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Acupuncture for glucose and lipid metabolic disorders of polycystic ovarian syndrome: A systematic review protocol

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ABSTRACT

Abstract

Background

Polycystic ovary syndrome (PCOS) is a common gynecological disease ~~which~~ that is often accompanied by some metabolic abnormality such as insulin resistance and dyslipidemia. As a non-pharmacological therapy, acupuncture is widely used for the treatment of PCOS but the effectiveness for insulin resistance and lipid metabolic disorder remains controversial.

Objectives

To assess the effectiveness and safety of acupuncture for insulin resistance and lipid metabolic disorder of women with PCOS.

Search methods

Eight databases will be searched from inception to June~~February~~ 2021, three clinical trial registration platforms will be searched for relevant trials.

Selection criteria

Randomized controlled trials (RCTs) of acupuncture therapy for insulin resistance and lipid metabolic of PCOS will be included.

Data collection and analysis

Study screening, data collection, and analysis will be performed by two or more reviewers independently. We will calculate mean difference（MD）, standard mean difference (SMD) with 95% confidence intervals (CIs). Data synthesis will be performed with RevMan V.5.3 software and with Stata V.15.0 software when necessary.

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KEYWORDS

Polycystic ovary syndrome, Acupuncture Therapy, Insulin resistance, lipid metabolism, Systematic review

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1 Study registration and design

Thesystematic review protocol has been registered prospectively in the International Prospective Register of Systematic Reviews (PROSPERO) (CRD42020177846). This protocol is reported in line with the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) statement guidelines. The PRISMA-P checklist is shown in the S1 Appendix.

And the study will be performed according to the Cochrane Handbook for Systematic Reviews of Interventions and presented based on Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines.

2 Criteria for including studies in this reviewTypes of studies

Randomized controlled trials (RCTs)of acupuncture therapy for IR and lipid metabolic of PCOSwill be included.Summary results of ongoing and completed trials published on the clinical trial registration platform will also be included. The sample size of both experimental and control groups for each individual included trial should be larger than 20respectively.

Types of participants

Participants who were diagnosed with PCOS according to the ESHRE and ASRM consensus in Rotterdam in 2003, will be included regardless of their age, race, and background. The Rotterdam consensus required at least 2 out of 3 criteria including 1) Oligo-and/or anovulation, 2) Clinical and/or biochemical signs of hyperandrogenism, 3) Polycystic ovaries, and exclusion of other aetiologies(such as congenital adrenal hyperplasias, androgen-secreting tumors, Cushing's syndrome)[1].

If the trials did not use the Rotterdam consensus, but the diagnostic criteria were clearly stated, we will evaluate the diagnostic criteria to confirm whether they meet the Rotterdam consensus. The authors will be contacted to obtain clarification if there is insufficient information. If the clarification is not available, the trials will be excluded.

Types of interventions

Experimental interventions

The interventions considered in the review were described as acupuncture, which is defined as needles be inserted into acupoints, pain points, or trigger points. The interventions including manual acupuncture, electro-acupuncture, combined acupuncture with moxibustion, acupuncture combined with lifestyle management (such as exercise, control diet), or acupuncture combined with metformin. Trials in which any one of the above treatments combined with a basic treatment(such as Diane-35clomiphene) which is used in control groups, will also be included.

Other stimulations to specific points such as catgut embedding, point injections, or acupoints stimulation without needle insertion (such as acupressure, massage) will be excluded. Trials in which patients have previously been treated with insulin sensitizer or insulin secretagogues before the study started will be excluded.

Control interventions

Eligible comparators were placebo, sham acupuncture, no treatment, lifestyle management, metformin, and metformin combined with sham acupuncture or lifestyle management. And any one of the above treatments combined with the same basic treatment(such as Diane-35, clomiphene), will also be included.

Studies only compared different forms or methods of acupuncture, and compared acupuncture with a different type of Chinese Medicine (such as Chinese herbs) will be excluded.

Types of outcome measures

Primary outcome

Homeostasis model assessment of insulin resistance (HOMA-IR)[33]. If HOMA-IR was not directly reported in articles, it will be calculated by available values of fasting insulin FINS and fasting plasma glucose (FPG). HOMA-IR= FINS μU/ml ×FPG mmol/L /22.5.

Serum triglyceride (TG).

Secondary outcomes

Serum biochemical parameters: Total cholesterol(TC), High-density lipoprotein cholesterol(HDL-C), Low-density lipoprotein cholesterol(LDL-C).

Anthropometric measures: Body mass index(BMI), Waist circumference(WC), Waist-to-hip ratio(WHR).

Adverse events related to acupuncture.

3 Electronic searches

The following databases will be searched from inception to June 2021, regardless of the publication status: Cochrane library, PubMed, EMBASE, Web of Science, China National Knowledge Infrastructure (CNKI), Chinese Biomedical Literature Database (CBM), Wan-Fang database, Chinese Scientific Journal Database (VIP). There is no language restriction.

The search terms consisted of four parts: population (PCOS), intervention (acupuncture), outcome (eg, HOMA-IR,glucose metabolism, lipid metabolism, glycolipid metabolism), study design (RCT). Searches will combine medical subject headings terms and free words in title and abstract. The search strategy for PubMed is shown in theS2 Appendix.

4 Searching other resources

RCTs will also be obtained from the reference lists of relevant studies and published systematic reviews. The ClinicalTrials.gov, the Chinese clinical Trial Registry, and the WHO International Clinical Trial Registry Platform will be searched for ongoing or unpublished trials.

5 Data collection and analysisSelection of studies

The search results will be imported into Endnote X9. After removing duplicate records, titles and abstracts will be checked to identify applicable studies by two independent reviewers (BH and TP). Then the full texts will be read for further selected according to the inclusion criteria. Excluded studies will be listed with reasons. Any disagreements will be resolved by discussion. The fFlow diagram of the study selection process is shown as the S1 Fig.

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6 Data extraction and management

Information will be extracted from the included studiesby two independent reviewers (BH and TP) using a data extraction form in excel, which included citation information (title, authors, source of publication, publication year, country, sponsor), study methods (design, sample size, method of randomization, allocation concealment, blinding), participant characteristics (age, diagnostic criteria), intervention details (type of acupuncture/control, treatment duration, treatment frequency), results (outcome measures, adverse events), and so on. Any discrepancy in the process of cross-checking will be resolved by consensus.

7 Risk-of-Bias Assessments

Two independent reviewers (YC, YW) will evaluatethe risk of bias using the following domains described in Cochrane's tool: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other bias. The risk of bias for each domain of ~~trials~~ RCTs will be classified as low risk, high risk, and unclear risk. Any disagreement will be resolved by consultation among the reviewers (LH, SW).

Meanwhile the methodological quality of each included trial will be classified as high quality, low quality, or moderate quality base on the following criteria according to Zhao et al[35]: (1) trial will be considered high quality when both randomization and allocation concealment are assessed as low risk of bias, and all other items are assessed as low or unclear risk of bias; (2) trial will be considered low quality if either randomization or allocation concealment is assessed as high risk of bias, regardless of the risk of other items; (3) trial will be considered moderate quality if they do not meet criteria for high or low risk.

8 Measures of treatment effect

RevMan V.5.3 will be used for data synthesis and analysis. For the outcomes are continuous data, the mean difference MD will be used to assess the treatment effect with 95% CIs if the studies used the same measurement scales. And the standard mean difference (SMD) will be used if different scales were used.

It is possible that individual studies may consist of multiple groups[36], such as different non-acupuncture control interventions eg, placebo, sham acupuncture, or no treatment. We will combine the groups from multiple arm studies into a single group according to the data merging methodology of subgroups before data synthesis.

9 Dealing with missing data

Original authors of the trial will be contacted for the relevant missing data. If missing data cannot be obtained, an imputation methodwill be used[31, 34]. We will conduct sensitivity analysis to assess the impact on the overall treatment effects. And the potential impact of the effect of missing data on the overall treatment effects of the review will be addressed in the discussion.

10 Assessment of heterogeneity

Statistical heterogeneity between different trials will be evaluated by the I^2 statistic with Q statistic test and visual inspection of forest plots. The I^2 statistic of 25%, 50%, and 75% indicates low, medium, and high heterogeneity, respectively[37]. I^2 value 50% indicates significant heterogeneity. When I^2 value 50%, clinical, methodological, or statistical heterogeneity will be assessed to find possible sources of heterogeneity firstly. If there is clinical or methodological heterogeneity, subgroup analysis or meta-regression analyses (with Stata V.15.0 software) will be used to explorethe source of heterogeneity. If there is statistical heterogeneity, data will be pooled based on random-effects model. And sensitivity analysis will also be performed to investigate the influence of every single study on the overall analyses.If there is significant heterogeneity among trials and cannot be explained, a descriptive analysis will be performed instead of a meta-analysis.

Assessment of reporting biases

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11 A funnel plot, as well as statistical tests (Egger test and Begg test by Stata V.15.0 software), will be used to assess reporting bias, if more than 10 trials are included for meta-analysis[38, 39].

12 Data synthesis

Data synthesis will be performed with the RevMan software (V.5.3) according to Cochrane Handbook for Systematic Reviews of Interventions if studies are sufficiently homogeneous. The Inverse Variance (IV) method and random-effects model with 95% CI will be used to calculate a pooled estimate of treatment effect since all the prespecified outcomes are continuous variables and a certain degree of heterogeneity is expected among trials that will be included.

However, if quantitative synthesis is not appropriate, a systematic narrative synthesis will be provided to summarize and explain the characteristics and findings of the included studies[31].

13 Subgroup analysis

We plan to conduct subgroup analysis based on different types of experimental intervention, control group, and different methodological quality. If there is still significant heterogeneity, the source of heterogeneity will be explored and trials will be further classified to perform subgroup analysis.

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15 Summary of evidence

The quality of evidence for all outcomes will be judged using the Grading of Recommendations Assessment, Development and Evaluation working group methodology[31]. It will be adjudicated as 'high', 'moderate', 'low' or 'very low' based on:risk of bias, inconsistency, indirectness, imprecision, publication bias, andadditional domains[40]. The results will be presented in 'summary of findings' tables.

16 Summary of evidence

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