INPLASY PROTOCOL

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Review Stage at time of this submission: Preliminary searches.

Conflicts of interest: None.

Effect of down-regulation of serum MMP-3 levels by traditional Chinese medicine ingredients combined with methotrexate on the progression of bone injury in patients with rheumatoid arthritis: a protocol for a systematic review and meta-analysis

Sun, Y; Huang, YC; He, LS; Wang, ZZ; Chen, TT; Li, XP; Lin, KX; Chen, JY; Gao, YXX[4].

Review question / Objective: To evaluate the efficacy and safety of traditional Chinese medicine components combined with methotrexate in the treatment of bone injury in patients with rheumatoid arthritis.

Rationale: To evaluate the effect of down-regulation of serum MMP-3 level by traditional Chinese medicine ingredients combined with methotrexate on the progression of bone injury in patients with rheumatoid arthritis by serum MMP-3, ESR,CRP, CCPand RF.

INTRODUCTION

Review question / Objective: To evaluate the efficacy and safety of traditional Chinese medicine components combined with methotrexate in the treatment of bone injury in patients with rheumatoid arthritis.

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rheumatoid arthritis by serum MMP-3, ESR,CRP, CCPand RF.

Condition being studied: A large number of clinical studies have confirmed that after treatment with traditional Chinese medicine ingredients such as sinomenine, the serum matrix metalloproteinase（MMP-3） level of patients with rheumatoid arthritis shows a significant decrease, while MMP-3 can be involved in degrading bone matrix in humans, so in the progression of bone and joint injury in patients with rheumatoid arthritis (RA), serum MMP-3 can be used as an important biochemical marker. The traditional Chinese medicine ingredients commonly used in clinical practice include total glucosides of total glucosides of paeony, sinomenine, and tripterygium glycosides, which have the characteristics of DMARDs and non-steroidal anti-inflammatory drugs, while they can reduce the toxic side effects of methotrexate, and their combination with other drugs such as methotrexate and leflunomide has become an important regimen for the treatment of rheumatoid arthritis in clinical practice. Therefore, we designed this study protocol to evaluate the adjuvant effect of commonly used traditional Chinese medicine ingredients combined with methotrexate in the treatment of osteoarticular injury in rheumatoid arthritis.

METHODS

Search strategy: The search time was set from 2000 to September 2020 in this study. EMBASE database, Cochrane Library, Pubmed, Web of Science, Science direct, Chinese National Knowledge Infrastructure (CNKI), Chinese Biomedical CD-ROM Database (CBM), Chinese Science and Technology Journal Database (VIP), VIP database and Wanfang Database were used as search sources to select the traditional Chinese medicine ingredients that reduce serum MMP-3 and use methotrexate in the treatment of rheumatoid arthritis. Clinical randomized controlled trials were used, and inclusion

criteria and exclusion criteria were set for screening.

Participant or population: Inclusion: Rheumatoid arthritis patients of different ages can be included in the study, regardless of nationality, gender, race, occupation and education.Exclusion：Degenerative arthritis, Suppurative arthritis, Gouty arthritis, Ankylosing spondylitis, Reactive arthritis, Osteoarthritis, Synovitis.

Intervention: This study focuses on the clinical trial of traditional Chinese medicine combined with methotrexate in the treatment of rheumatoid arthritis. the results will provide advice and advice for clinicians. Therefore, the experimental group only received traditional Chinese medicine ingredients combined with methotrexate treatment, without any combination of other drugs and treatment, serum MMP-3 levels and disease activity indicators will be included. Comprehensive therapy can not evaluate the efficacy of traditional Chinese medicine ingredients combined with methotrexate will be excluded.

Comparator: Studies of control groups will be treated with treatment and other interventions?(e.g, Methotrexate monotherapy).

Study designs to be included: All relevant RCTs published in English and Chinese on traditional Chinese medicine combined with methotrexate in the treatment of rheumatoid arthritis can be included. Non-randomized controlled trials, reviews, case reports, experimental studies, expert experience and duplicate publications will be excluded.

Eligibility criteria: This study only selected the clinical control study of traditional Chinese medicine combined with methotrexate published in Chinese and English in the treatment of patients with rheumatoid arthritis. However, animal trials, reviews, case reports and non-randomized controlled trials were excluded.

Information sources: The details were adjusted according to the specific databases including CBM, CNKI, WF, VIP, Web of Science, Embase, PubMed, Cochrane Library, WHO ICTRP, ChiCTR, Science Direct , Clinical Trials, Grey Literature Database. No limitation on language or publication types restriction will be applied.

Main outcome(s): The ACR20 score and serum MMP-3 level in patients with rheumatoid arthritis will be evaluated as the main outcome.

Additional outcome(s): The improvement of joint BMD, CDAI and other clinical related symptoms were used as secondary evaluation indicators.

Data management: Two independent examiners will extract data from eligible studies and enter the following information in the data extraction table. When consensus cannot be reached by discussing the extraction of data, the decision will be made by the third author.

Quality assessment / Risk of bias analysis: Literature retrieval, screening and data extraction are carried out independently by two researchers through standardized qualification forms.If there is any disagreement, a third party should be consulted to assist in the judgment, and if there is any omission, the author should be contacted to supplement it.The general information of the selected articles will be extracted, including the first author, country, year of publication, study design, follow-up time, course of disease, sample size, detailed intervention measures, control treatment and so on.When the information of the article is sufficient or unclear, one of the authors will contact the original author by email or phone and ask for detailed supplementary information.

Strategy of data synthesis: RevMan5.3.5 will be used for all statistical analysis. Depending on the level of heterogeneity included in the study, a fixed effect model (I^2 50%) or a random effect model (I^2 50%)

was selected.Dichotomy data were analyzed with 95% CI with RR, and continuous data with 95% CI with MD/SMD. Meaningful heterogeneity will be explained by any additional assessment, including sensitivity analysis or subgroup analysis, depending on the data.

Subgroup analysis: If necessary, a subgroup analysis will be carried out according to different types of traditional Chinese medicine components, participant characteristics and result measurements.

Sensibility analysis: Sensitivity analysis is mainly used to evaluate the robustness of the primary outcome measures. The method is that removing the low-level quality study one by one and then merges the data to assess the impact of sample size, study quality, statistical method, and missing data on results of meta-analysis.

Language: English.

Country(ies) involved: China.

Keywords: Traditional Chinese medicine ingredients, Methotrexate, Rheumatoid arthritis(RA), MMP-3, Bone injury.

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