INPLASY PROTOCOL

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Conflicts of interest:
The study has no conflicts interest.

Tanshinone for polycystic ovary syndrome: a protocol of systematic review and meta-analysis

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Review question / Objective: **1. Type of participants: patients who were diagnosed with PCOS, there will be no limitation on age, origin and nationality. 2. Intervention: Tanshinone alone or basic treatment combined with tanshinone, at any dose and route. 3.Control:conventional ovulation inducing agents, such as clomiphene, letrozole and metformin. 4. Outcomes: Primary outcomes: ovulation rates Secondary outcomes:a) sex hormone level; b)fasting serum glocuse; c) fasting insulin; d) total cholesterol; e) triglycerides; f) low density lipoprotein; g)high density lipoprotein; h) adverse events. Types of studies: published and unpublished randomized control trials (RCTs) were eligible for inclusion. we excluded non-RCTs as they are associated with a high risk of bias.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 06 October 2020 and was last updated on 06 October 2020 (registration number INPLASY2020100017).

INTRODUCTION

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Condition being studied: PCOS is a common endocrine disorder in women, it is the leading cause of infertility and amenorrhea. Due to its high recurrence rate, poor prognosis and serious complications, more works on the research of PCOS are needed. In recent years, studies have found that the prevalence of IR in PCOS is higher, reaching 50-80% , and it is believed that IR is a direct cause of anovulation. Restoring natural and regular ovulatory menstruation is critical for PCOS treatment, but there is still no perfect treatment. Various ovulation-inducing agents are used for PCOS therapy, but they all have certain deficiencies and side effects. Therefore, traditional Chinese medicine, as the main component of complementary treatments, has attracted attention as a place for the treatment of PCOS. Among them, tanshinone is a common Chinese patent medicine widely used for PCOS patients who are hyperandrogenism and IR. It is known to affect activating blood and dissolving stasis. There has some studies description of the safety and efficacy of tanshinone. However, systematic review or meta-analysis including RCT studies designed as tanshinone therapy, is not reported. This study will provide evidence about the safety and efficacy of tanshinone in the treatment of PCOS.

METHODS

Search strategy: Two authors will independently search the following electronic databases: PubMed, Cochrane Library, EMBASE, Web of Science, CINAHL, and China National Knowledge Infrastructure(CNKI) to the present. Also, we will retrieve unpublished trials on ClinicalTrials.gov. The keywords of our search terms were ("Tanshinone") AND ("polycystic ovary syndrome" OR"PCOS").

Participant or population: All eligible patients were defined as diagnosed with PCOS. There will be no limitations on age, origin, and nationality.

Intervention: We will include studies that the intervention group received tanshinone.

Comparator: All eligible participants in the control group will include any type of intervention.

Study designs to be included: Published and unpublished randomized control trails(RCTs) were eligible for inclusion.

Eligibility criteria: 1. Type of participants: patients who were diagnosed with PCOS, there will be no limitation on age, origin and nationality. 2. Intervention: Tanshinone alone or basic treatment combined with tanshinone, at any dose and route. 3. Control: conventional ovulation inducing agents, such as clomiphene, letrozole and metformin. 4. Outcomes: Primary outcomes:ovulation rates Secondary outcomes: a) sex hormone level; b) fasting serum glucose; c) fasting insulin; d) total cholesterol; e) triglycerides; f) low density lipoprotein; g)high density lipoprotein; h) adverse events. Types of studies:published and unpublished randomized control trails(RCTs) were eligible for inclusion. we excluded non-RCTs as they are associated with a high risk of bias.

Information sources: PubMed, Cochrane Library, EMBASE, Web of Science, CINAHL, China National Knowledge Infrastructure (CNKI) and ClinicalTrials.gov.

Main outcome(s): Ovulation rate.

Additional outcome(s): Total response rate, sex hormone level, fasting serum glucose, fasting insulin, TC, TG, LDL, HDL, and adverse events.

Quality assessment / Risk of bias analysis: If more than ten studies are included, we will generate Funnel plots and egger's regression text to analyze publication bias.

Strategy of data synthesis: 1. Data extraction: Two reviewers will independently extract detailed data and information from articles, and a third viewer will discuss any disagreement. We will extract the data of necessary information(title, first author, country, publication year), participants' characteristics (sample size, average age, trial design, trial methods, trial setting, the inclusion and exclusion criteria), interventions(doses of tanshinone, type, treatment duration, and follow-up time), comparisons(details of intervention and control groups), and outcomes(results, findings, and adverse events). 2. Measurement of the treatment effect: We used the Cochrane Review Manager (RevMan 5.3) software for data analysis. For continuous variables, we estimated by standardized mean difference (MD) and 95% confidence intervals (CIs), the effect size of dichotomous variables will be estimated using risk ratio and 95% CIs. We will apply I2 statistic to employ statistical heterogeneity. When I2 <50%, we will using a fixed-effect model, otherwise use a random-effect model. 3. Dealing with missing data: If the data not provided or insufficient, we will contact the authors and attempt to get detailed information. When the data are unavailable, we only analyze available data. 4. Assessment of heterogeneity: We will evaluate study heterogeneity by I2 statistic and the chi-square test, and when P 50%, the studies considered to have significant heterogeneity. If significant heterogeneity is detected, we will conduct a subgroup analysis.

Subgroup analysis: We will conduct the subgroup analysis to identify substantial heterogeneity according to the study information, patient's characteristics, type of inventing measures, and outcome indicators.

Sensibility analysis: The sensitivity analysis will be conducted to test the robustness of the study. We will eliminate low qualities studies 1 by 1 to evaluate the reliability of the results of the meta-analysis.

Language: English, Chinese.

Country(ies) involved: China.

Keywords: Tanshinone, polycystic ovary syndrome, randomized controlled trials, systematic review.

Contributions of each author:
Author 1 - Yijiao Yang - drafted the manuscript.
Author 2 - Honglin Liu - The author provided statistical expertise.
Author 3 - Yue Xia - The author contributed to the development of the selection criteria, and the risk of bias assessment strategy.
Author 4 - Xia Peng - The author contributed to the development of the selection criteria, and the risk of bias assessment strategy.
Author 5 - Xiaorong Ni - The author read, provided feedback and approved the final manuscript.