INPLASY PROTOCOL

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Corresponding author:
Ziyi Hu

15170042768@163.com

Author Affiliation:
Jiangxi University of Traditional Chinese Medicine

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Conflicts of interest:
None.

Efficacy and safety of Guizhi-Shaoyao-Zhimu Decoction in the Treatment of Rheumatoid Arthritis: A protocol for systematic review and meta-analysis

Ye, J[1]; Li, RL[2]; Hu, ZY[3]; Zhang, P[4]; Liu, LJ[5].

Review question / Objective: **Rheumatoid arthritis (RA) is a significant public health problem associated with a substantial burden of functional disability. The Guizhi-Shaoyao-Zhimu decoction (GSZD), a traditional medicine, has been used in China for a long time to treat RA. This study aimed to systematically investigate the efficacy and safety of GSZD in the treatment of RA.**
Condition being studied: **Rheumatoid arthritis(RA) is a chronic autoimmune disease characterized by persistent synovitis, progressive joint injury, deformity, and even disability. The global prevalence of RA was 460 per 100,000 population . Fatigue, joint inflammation, and deformity are the main complications of rheumatoid arthritis, which can damage physical function, work efficiency, and activities of daily life, as well as overall emotional health. RA is associated with the enormous economic burden of individual patients, their families, and society. It is estimated that the total annual financial burden in Europe and the United States is 45.3 billion euros and 41.6 billion euros, respectively. RA is considered a multifactorial disease, where various genetic and environmental factors.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 30 December 2020 and was last updated on 30 December 2020 (registration number INPLASY2020120147).

INTRODUCTION

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METHODS

Participant or population: Patients who met the standard of RA diagnosis will be included.

Intervention: The treatment group was treated alone with GSZD, or GSZD combined with western medicine.

Comparator: The control group was treated with western medicine without GSZD.

Study designs to be included: Randomized controlled trials (RCTs) will be included in this review, regardless of whether the blind method and allocation concealment are used.

Eligibility criteria: 1. Inclusion criteria 1.1. Type of studies. Randomized controlled trials (RCTs) will be included in this review, regardless of whether the blind method and allocation concealment are used. 1.2. Type of participants. Patients who met the standard of RA diagnosis will be included. 1.3. Type of interventions. The treatment group was treated alone with GSZD, or GSZD combined with western medicine. 1.4. Type of comparators. The control group was treated with western medicine without GSZD. 1.5. Types of outcome measures. 1.5.1. Primary Outcome. The total effective rate and Visual Analogue Scale(VAS) score 1.5.2. Secondary outcomes. (1) Swollen joint count(SJC); (2) Morning stiffness time; (3) Inflammatory indicators (such as CRP and ESR); (4) Rheumatoid factor(RF); (5) Incidence of adverse events. 2.Exclusion criteria (1) Republished literature; (2) Research on insufficient data or lack of access to the full text; (3) Case report, Reviews, Basic research, nonRCT.

Information sources: We will search the following databases from the establishment to February 2021: PubMed, Embase, the Cochrane Library, China National Knowledge Infrastructure, the Chongqing VIP Chinese Science and Technology Periodical Database, Wanfang Database, and China Biomedical Literature Database.

Main outcome(s): The total effective rate and Visual Analogue Scale(VAS) score.

Additional outcome(s): (1) Swollen joint count(SJC); (2) Morning stiffness time; (3) Inflammatory indicators (such as CRP and ESR); (4) Rheumatoid factor(RF); (5) Incidence of adverse events.

Quality assessment / Risk of bias analysis: There may be biases in clinical trials from selecting and assigning subjects, implementing interventions, following up matters, and measuring and reporting findings at every stage. Thus, RCTs will be evaluated through the bias risk assessment tool (Cochrane Handbook for Systematic Reviews of Interventions). It includes the following six items: random sequence generation; allocation concealment; blinding of participants, caregivers, outcome assessors; incomplete outcome data; selective outcome reporting; and other bias. According to each study's results, the two researchers made 'low-risk' 'high-risk' or 'unclear risk' assessment of the above six items, independently. If the two researchers occur different opinions,

the objection will be decided by the third reviewer.

Strategy of data synthesis: RevMan5.3 software will conduct this meta-analysis. A random-effects model will be used to estimate the pooled primary and secondary outcomes. The forest plots will display the results of the meta-analysis. If the products are not suitable for meta-analysis, we will conduct a descriptive analysis. Only when more than 10 RCTs are included can we use funnel charts to assess publication bias.

Subgroup analysis: According to the treatment group with GSZD alone or combined with Western medicine, we will conduct a separate meta-analysis. We will carry out a subgroup analysis according to different dosage forms of GSZD, Chinese herbal compound, and extra western medicine in the control group.

Sensibility analysis: We will use the leave-one-out method for sensitivity analysis to judge the stability of outcome indicators.

Country(ies) involved: China.

Keywords: Rheumatoid Arthritis, Guizhi-Shaoyao-Zhimu Decoction, protocol, systematic review.

Contributions of each author:
Author 1 - Jing Ye - The author drafted the manuscript.
Author 2 - Renliang Li - The author provided statistical expertise.
Author 3 - Ziyi Hu - The author contributed to the development of the selection criteria, and the risk of bias assessment strategy.
Author 4 - Ping Zhang - The author read, provided feedback and approved the final manuscript.
Author 5 - Liangji Liu.