INPLASY PROTOCOL

To cite: Qu et al. Efficacy and safety of Chinese medicinal formula containing Cortex Phellodendri for gout: a protocol for systematic review and meta-analysis. Inplasy protocol 202250109. doi: 10.37766/inplasy2022.5.0109

Received: 17 May 2022

Published: 17 May 2022

Corresponding author:
Xiaohu Tang

h.tang0718@163.com

Author Affiliation:
Yunnan University of Chinese Medicine.

Support: **2018 No.131; 2022Y362; H-2019077.**

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

Conflicts of interest:
None declared.

Efficacy and safety of Chinese medicinal formula containing Cortex Phellodendri for gout: a protocol for systematic review and meta-analysis

Qu, PD[1]; Huang, J[2]; Wang, SQ[3]; Hu, Q[4]; Li, S[5]; Wang, W[6]; Peng, JY[7]; Tang, XH[8].

Review question / Objective: **The purpose of this study was to compare the efficacy and safety of Chinese medicinal formula containing Cortex Phellodendri and traditional western medicine in the treatment of gout.**
Information sources: **The following databases will be searched on the same day: Web of Science, PubMed, Cochrane Library, Embase, China National Knowledge Infrastructure (CNKI), Wanfang Data Knowledge Service Platform (Wanfang), Weipu Chinese Science and Technology Journal Full-text Database (VIP) and Chinese Biomedical Literature Database (CBM). The retrieval time is from the inception of the database to May 2022. At the same time, we will retrieve other resources to make up for the shortage of electronic database, mainly searching for the clinical trial registries and grey literature about Chinese herbal decoction containing Cortex Phellodendri for gout on the corresponding website. In addition, the relevant journals, in the reference literature, will be searched and tracked.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 17 May 2022 and was last updated on 20 May 2022 (registration number INPLASY202250109).

INTRODUCTION

Review question / Objective: **The purpose of this study was to compare the efficacy and safety of Chinese medicinal formula containing Cortex Phellodendri and traditional western medicine in the treatment of gout.**

Condition being studied: **Gout is caused by serum uric acid (SUA) exceeding its saturation in blood or tissue fluid, which leads to the formation and deposition of sodium urate crystals in local joints, and then induces local inflammatory response and tissue destruction. Hyperuricemia is a metabolic syndrome caused by purine**

metabolic disorder, which is characterized by SUA levels exceeding 420 μmol/L twice in different days. It is found that urate crystals can be deposited in the joints and surrounding tissues of patients with asymptomatic hyperuricemia with the wide application of advanced imaging methods such as high-frequency ultrasound and dual energy CT. These suggest that hyperuricemia and gout are a continuous pathological process. Gout and hyperuricemia are independent risk factors for chronic kidney disease, hypertension, cardiovascular and cerebrovascular diseases and diabetes, and independent predictors of premature death. Both of them have become another common metabolic disease after diabetes. In 2019, allopurinol, febuxostat, benzbromarone, colchicine and NSAIDs were recommended by the Chinese Society of Endocrinology, Chinese Medical Association as the first choice for the treatment of gout and / or hyperuricemia. Although the use of these drugs has indeed achieved certain curative effects, there are also some problems that cannot be ignored. In recent years, it has been gradually recognized all over the world that the advantages of traditional Chinese medicine in the prevention and treatment of gout. In traditional Chinese medicine, gout is closely related to dampness, heat, sputum, and stasis, which can be effectively treated by heat-clearing and dampness-dying medicine. Cortex Phellodendri, as a kind of heat-clearing and dampness-dying medicine, has been widely used in the treatment of gout in the form of combination. However, there is no systematic evaluation and meta-analysis on the efficacy and safety of Chinese medicinal formula containing Cortex Phellodendri in the treatment of gout.

METHODS

Participant or population: The patients are adults (aged≥18 years) and must meet internationally recognized diagnostic criteria for gout, such as the diagnostic criteria of American College of Rheumatology (ACR) in 1997, European League Against Rheumatism (EULAR) in 2011, Chinese diagnostic criteria, etc. There are no restrictions on the severity of symptoms, country of origin, educational background and gender. It will be excluded that pregnant women, patients with cancer, mental illness and severe heart, liver and kidney complications.

Intervention: For intervention group, it is included that using oral Chinese medicinal formula containing Cortex Phellodendri or in combination with conventional treatment of western medicine such as febuxostat, allopurinol, colchicine and so on. It will be excluded that oral Chinese medicine combined with external application of Chinese medicine, acupuncture or other therapies.

Comparator: For comparison group, it is contained that using conventional treatment of western medicine or placebo only.

Study designs to be included: Only clinical randomized controlled trials (RCTs) will be considered.

Eligibility criteria: The outcomes contain laboratory indicators and scale scores in the form of continuous data or dichotomous data, such as clinical efficacy, serum uric acid (SUA), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), white blood cell (WBC), adverse events (AEs), visual analogue scale (VAS), interleukin-1β (IL-1β) or tumor necrosis factor-α (TNF-α). The publication date of the report is limited to May 2022 and the language of the report is limited to Chinese and English. In addition, studies that cannot obtain abstract or full text, cannot provide accurate data and cannot provide consistent outcome indicators will be excluded.

Information sources: The following databases will be searched on the same day: Web of Science, PubMed, Cochrane Library, Embase, China National Knowledge Infrastructure (CNKI), Wanfang Data Knowledge Service Platform (Wanfang), Weipu Chinese Science and Technology Journal Full-text Database (VIP) and Chinese Biomedical Literature

Database (CBM). The retrieval time is from the inception of the database to May 2022. At the same time, we will retrieve other resources to make up for the shortage of electronic database, mainly searching for the clinical trial registries and grey literature about Chinese herbal decoction containing Cortex Phellodendri for gout on the corresponding website. In addition, the relevant journals, in the reference literature, will be searched and tracked.

Main outcome(s): The primary outcomes are composed of the clinical efficacy, serum uric acid (SUA), adverse events (AEs), interleukin-1β (IL-1β), tumor necrosis factor-α (TNF-α) and visual analogue scale (VAS).

Additional outcome(s): The secondary outcomes include erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and white blood cell (WBC).

Data management: Two reviewers will independently manage records and data throughout the review by using the same qualification evaluation form and the same version of document management software. Any differences will be discussed or made in consultation with the third reviewer to resolve.

Quality assessment / Risk of bias analysis: The risk of bias of qualified studies will be assessed according to Cochrane Collaboration risk-of-bias tool. Seven items will be evaluated into 3 levels which is low risk, high risk and unclear risk, including random sequence generation, allocation concealment, blind methods, blind assessment of results, incomplete result data, selective reports and other biases. The final assessment results will be exchanged and checked by 2 reviewers (Size Li and Wei Wang). The third author (Pengda Qu) will participate in the discussion and determine the final result when the results are inconsistent.

Strategy of data synthesis: Review Manager (RevMan) 5.3 software will be used for the meta-analysis. Mean difference (MD) with 95% confidence interval (95% CI) is used as the effect index for continuous data, and other types of data are combined for analysis after being converted to MD. Relevant risk (RR) with 95% confidence interval (95% CI) is used as the effect index for the dichotomous data, and other dichotomous data will be converted into RR. The heterogeneity of the included studies will be tested by chi square test and I^2 test for analysis. Heterogeneity will be evaluated by Chi-squared test and I^2 test. If there is no significant statistical heterogeneity ($P \geq .10$ and $I^2 < 50\%$), a fixed effect model will be used. Otherwise ($P < .10$ and $I^2 \geq 50\%$), the random effect model will be used.

Subgroup analysis: If there is significant statistical heterogeneity in meta-analysis, subgroup analysis will be conducted to investigate possible sources of heterogeneity, including treatment time, age, gender, study quality, etc.

Sensitivity analysis: For evaluating the stability of the combined results, sensitivity analysis will be done by excluding included studies one by one, reanalyzing the remaining studies, and comparing the differences between the excluded results and the original results.

Language: Chinese and English.

Country(ies) involved: China.

Keywords: Cortex Phellodendri, Chinese medicinal formula, gout, meta-analysis, protocol.

Contributions of each author:
Author 1 - Pengda Qu.
Author 2 - Jing Huang.
Author 3 - Shiqi Wang.
Author 4 - Qian Hu.
Author 5 - Size Li.
Author 6 - Wei Wang.
Author 7 - Jiangyun Peng.
Author 8 - Xiaohu Tang.