INPLASY PROTOCOL

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Conflicts of interest:
The authors declare no conflict of interest.

Efficacy of coenzyme Q10 supplementation on glucose metabolism, lipid profiles and biomarkers of inflammation in women with polycystic ovary syndrome: a protocol for a systematic review and meta-analysis

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Review question / Objective: **The objective of the present meta-analysis will be to assess the efficacy and safety of coenzyme Q10 (CoQ10) in the treatment of women with polycystic ovary syndrome (PCOS).**
Condition being studied: **Polycystic ovary syndrome (PCOS) is one of the common gynecological endocrine system diseases. It is characterized by excessive androgen, rare or anovulation and polycystic ovary morphology. The incidence of PCOS in women of childbearing age is 6% ~ 20%. Coenzyme Q10(CoQ10) is a fat-soluble natural vitamin, which has a continuous oxidation-reduction cycle and is an effective antioxidant that can protect ovaries from oxidative damage. Studies have shown that dietary supplementation of CoQ10 can improve the metabolic and endocrine indexes of PCOS patients, as well as insulin resistance and endothelial cell function. PCOS is the most common endocrine disease in women of childbearing age. This study aims to systematically summarize and analyze the scientific literature on glucose metabolism index, Inflammatory factor and sex hormone level of PCOS patients treated with CoQ10, so as to provide a reference basis for clinical treatment.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 05 October 2020 and was last updated on 05 October 2020 (registration number INPLASY2020100013).

INTRODUCTION

Review question / Objective: **The objective of the present meta-analysis will be to assess the efficacy and safety of coenzyme Q10 (CoQ10) in the treatment of women with polycystic ovary syndrome (PCOS).**

Rationale: Currently, there is no systematic review of the efficacy and safety of CoQ10 therapy for women with PCOS, so this meta-analysis aims to explore it in a comprehensive manner. At the same time, we will provide high-quality evidence to help patients and clinicians choose better treatment strategy for PCOS.

Condition being studied: Polycystic ovary syndrome (PCOS) is one of the common gynecological endocrine system diseases. It is characterized by excessive androgen, rare or anovulation and polycystic ovary morphology. The incidence of PCOS in women of childbearing age is 6% ~ 20%. Coenzyme Q10(CoQ10) is a fat-soluble natural vitamin, which has a continuous oxidation-reduction cycle and is an effective antioxidant that can protect ovaries from oxidative damage. Studies have shown that dietary supplementation of CoQ10 can improve the metabolic and endocrine indexes of PCOS patients, as well as insulin resistance and endothelial cell function. PCOS is the most common endocrine disease in women of childbearing age. This study aims to systematically summarize and analyze the scientific literature on glucose metabolism index, Inflammatory factor and sex hormone level of PCOS patients treated with CoQ10, so as to provide a reference basis for clinical treatment.

METHODS

Search strategy: We will retrieve the following electronic databases from the built-in until March 2021: Cochrane Library, PubMed, EMBASE, and Web of Science, China National Knowledge Infrastructure (CNKI), Chinese Biomedical Literature Database (CBM), Clinical Trials. gov, Chinese Scientific Journal Database (VIP) and Wang-fang database. We adopt the combination of heading terms and free words as search strategy which decided by all the reviewers. We will apply a search method combining MeSH terms and free words. Search terms will be as follows: Polycystic ovary syndrome, PCOS, coenzyme Q10, CoQ10, randomized controlled trials, etc.

Participant or population: Adult women diagnosed with PCOS according to Rotterdam criteria in 2003. Adolescents (under 18) and postmenopausal women (over 50) will be excluded from the review.

Intervention: Intervention strategies include CoQ10 or CoQ10 combined with traditional Chinese medicine or western medicine or lifestyle interventions such as diet and exercise. CoQ10 can be used at any dose, frequency and duration.

Comparator: The control included blank, placebo, traditional Chinese medicine (TCM) treatment, western medicine treatment, or lifestyle intervention such as diet and exercise.

Study designs to be included: The search results will be limited to human studies only, and all included studies were randomized controlled trial (RCTs) without any language restrictions.

Eligibility criteria: Inclusion criteria :(1) Women diagnosed with polycystic ovary syndrome; (2) Intervention treatment was CoQ10 or CoQ10 combined with traditional Chinese medicine or western medicine or lifestyle interventions such as diet and exercise; (3) The control includes blank, placebo traditional Chinese medicine (TCM) treatment, western medicine treatment, or lifestyle intervention such as diet and exercise; (4) Randomized controlled trials were included, and the use of random or blind methods and published language were not restricted. Exclusion criteria :(1) adolescents (under 18 years of age), postmenopausal women (over 50 years of age), pregnant and lactation women;(2) Patients who had taken drugs affecting hormone levels, such as antioxidants, ovulation inducers or oral contraceptives, within three months before the experiment;(3) Other causes of menstrual disorders and androgen overload, such as congenital adrenal hyperplasia, androgen secreting tumors, Cushing's syndrome, etc.

Information sources: We will retrieve the following electronic databases from the built-in until March 2021: Cochrane Library,

PubMed, EMBASE, and Web of Science, China National Knowledge Infrastructure (CNKI), Chinese Biomedical Literature Database (CBM), Clinical Trials. gov, Chinese Scientific Journal Database (VIP) and Wang-fang database. We adopt the combination of heading terms and free words as search strategy which decided by all the reviewers. We will apply a search method combining MeSH terms and free words. Search terms will be as follows: Polycystic ovary syndrome, PCOS, coenzyme Q10, CoQ10, randomized controlled trials, etc. Meanwhile, we will retrieve other resources to complete the deficiencies of the electronic databases, primarily searching for the grey literature on the corresponding website. If necessary, we will contact the corresponding author of the relevant study by E-mail or telephone to obtain sufficient information.

Main outcome(s): Primary outcomes consist of menstrual cycle regulation, body mass index (BMI), homeostasis model assessment of insulin resistance (HOMA-IR), leutinizing hormone (LH), follicle stimulating hormone (FSH), testosterone (T), estradiol (E2), progesterone (P), serum sex hormone binding globulin (SHBG), dehydroepiandrosterone sulphate (DHEAS) and free androgen index (FAI).

Additional outcome(s): Secondary outcomes were Ferriman-Gallway score, acne score, waist to hip ratio (WHR), Total cholesterol (TC), triglyceride (TG), low-density lipoprotein (LDL), high-density lipoprotein (HDL), fasting plasma glucose (FPS), fasting insulin (FINS), insulin sensitivity index (ISI), interleukin-1 (IL-1), interleukin-8, tumor necrosis factor alpha (TNF-α), and adverse reactions, etc.

Data management: Endnote X9.1 software was used to manage the retrieved literature and delete duplicate literature. Two researchers trained in methodology independently selected the relevant literature. If there is a difference, a third investigator will decide. We will then extract the data into a Microsoft Excel spreadsheet.

Quality assessment / Risk of bias analysis: Two independent reviewers will use the Cochrane Risk Assessment tool to assess the methodological quality of individual studies. These include randomization, allocation concealment, blinding of participants and staff, blinding of outcome assessments, integrity of outcome data, selective reporting, and other biases. Each entry will be assigned a rating of low, high, or unknown risk. If both reviewers have different opinions, the third reviewer will give the decision.

Strategy of data synthesis: We will use the Review Manager version 5.3 software for data synthesis. Dichotomous data were represented by RR and continuous data were represented by MD or SMD. If there is no heterogeneity ($I2<50\%$, $P\geq0.1$), the fixed-effect model was used to synthesize the data. Otherwise ($I2\geq50\%$, $P<0.1$), a random effect model was used for analysis. If there is significant heterogeneity, subgroup analysis or sensitivity analysis will be performed to identify the cause.

Subgroup analysis: If there is significant heterogeneity in study results, we will conduct subgroup analysis according to different reasons. The heterogeneity was mainly manifested in race, age, gender, coenzyme Q10 dose and course of treatment, etc.

Sensibility analysis: Sensitivity analysis was used to evaluate the robustness of the main efficacy indicators. The method is to eliminate the low-quality studies one by one, merge the data, and evaluate the impact of sample size, statistical methods, study quality, and missing data on the analysis results.

Language: All included studies were randomized controlled trials (RCTs) without any language restrictions.

Country(ies) involved: China.

Keywords: coenzyme Q10, glucose metabolism, lipid profiles, inflammation, polycystic ovary syndrome, protocol.

Dissemination plans: The final results will be published in a peer-reviewed journal based on PRISMA guidelines.

Contributions of each author:

Author 1 - Min Liu - The author performed statistical analysis, drafted and revised the manuscript.
Author 2 - Hongqiu Zhu - The author read, provided feedback and approved the final manuscript.
Author 3 - Xiaodan Hu - The author will extract data, assess the risk of bias.
Author 4 - Ying Zhu - The author will extract data, assess the risk of bias.
Author 5 - Haiyan Chen - The authors performed statistical analysis.