INPLASY PROTOCOL

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Conflicts of interest:
There is no conflict of interest.

Comparative efficacy and safety of traditional Chinese medicine for lipodermatosclerosis - A protocol for systematic review and network meta-analysis

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Review question / Objective: **To the best of our knowledge, as a clinical irreplaceable treatment method for LDS, TCM has not been Compared of the safety and effectiveness so far. As an extension of traditional meta-analysis, NMA can make full use of clinical data, and compare efficacy of more than three treatment methods. Therefore, we will use it to compare the safety and effectiveness of TCM for LDS.**
Information sources: **We will search Web of Science, PubMed, China BioMedical Literature (CBM), EMBASE, Cochrane Library, China National Knowledge Infrastructure (CNKI), and Wanfang database from January 2015 to September 2020, without restrictions for language, or publication status. In addition, we will search the ongoing trial registered on the International Clinical Trial Registration Platform.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 23 October 2020 and was last updated on 23 October 2020 (registration number INPLASY2020100090).

INTRODUCTION

Review question / Objective: **To the best of our knowledge, as a clinical irreplaceable treatment method for LDS, TCM has not been Compared of the safety and effectiveness so far. As an extension of traditional meta-analysis, NMA can make full use of clinical data, and compare efficacy of more than three treatment methods. Therefore, we will use it to compare the safety and effectiveness of TCM for LDS.**

Condition being studied: Lipodermatosclerosis (LDS), also known as Localized Scleroderma or Dermato-sclerosis, is first described in 2009 as the C4b stage of varicose veins of the lower extremities by Shiman M I. Today, it is generally believe that LDS is a part of the pathological progress in the progression of CVD. It is a non-bacterial inflammatory reaction of the skin and fat caused by the activation of leukocytes and inflammatory mediators under a background of venous hypertension. Its main clinical manifestations are erythema, induration, hyperpigmentation, and rough and thickened skin. It may also eventually lead to refractory ulcers, skin necrosis and cancer, which negatively affects the quality of life, increases psychological burden, and even enormously threaten patients' lives. CVD is more common in industrialized countries and generally occurs in the middle-aged and older women. A study shows that the incidence of CVD ranges from 10% to as high as 30%, and approximately 10% of CVD patients will develop LDS. Recent research showed that the incidence of LDS connected with ulceration is estimated to be approximately 13%, increasing annually. Another study based on skin disease types in the obese patients found that the incidence rate of LDS in obese population was 0.5%.

METHODS

Participant or population: The diagnosis of LDS will follow the guidelines for LDS, regardless of age, severity, duration, race or gender.

Intervention: The treatment group must have been treated with TCM on the basis of conventional treatment.

Comparator: The control group have been treated with western medicine.

Study designs to be included: We will collect all relevant RCTs of TCM for LDS published in Chinese or English.

Eligibility criteria: We will include the following criteria: 1) patients diagnosed with LDS; 2) patients in the experimental group were treated with traditional Chinese medicine on the basis of traditional western medicine. 3) The control group was treated with traditional western medicine. 4) The type of study was randomized controlled trial.

Information sources: We will search Web of Science, PubMed, China BioMedical Literature (CBM), EMBASE, Cochrane Library, China National Knowledge Infrastructure (CNKI), and Wanfang database from January 2015 to September 2020, without restrictions for language, or publication status.In addition, we will search the ongoing trial registered on the International Clinical Trial Registration Platform.

Main outcome(s): The outcomes of our interest are chronic venous insufficiency questionnaire(CIVIQ), venous clinical severity score(VCSS) and the level of transforming growth factor-β1(TGF-β1) in serum, and the details are as follows: 1. According to the method of CIVIQ, the scale of 1 to 5 was adopted. The assessment included social activities, mental and psychological, physical fitness and pain. 2. According to the VCSS, each score was divided into four grades: 0, 1, 2 and 3. The main indicators included pain, edema, varicose vein, pigmentation, inflammatory reaction, Scleroderma and ulcer. 3. the level of transforming growth factor-β1(TGF-β1) in serum. The literature included must cover one or more indicators above.

Quality assessment / Risk of bias analysis: According to the Cochrane Handbook, the two researchers independently evaluated the quality of the input articles from seven aspects. For each item, the correct use of method is low risk, unclear risk is unclear risk, and incorrect or unused method is high risk. Two researchers will completed and cross checked independently, If there is a disagreement, they will discuss with a third researcher.

Strategy of data synthesis: STATA14.0 software and MCMC method will be used

for Bayesian meta-analysis to extract data from included studies. We will use three Markov chains to simulate, and set the number of iterations to be 50000. STATA14.0 will be used to draw the reticular diagram to show the comparison of different interventions more vividly. We will calculate RoR and its corresponding 95% confidence interval (CI). The closer the lower limit of 95%CI is to 1, the better the consistency. When the RoR is about 1, fixed effect model will be adopted. Otherwise, random effect model will be adopted. We will use odds ratio (OR) and 95% CI (P<0.05) to express Dichotomous data, rank the efficacy of various interventions with WinBUGS1.4.3 and record the area under the curve.

Subgroup analysis: If there is enough data, we will consider grouping analysis.

Sensibility analysis: Sensitivity analysis can also be understood as robustness analysis, which is an important method to evaluate the robustness and reliability of the combined results of meta-analysis. the common sensitivity analysis method is exclude each study one by one and then merge the effects. After excluding one article, if the heterogeneity changes, we think that the study may be the source of it.

Country(ies) involved: China.

Keywords: Lipodermatosclerosis, traditional Chinese medicine, network meta-analysis, protocol

Contributions of each author:
Author 1 - Mengmeng Du - The author is responsible for data collection, statistical analysis and drafting.
Author 2 - Yudong Zhang - The author is responsible for fund support.
Author 3 - Xiaohua Shi - The author is responsible for data collection, statistical analysis and drafting.
Author 4 - Ming Liu - The author is responsible for the information feedback and the final manuscript.