INPLASY PROTOCOL

Corresponding author:
Hongqiang An

Wujianlin201801@163.com

Author Affiliation:
Shandong University of Traditional Chinese Medicine

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We declare no conflicts of interest.

Comparison of efficacy and safety of Chinese patent medicine in the treatment of postmenopausal osteoporosis — A protocol for systematic review and network meta-analysis

An, H[1]; Zhao, J[2]; Wang, J[3]; Li, C[4]; Jiang, Z[5]; Yao, J[6]; Zhang, X[7]; Wu, J[8].

Review question / Objective: Postmenopausal osteoporosis (PMOP) is the focus and difficult problem in the world at present, and we found that Chinese patent medicine(CPM) shown a more miraculous effect. Many kinds of Chinese patent medicine have been proved to be effective in the treatment of this disease, but it is still unclear which kind of Chinese patent medicine has the best effect. Therefore, we propose a network meta-analysis(NMA) protocol to observe the efficacy of various CPM for this disease and provide guidance for clinical practice.

INTRODUCTION

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efficacy of various CPM for this disease and provide guidance for clinical practice.

Condition being studied: As a kind of primary osteoporosis, postmenopausal osteoporosis（PMOP）is caused by the decrease of ovarian function and the rapid decrease of plasma estrogen level in postmenopausal women, which leads to the decrease of bone mass ,thus leading to the rapid increase of the incidence of osteoporosis. PMOP is a major health risk for older persons. It often results in high morbidity and mortality rates for brittle fractures, as well as increased socio-economic costs. With the advent of aging society and people's life expectancy, the cost of fracture care caused by osteoporosis will increase the medical burden of the whole society. According to statistics, there are 10 million cases of bone fracture caused by osteoporosis worldwide every year, and two-thirds of them are women. Organizations such as the IOF are also studying the epidemiology of osteoporosis and fractures. Research now suggests that people with high rates of osteoporosis are moving from Europe to Asia. The number of fractures in elderly patients in Asia is expected to increase eightfold between 2000 and 2050. In addition, 50 percent of hip fractures worldwide occur in Asia.

METHODS

Participant or population: According to the PMOP Diagnostic Criteria issued by the American Association of Clinical Endocrinologists (AACE), we will include patients diagnosed with PMOP.

Intervention: The treatment group was treated with a CPM or CPM combined with conventional western medicine(CWM).

Comparator: The control group was treated with CWM only.

Study designs to be included: We will include published randomized controlled trials (RCTS) in China and internationally.

Whether blind or not, and language is limited to Chinese and English.

Eligibility criteria: Patients diagnosed with PMOP, regardless of age, race, ethnicity, primary disease or Clinical stage.

Information sources: We will use computers to search Embase, Pubmed, Cochrane Library, Web of Science, CNKI, WanFang, VIP, CBM databases, and the ClinicalTrials.gov clinical registration system to collect RCT for PMOP.

Main outcome(s): Main outcome indicators: new fracture; Quality of life; Severe side effects; Death caused directly or indirectly.

Additional outcome(s): Additional outcome : bone mineral density(BMD), estradiol, serum calcium, serum phosphorus, serum alkaline phosphatase, bone glaprotein, tartrate-resistant acid phosphatase, bone alkaline phosphatase, pain degree ,Clinical efficiency.

Quality assessment / Risk of bias analysis: We will evaluate the quality of the included literature using the bias risk assessment tool recommended by Cochrane System Reviewers' Manual 5.3. Including: Random method; Allocation hiding; Blind the researchers and participants; Blind the research results; The integrity of the result data; Selective reporting of research results; Whether there are other sources of bias. Each evaluation result will be divided into low risk of bias, high risk of bias and unclear.

Strategy of data synthesis: Counting data will adopt odds ratio (OR), and continuous variable data will adopt either mean difference (MD) or standardized mean difference (SMD). As treatment effects, both are represented as the effect value and its 95% Confidence interval (CI). RevMan 5.3 software will be used for bias evaluation, and Stata 16.0 software will be used for heterogeneity analysis and evidence diagrams for NMA. We will determine the size of heterogeneity quantitatively by I 2. When I 2 < 50% and P > 0.1, we will assume that there is no

statistical heterogeneity in each study, and we will use the fixed-effect model for Meta-analysis. When I $2\geq50\%$ and $P\leq 0.1$, statistical heterogeneity among studies will be considered. At this time, the source of heterogeneity needs to be further analyzed. After excluding the clinical heterogeneity factors, the random-effect model is used for Meta-analysis. If clinical heterogeneity exists, we will use subgroup analysis and meta-regression analysis. If the source of heterogeneity is unknown, meta-analysis is abandoned and descriptive analysis is adopted. Sensitivity analysis will be used to determine the robustness of the results.

Subgroup analysis: If the evidence is sufficient, subgroup analysis will be considered to seek the source of heterogeneity.

Sensibility analysis: Then the sensitivity analysis will be performed by excluding every article. If the heterogeneity changes, the excluded article may be the reason for the heterogeneity.

Country(ies) involved: China.

Keywords: Osteoporosis; Postmenopausal; Chinese patent drugs; network meta-analysis; protocol.

Contributions of each author:
Author 1 - Hongqiang An.
Author 2 - Jifeng Zhao.
Author 3 - Jiahao Wang.
Author 4 - Chuancheng Li.
Author 5 - Zhenyuan Jiang.
Author 6 - Junpeng Yao.
Author 7 - Xiao Zhang.
Author 8 - Jianlin Wu.