INPLASY PROTOCOL

To cite: Jiang et al. Comparative efficacy and safety of Traditional Chinese Patent Medicine for Anxiety disorders in children or adolescence - A protocol for systematic review and network meta-analysis. Inplasy protocol 202080048. doi: 10.37766/inplasy2020.8.0048

Received: 11 August 2020

Published: 11 August 2020

Corresponding author:
Zhenyuan Jiang

J15562437830@163.com

Author Affiliation:
Shandong University of Traditional Chinese Medicine

Support: **Medicine project (2019-0108)**

Review Stage at time of this submission: **Preliminary searches.**

Conflicts of interest:
We declare no conflicts of interest.

Comparative efficacy and safety of Traditional Chinese Patent Medicine for Anxiety disorders in children or adolescence - A protocol for systematic review and network meta-analysis

Jiang, ZY[1]; Wang, JH[2]; Yu, XW[3]; LI, CC[4]; Shao, YZ[5]; Wang, ZL[6].

Review question / Objective: **Chinese patent medicines play an irreplaceable role in the treatment of this disease. At present, there is no comparison of the safety and effectiveness of various Chinese patent medicines curing anxiety in adolescents. So we take advantage of the method of network meta-analysis to systematically compare the efficacy of various Chinese patent medicines curing this disease.**

Condition being studied: **Anxiety is the appearance of inner fear and restlessness for no obvious reason, often accompanied by autonomic dysfunction, and the clinical symptoms are persistent mental stress or episodic panic. Adolescents and children are in a special period of physical and mental development. Due to their young age and poor mental endurance, they are vulnerable to adverse life events. Therefore, Anxiety symptoms are very common especially in adolescents and children. Relevant research shows that about 5%-20% of children and adolescents worldwide have anxiety disorders; A Norwegian survey on the stability, changes and incidence of anxiety symptom clusters among 13-16-year-olds found that the incidence of high-level anxiety was 8.2%. Children suffering from anxiety disorders are vulnerable to other mental problems and related physical symptoms in the later growth process than other children.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 11 August 2020 and was last updated on 11 August 2020 (registration number INPLASY202080048).

INTRODUCTION

Review question / Objective: **Chinese patent medicines play an irreplaceable role in the treatment of this disease. At present, there is no comparison of the safety and effectiveness of various Chinese patent medicines curing anxiety in adolescents.**

So we take advantage of the method of network meta-analysis to systematically compare the efficacy of various Chinese patent medicines curing this disease.

Condition being studied: Anxiety is the appearance of inner fear and restlessness for no obvious reason, often accompanied by autonomic dysfunction, and the clinical symptoms are persistent mental stress or episodic panic. Adolescents and children are in a special period of physical and mental development. Due to their young age and poor mental endurance, they are vulnerable to adverse life events, Therefore, Anxiety symptoms are very common especially in adolescents and children. Relevant research shows that about 5%-20% of children and adolescents worldwide have anxiety disorders; A Norwegian survey on the stability, changes and incidence of anxiety symptom clusters among 13-16-year-olds found that the incidence of high-level anxiety was 8.2%. Children suffering from anxiety disorders are vulnerable to other mental problems and related physical symptoms in the later growth process than other children.

METHODS

Participant or population: Adolescents and children diagnosed with anxiety disorders will be included. The diagnosis of anxiety will follow the Hamilton Anxiety Scale (HAMA) and Anxiety Self-Rating Scale (SAS).

Intervention: The experimental group was treated with traditional Chinese patent medicines combined with conventional Western medicine. Chinese patent medicines included Xiaoyao Pills, Wuling Capsules, Shugan Jieyu Capsules, and Xuefu Zhuyu Oral Liquid. The control group received Western medicine treatment, including oral medication or mental behavior therapy. RCTs that use two or more proprietary Chinese medicines or combined acupuncture, moxibustion and other traditional Chinese medicine methods are excluded.

Comparator: The control group received Western medicine treatment, including oral medication or mental behavior therapy.

Study designs to be included: We will include all RCTs using TCPM for the treatment of anxiety in adolescents and children.

Eligibility criteria: We include studies if they meet the following criteria: 1)Adolescents and children diagnosed with anxiety disorders according to the Hamilton Anxiety Scale (HAMA) and Anxiety Self-Rating Scale (SAS); 2) The experimental group was treated with traditional Chinese patent medicines combined with conventional Western medicine; 3) The control group received Western medicine treatment, including oral medication or mental behavior therapy; 4)study types are randomized controlled trials.

Information sources: We will search the Cochrane Library, PubMed, Embase, Clinical Trials, CNKI Database, VIP, Wanfang Database, and China Biomedical Database. The search strategy will be constructed in the form of Medical Subject Headings (MeSH) combine with keywords. We will also search ongoing trial registers in the trial registry websites.

Main outcome(s): According to the Hamilton Anxiety Scale, a 5-point scale of 0-4 is adopted. The main indicators are: total clinical effective rate, improvement of anxiety mood, insomnia remission rate, improvement of cognitive function; secondary indicators including relapse rate, plant Nervous system symptoms and the rate of improvement in behavior when talking to people. The included literature must cover one or more main indicators.

Quality assessment / Risk of bias analysis: The quality of each trial will be assessed by two researchers independently based on the Cochrane Risk of Bias Risk Assessment Tool recommended by Cochrane Handbook version 5.1.0. Use the decision words "high risk", "low risk", and "unclear risk" to evaluate the quality of the

input article in 7 aspects, including: whether the random sequence is sufficient; whether there is hidden allocation; whether blinding is used; whether the result data is complete; Whether there is selective reporting; whether there is publication bias; others.

Strategy of data synthesis: We will use Stata 14.0 software and Markov chain-Monte Carlo (MCMC) method to conduct Bayesian meta-analysis. Three Markov chains will be used for simulation, and the number of iterations will be set at 50,000 (the first 20,000 are used for annealing to eliminate the effect of the initial value, and the last 30,000 are used for sampling). The reticular diagram will be drawn by Stata 15.0 software to show the direct and indirect comparison between different interventions. The relative odds ratio (RoR) and its 95% confidence interval (CI) are calculated to evaluate the consistency of each closed loop. The lower limit of 95% CI is equal to 1, indicating good consistency. If RoR is close to 1, direct evidence and indirect evidence are consistent, and the fixed effect model is adopted for analysis. Otherwise, the closed-loop is considered to have obvious inconsistencies, and the random effect model is used for analysis. Dichotomous data will be represented by odds ratio (OR) and 95% CI, and $P < 0.05$ was considered statistically significant. WinBUGS 1.4.3 will be used to rank the efficacy of different interventions and the area under the curve will be recorded (the area under the curve will be expressed as a percentage, the larger the value, the better the effect).

Subgroup analysis: Subgroup analysis will be considered if sufficient data is available.

Sensibility analysis: Sensitivity analysis will be conducted with symptom improvement rate to evaluate clinical similarity and methodology of included studies to determine the reliability of the results of this study.

Country(ies) involved: China.

Keywords: Traditional Chinese patent medicine (TCPM), Anxiety disorders in childhood or adolescence, Network meta-analysis, Protocol.

Contributions of each author:

Author 1 - Zhenyuan Jiang - Author 1 drafted the manuscript.

Author 2 - Jianhao Wang - The author provided statistical expertise.

Author 3 - Xiaowen Yu - The author contributed to the development of the selection criteria, and the risk of bias assessment strategy.

Author 4 - ChuanCheng Li - The author read, provided feedback and approved the final manuscript.

Author 5 - Yuze Shao - The author read, provided feedback and approved the final manuscript.

Author 6 - Zhonglin Wang - The author read, provided feedback and approved the final manuscript.