INPLASY PROTOCOL

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None declared.

Efficacy of integrated traditional Chinese medicine and Western medicine in the treatment of female precocious puberty A protocol for systematic review and meta-analysis of randomized controlled trials

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Review question / Objective: **Compare the efficacy of integrated traditional Chinese medicine and Western medicine therapy and Western medicine alone for female precocious puberty.**
Eligibility criteria: **Literature inclusion criteria: All included RCTS required that the study subjects should be girls who had developed secondary sexual characteristics before the age of 8 years or had menarche before the age of 10 years. The treatment group was treated with integrated traditional Chinese and western medicine, and the control group was treated with western medicine alone (such as GnRH-a). Literature exclusion criteria (1) Non - RCT literature; (2) RCT of traditional Chinese medicine versus traditional Chinese medicine, and RCT of traditional Chinese medicine versus western medicine; (3) Precocious puberty caused by organic lesions or tumors or other diseases.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 14 October 2022 and was last updated on 14 October 2022 (registration number INPLASY2022100060).

INTRODUCTION

Review question / Objective: **Compare the efficacy of integrated traditional Chinese medicine and Western medicine therapy and Western medicine alone for female precocious puberty.**

Condition being studied: **Precocious puberty is a disease of growth and development, which is mainly characterized by a significant advance in the age of sexual development. It is generally believed that girls who show secondary sexual characteristics before the age of 8, boys before the age of 9, or**

girls who have signs of menstruation before the age of 10 can be clinically diagnosed as precocious puberty. Precocious puberty can be caused by physiological and psychological two exposures. At present, due to the imbalance of children's dietary structure, environmental pollution and social media, the incidence of precocious puberty in China is increasing year by year. According to some statistics, the incidence of precocious puberty in China has reached 1%, and it can reach 3% in some economically developed areas. The height of children with precocity may be higher than that of children of the same age in the early stage, but due to the rapid growth of bone, the epiphyseal fusion may be premature, and the adult stature may be shorter. In addition, the early development of female breasts and early menstruation will affect the daily life and increase the psychological pressure of children, especially for some children with immature intelligence and psychology.

GnRH-a is currently the first choice for the treatment of precocious puberty. In addition, Chinese pediatric clinicians are committed to the use of traditional Chinese medicine in the treatment of precocious puberty and have achieved certain results. The research on the treatment of precocious puberty with integrated traditional Chinese and western medicine is also deepening, but its clinical efficacy and safety are still unclear and lack of systematic evaluation. Combined with China's national conditions, we plan to conduct this systematic review and meta-analysis to compare the efficacy of integrated traditional Chinese medicine and Western medicine therapy and Western medicine alone for female precocious puberty.

METHODS

Participant or population: female meeting diagnostic criteria for precocious puberty.

Intervention: The experimental group was treated with integrated traditional Chinese and western medicine.

Comparator: The control group was treated with western medicine alone.

Study designs to be included: RCTs.

Eligibility criteria: Literature inclusion criteria: All included RCTS required that the study subjects should be girls who had developed secondary sexual characteristics before the age of 8 years or had menarche before the age of 10 years. The treatment group was treated with integrated traditional Chinese and western medicine, and the control group was treated with western medicine alone (such as GnRH-a). Literature exclusion criteria (1) Non - RCT literature; (2) RCT of traditional Chinese medicine versus traditional Chinese medicine, and RCT of traditional Chinese medicine versus western medicine; (3) Precocious puberty caused by organic lesions or tumors or other diseases.

Information sources: Electronic databases will be systematically searched for relevant reports from their inception to October 18,2022: PubMed,Wanfang,Chinese biomedical literature database(CBM),the Chongqing VIP Chinese Science and Technology Periodical(VIP),and China national knowledge infrastructure(CNKI). The retrieval type we will use: (precocious puberty OR sexual premature granule OR sexual precocious puberty OR sex precocity) AND (traditional Chinese medicine OR Chinese herbal medicine OR Chinese herbs OR Chinese medicinal herb OR Chinese medicine). We will search using a combination of subject terms and free words, with no language restrictions. In addition, we will also refer to the references of all relevant systematic review articles and conduct backtracking retrieval after reading the title to ensure that all the required literature is obtained.

Main outcome(s): The main outcomes of this study are the total effective rate and adverse reaction rate.

Additional outcome(s): (1) Height, weight, growth rate、 bone age and bone age index、 breast Tanner staging score.
(2) Imaging examination: mammary nucleus diameter, uterine volume, ovarian volume, and follicle size.
(3) Laboratory indicators: serum follicle-stimulating hormone (FSH), luteinizing hormone (LH), estradiol (E2) levels.

Quality assessment / Risk of bias analysis: We will evaluate the quality of the literature according to the risk of bias assessment tool recommended by the Cochrane Handbook of Systematic Reviews of interventions. The evaluation will be carried out strictly in accordance with the 7 aspects specified in the Cochrane Systematic Assessment Manual, and the methodological quality of the included studies will be judged on three levels of quality: "low risk", "high risk" and "undetermined risk". The evaluation will be conducted independently by 2 investigators, with a third party assisting in the determination if the results are inconsistent. The risk of bias will be expressed as a risk of bias summary and risk of bias graph respectively.

Strategy of data synthesis: Review Manager software version 5.3 will be used for meta-analysis. Relative risk (RR) with 95% confidence interval (CI) will be calculated for dichotomous data, and mean difference (MD) with 95% CI will be calculated for continuous data. P<.05 is a statistically significant difference for all analyses. The level of statistically significant heterogeneity will be set at P.1 and I2 50%, meta-analysis will adopt fixed-effect; If P .1 or I2 > 50%, meta-analysis will adopt random -effect. If the random - effect is used, we will perform subgroup analysis or sensitivity to clarify the source of heterogeneity. If quantitative synthesis is not possible, we will perform a descriptive analysis.

Subgroup analysis: We will explore the sources of heterogeneity through subgroup analysis based on age, gender, duration of disease, different interventions, duration of treatment, etc. A subgroup analysis will be performed to determine the potential heterogeneity and inconsistency clinically and statistically. A meta-regression analysis will be implemented to quantify the inter-subgroup difference and explore statistical significance.

Sensitivity analysis: To determine whether the decisions at each step are robust and impact the combined results, a sensitivity analysis will be conducted. Each time a study is excluded, a new meta-analysis is conducted separately to see if the effect size changes. We will also use this method to explore the sources of heterogeneity if there is significant heterogeneity in the studies.

Country(ies) involved: China.

Keywords: efficacy, integrated traditional Chinese medicine and Western medicine, precocious puberty, protocol, Western medicine.

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