INPLASY PROTOCOL

To cite: Jiang et al. Traditional Chinese medicine on treating Kawasaki disease: A systematic review and meta-analysis protocol. Inplasy protocol 2020120066. doi: 10.37766/inplasy2020.12.0066

Received: 12 December 2020

Published: 12 December 2020

Corresponding author:
Yong Jiang

jiangyong@pyztcm.com

Author Affiliation:
Chengdu University of Traditional Chinese Medicine, School of Basic Medical Sciences

Support: **NSFC Grant No.61801058.**

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

Conflicts of interest:
None.

Traditional Chinese medicine on treating Kawasaki disease: A systematic review and meta-analysis protocol

Jiang, YC[1]; Zhao, M[2]; Fang, ZP[3]; Chen, ZX[4]; Jiang, Y[5].

Review question / Objective: **The purpose of this study was to explore the efficacy and safety of traditional Chinese medicine in the treatment of KD.**
Condition being studied: **Kawasaki disease (KD), also known as cutaneous mucosal lymph node syndrome, is an acute, systemic vasculitis in infants under 5 years old. The etiology and pathogenesis of this disease are still unclear. The pathological change is systemic vasculitis. The main clinical manifestations were fever, conjunctival hyperemia, erythema multiforme and cervical lymph node enlargement. Severe cases can appear myocardial ischemia, myocardial infarction, and even sudden death. This disease makes the quality of life and life of children seriously threatened. In recent years, the incidence rate of this disease has been increasing year by year in many countries, especially in Asian countries, and has become the main cause of acquired heart disease in developed countries. At present, the treatment of KD is still dominated by conventional western medicine, and surgical treatment is taken when necessary, but the side effects of drugs are more and the success rate of operation is low. Many experiments have proved that traditional Chinese medicine has a good therapeutic effect on KD. This paper aims to evaluate the efficacy and safety of traditional Chinese medicine in the treatment of KD.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 12 December 2020 and was last updated on 12 December 2020 (registration number INPLASY2020120066).

INTRODUCTION

Review question / Objective: **The purpose of this study was to explore the efficacy and safety of traditional Chinese medicine in the treatment of KD.**

Condition being studied: **Kawasaki disease (KD), also known as cutaneous mucosal**

lymph node syndrome, is an acute, systemic vasculitis in infants under 5 years old. The etiology and pathogenesis of this disease are still unclear. The pathological change is systemic vasculitis. The main clinical manifestations were fever, conjunctival hyperemia, erythema multiforme and cervical lymph node enlargement. Severe cases can appear myocardial ischemia, myocardial infarction, and even sudden death. This disease makes the quality of life and life of children seriously threatened. In recent years, the incidence rate of this disease has been increasing year by year in many countries, especially in Asian countries, and has become the main cause of acquired heart disease in developed countries. At present, the treatment of KD is still dominated by conventional western medicine, and surgical treatment is taken when necessary, but the side effects of drugs are more and the success rate of operation is low. Many experiments have proved that traditional Chinese medicine has a good therapeutic effect on KD. This paper aims to evaluate the efficacy and safety of traditional Chinese medicine in the treatment of KD.

METHODS

Participant or population: Participants in the selected articles had no restrictions on gender, region, nationality, belief, race, origin and course of disease, except that the age was less than or equal to 5 years old.

Intervention: The experimental group was treated with traditional Chinese medicine on the basis of conventional western medicine. The use of traditional Chinese medicine is limited to prescription drugs and proprietary Chinese medicine. Prescription drugs require definite dosage, but there are no restrictions on drug composition, dosage form and dosage. The dosage forms can be soup, paste, pill or powder, etc. Acupuncture, massage and other traditional Chinese medicine treatment methods will be excluded.

Comparator: The control group was treated with conventional western medicine or surgery. Conventional western medicine generally includes oral aspirin, glucocorticoid or intravenous gamma globulin. Coronary artery bypass grafting, interventional catheterization and heart transplantation are commonly used in surgery. Specific drugs, doses and methods are not limited. The control group was excluded from traditional Chinese medicine treatment.

Study designs to be included: We will search all the studies that traditional Chinese medicine is used as the main intervention for KD. Non-randomized controlled trials (non-RCTs), quasirandomized controlled trials (qRCTs), summaries of personal experience, case reports, and crossover studies will be excluded. There are no language restrictions.

Eligibility criteria: Inclusion criteria for study selection:Types of studies. We will search all the studies that traditional Chinese medicine is used as the main intervention for KD. Non-randomized controlled trials (non-RCTs), quasi-randomized controlled trials (qRCTs), summaries of personal experience, case reports, and crossover studies will be excluded. There are no language restrictions. Types of participants. Participants in the selected articles had no restrictions on gender, region, nationality, belief, race, origin and course of disease, except that the age was less than or equal to 5 years old. Types of interventions. There is no requirement for the intervention course, the specific contents of the control group and the experimental group are as follows. Control interventional. The control group was treated with conventional western medicine or surgery. Conventional western medicine generally includes oral aspirin, glucocorticoid or intravenous gamma globulin. Coronary artery bypass grafting, interventional catheterization and heart transplantation are commonly used in surgery. Specific drugs, doses and methods are not limited. The control group was excluded from traditional Chinese

medicine treatment. 2.2.3.2.Experimental interventional. The experimental group was treated with traditional Chinese medicine on the basis of conventional western medicine. The use of traditional Chinese medicine is limited to prescription drugs and proprietary Chinese medicine. Prescription drugs require definite dosage, but there are no restrictions on drug composition, dosage form and dosage. The dosage forms can be soup, paste, pill or powder, etc. Acupuncture, massage and other traditional Chinese medicine treatment methods will be excluded.

Information sources: Ongoing experiments which have been registered on World Health Organization International Clinical Trials Registry Platform (ICTRP) or Chinese Clinical Trial Registry. Try to contact the researchers to inquire about the progress of the trial and provide the latest test data. As for grey literature, we will retrieve on the following websites: GreyNet International, SIGLE (The System for Information on Grey Literature in Europe), Open Gery, Gery Literature Report.

Main outcome(s): Primary outcomes. The main results were clinical symptoms (fever, conjunctival membrane congestion, lip and oral manifestations, hand and foot symptoms, skin manifestations and cervical lymph node enlargement) and changes in coronary artery (coronary aneurysm, coronary artery stenosis or expansion). Secondary outcomes. The secondary evaluation criteria were: blood routine (WBC count, ESR, CRP), immunological indexes (Ab, blood circulation immune complex), ECG, chest X-ray and echocardiography. More importantly, the incidence of adverse reactions in the trial will also be recorded.

Quality assessment / Risk of bias analysis: As for the risk of bias in the literature, two researchers will independently use the tool for assessing risk of bias recommended by Cochrane Handbook for Systematic Reviews of Interventions 5.1.0 (Cochrane Handbook 5.1.0¡ªPart 2: 8.5šC8.7) to assess the quality of the included literature and risk of bias. The evaluation includes: selection bias (random sequence generation and allocation concealment), performance bias (participants and personnel blind method), detection bias (blind method of result evaluation), loss bias (incomplete result data), reporting bias (selective result report) and other bias (other sources of bias) The assessors read the full text carefully to judge the risk level, which is divided into low risk, high risk and unknown risk. If the research reported in the literature is not detailed enough, the judgment is usually the deviation of "unknown risk". For example, this study uses a random number table for grouping, so the generation of random sequences will be expressed as "low risk". If there is any difference, we will consult a third reviewer to solve the problem.

Strategy of data synthesis: The meta-analysis in this review will use Revman 5.3 and stata13.0 software. Relative risk (RR) was used as the result index of the two categorical variables. The confidence interval (CI) of the mean difference (MD) or standardized mean difference (SMD) was 95% for the result indicators of continuous variables. Heterogeneity testing will be used for inclusion studies and tested by chi square test. When P¡Ý.10 and I2¡Ü50%,, there was no significant statistical heterogeneity or difference, then fixed effect model was used. If P < .10 and / or I2 > 50%, there is significant heterogeneity between studies, then the random effect model is used. Further analysis of the source of heterogeneity, if necessary, grouping analysis. There are differences in clinical and methodological aspects. Therefore, this paper will choose random effects model learning. Finally, funnel plot was drawn to evaluate publication bias.

Subgroup analysis: Subgroup analysis to explore the differences in age, gender, interventions, and course of disease/ treatment. We used funnel plots to identify whether there was small study bias if 10 or more studies were included. The asymmetry of funnel plots suggests the possibility of small study effects, and the results of analysis were explained cautiously.

Sensibility analysis: Sensitivity analysis will be performed to test the robustness of findings if there are sufficient studies included. The factors on effect are as follows: 1. Methodologic quality: analysis will be performed excluding studies of poor methodologic quality; 2. Published status: analysis will be performed excluding unpublished studies; 3. Sample size: analysis will be performed excluding small sample size studies; 4. Diagnostic criteria: analysis will be performed in studies of the same diagnostic criteria; 5. Race/ethnicity: analysis will be performed in studies of the same race or ethnicity.

Country(ies) involved: China.

Keywords: Kawasaki disease, protocol, systematic review, traditional Chinese medicine.

Contributions of each author:
Author 1 - Yuchang Jiang.
Author 2 - Mao Zhao.
Author 3 - Zhipeng Fan.
Author 4 - Zhaoxing Chen.
Author 5 - Yong Jiang.