INPLASY PROTOCOL

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None declared.

Effectiveness of integrated Chinese herbal medicine Shoutai Pill and Western medicine in the treatment of recurrent pregnancy loss: A protocol for systematic review and meta-analysis

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Review question / Objective: **We provide a protocol to evaluate the efficacy of integrated Shoutai Pill and Western medicine to update the evaluation for the best available and security treatment for recurrent pregnancy loss(RPL).**
Condition being studied: **Recurrent pregnancy loss (RPL) is a distinct disorder defined by two or more consecutive pregnancy failures before 20 gestational weeks infertile couples. The incidence of this disease accounts for about 1%-5% of women of reproductive age and seriously affects their physical and psychological health. At present, the known etiology of this disease mainly includes abnormal anatomic structures, genetic abnormality, endocrine disorders, prethrombotic status, abnormal immune function, infection, etc. Excluding the above factors, approximately 40-50% of RPL remain unexplained, known as unexplained recurrent pregnancy loss (URPL). At present, the main therapeutic methods of RPL are surgical therapy, preimplantation genetic diagnosis (PGD), hormone therapy, anti-infection therapy, anticoagulation, and immunoregulatory therapy, etc. However, there is no effective treatment has been identified for URPL. Therefore, we still need to investigate effective treatments to reduce pregnancy losses and maintain successful pregnancy preservation in these patients.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 17 October 2021 and was last updated on 17 October 2021 (registration number INPLASY2021100062).

INTRODUCTION

Review question / Objective: **We provide a protocol to evaluate the efficacy of integrated Shoutai Pill and Western medicine to update the evaluation for the best available and security treatment for recurrent pregnancy loss(RPL).**

Rationale: **Recurrent pregnancy loss (RPL) is one of the most common complications of early pregnancy in humans. There is no**

effective treatment available in Western medicine. Shoutai Pill, a famous classic herbal formula in traditional Chinese medicine (TCM), is widely available in China for treating RPL but still lacks evidence-based medical evidence, which the clinical efficacy is questioned.

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METHODS

Search strategy: We made the retrieval formula according to the PICOS strategy. The search terms for literature searching were as follows: ("recurrent spontaneous abortion" OR "recurrent miscarriage" OR "habitual abortion" OR "recurrent pregnancy loss" OR "hua tai") AND("shou tai pill" OR "shoutai pill" OR"shoutai wan" OR "shou tai wan") AND ("clinical research" OR "randomized controlled trial" OR "randomization" OR "RCT" OR "random grouping"). We also manually searched the reference lists of all identified articles for possible related studies to supplement the relevant literature.

Participant or population: The included patients should be confirmed pregnant by serum human chorionic gonadotropin (HCG) or ultrasound in the first trimester of pregnancy with a diagnosis history of RPL regardless of maternal age, gestational age, race, nationality, education, or economic status. Studies involving other diseases will be ruled out, such as infections, abnormal parental karyotypes, endocrine disorders, and anatomic abnormality.

Intervention: We included studies using integrated Shoutai Pill or modified Shoutai Pill and Western medicine according to syndrome differentiation as the experimental intervention, regardless of the dose, method of dosing, or duration of administration.

Comparator: Placebo or western medicine

Study designs to be included: Only the clinical randomized controlled trial (RCT) focused on integrated Shoutai Pill and Western medicine for RPL will be included. The language is not limited. Non-RCTs or animal experiments were excluded.

Eligibility criteria: If trials included other cointerventions such as acupuncture, acupoint application, and moxibustion, they were excluded.

Information sources: We will search the following electronic databases with no limitations on language and publication status for RCTs examining the effect of integrated Shoutai Pill and Western medicine for the treatment of RPL from inception to 31 October 2021. 1. PubMed 2. Embase 3. Cochrane Library 4. Web of Science (WOS) 5. China National Knowledge Infrastructure (CNKI) 6. Chinese BioMedical database (CBM) 7. Chinese Scientific Journals Database (VIP) 8. Wanfang database. We will search for relevant conference papers, journal references, and magazines without an electronic version, and we will search Chinese Clinical Trials Registry (ChiCTR) (http://www.chictr.org.cn/), ClinicalTrials.gov (https://clinicaltrials.gov),

and Google scholar (http://scholar.google.com).

Main outcome(s): The primary outcome is the incidence of early pregnancy loss.

Additional outcome(s): The second outcome included the incidence of live birth, TCM syndromes and symptoms, serum D-dimer level, serum fibrinogen, and incidence of maternal and perinatal adverse events during treatment.

Data management: For all studies included, two authors will independently extract relevant information separately: publication of the year, author, participants, randomized method, random concealment, sample size, number of cases in each group, age, gender, condition, diagnostic criteria, blindness, intervention, control, duration of intervention, outcomes, and methodologic characteristics.

Quality assessment / Risk of bias analysis: The two researchers will evaluate the treatment of included literature based on the "risk of bias assessment tool" of the Cochrane Handbook. The items to be evaluated include random sequence generation, random allocation concealment, blind method implementation, outcome assessor, result data integrity, selective outcome report, and other biases. If there are disagreements, it will be arbitrated by Zhenni Mu.

Strategy of data synthesis: Review Manager 5.4 software will be used for statistical analysis. Dichotomous data will be analyzed by using the risk ratio with a 95% confidence interval (CI) and continuous variables will be analyzed by using the mean difference with 95% CI.

Subgroup analysis: If there is significant heterogeneity in our study, we will perform a subgroup analysis based on the type of control group, including types of TCM syndrome, sample size, age, dosage form, and course of treatment.

Sensitivity analysis: If there are enough RCTs in our study, we will conduct sensitivity analysis based on methodologic quality, sample size, and missing data to assess the robustness of the meta-analysis.

Language: The language is not limited.

Country(ies) involved: China.

Keywords: Chinese herbal medicine, recurrent pregnancy loss, protocol, systematic review, Shoutai Pill.

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