprehensive study, overviewing significant SRs for the quality and outcomes of CM on female infertility. We expect the results of this study will help clinicians and patients in making decisions to identify the appropriate treatment for female infertility.

This study will restrict to SRs published written in English and Korean. It is reasonable to include all the evidence for research topic without language limitations and restricting the language can cause language bias and lead to incorrect conclusions. However, according to a study, there is little evidence that language restrictions are biased in traditional medicine.[13] In addition, based on our preliminary review, most of English-language SRs will be included in the overview of SR contain a lot of RCTs conducted in China and so on.

Conflict of interest

The authors declare that they have no conflict of interest.

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Data availability

The data from this work will be made available upon request.

Authors' contribution

All authors planned the study and wrote the manuscript.

Ethical statement

Not applicable.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.imr.2020.01.010.

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