INPLASY PROTOCOL

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Anti-osteoporosis Effects and Possible Mechanisms of the Total Flavonoids of Epimedium in Rat Models of Postmenopausal Osteoporosis: A Systematic Review and Meta-Analysis

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Review question / Objective: Postmenopausal osteoporosis (PMOP) is a common disease affecting the health of middle-aged and elderly women, so it is very important to prevent it in advance. Epimedium is widely used to treat osteoporosis (OP) in China. We present here a systematic assessment of the effects of the total flavonoids of epimedium(TFE) on animal models from current studies. The possible mechanisms of TEF in the treatment of osteoporosis were reviewed. P:postmenopausal rat with osteoporosis; I:the total flavonoids of epimedium; C:placebo; O:bone mineral density; S: rct.

Eligibility criteria: Inclusion criteria:We considered studies to be eligible if they were randomised controlled studies;if they used ovariectomized rats for the experiment; and if they have clearly defined outcome indicator and easily extracted outcome data.

INTRODUCTION

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epimedium; C:placebo; O:bone mineral density; S: rct.

Condition being studied: Osteoporosis (OP)
is a common systemic bone disease, which is characterized by decreased bone mass, damage of bone tissue microstructure, increased bone brittleness and prone to fracture[1].
Osteoporosis is mainly divided into primary and secondary types.Primary osteoporosis includes postmenopausal osteoporosis (type I), geriatric osteoporosis (type II) and idiopathic osteoporosis (including adolescent). Secondary osteoporosis is more common in men and premenopausal women [2,3]. According to the White paper on Osteoporosis in China published by the International Osteoporosis Foundation, 210 million people in China have bone mass below the normal standard and are at risk of osteoporosis [4]. OP not only has seriously affected the daily life of patients and greatly increased the social burden,but also will become an important public health and social problem in China. According to statistics, there are more than 70 million patients with OP in China.OP has become the fourth most common chronic disease in China. Among people aged 50-60 years, the prevalence of OP was 20.7% in women. The prevalence of OP is significantly higher in people over 60 years old.The number of female patients in PMOP is particularly prominent [5].The treatments that have been proven to treat OP include diet modification, rehabilitation exercise and medication.But so far, there is no fully curative treatment for osteoporosis. Therefore, in the search for effective drugs to treat osteoporosis, much attention has been focused on traditional Chinese medicine.

METHODS

Search strategy: The search algorithm was adapted according to the different database requirements. For instance, the retrieval strategy for Web of Science was (((TS=("the total flavonoids of epimedium")) OR TS=(yinyanghuozonghuangtong)) OR TS=("yin yang huo zong huang tong")) AND TS=(osteoporosis).

Participant or population: postmenopausal rat with osteoporosis.

Intervention: The total flavonoids of epimedium.

Comparator: Placebo.

Study designs to be included: RCT.

Eligibility criteria: Inclusion criteria:We considered studies to be eligible if they were randomised controlled studies; if they used ovariectomized rats for the experiment; and if they have clearly defined outcome indicator and easily extracted outcome data.

Information sources: PubMed, Web of Science, Cochrane Library, Embase, Elsevier, Google Scholar, SpringerLink, China National Knowledge Infrastructure (CNKI), Chinese Biomedical Disc, Chinese VIP Database, and Wanfang Database.

Main outcome(s): Bone mineral density.

Data management: We used the PRISMA flow diagramt to chose the included studies.Than we imported the results of literature search into Endnote 20 software.The authors independently reviewed the studies to exclude those that met the exclusion criteria.First, we excluded duplicate references. Second,studies with titles and abstracts that did not in conformity with the inclusion criteria were excluded.Third, we downloaded the full text of the studies and read the included studies, and then excluded literature that did not in conformity with inclusion criteria.Any disagreement between the above two authors has been sent to a third independent author for discussion.

Quality assessment / Risk of bias analysis: We used SYRCLE's RoB tool to assess the quality of the included literatures. SYRCLE's RoB tool for assessing the risk of bias in animal experiments includes 10 items.According to the tool,"yes" mean low risk of bias; "no"mean high risk of bias; "unclear"mean details on correctly

assessing the risk of bias are poorly reported.

Strategy of data synthesis: Review Manager 5.4 statistical software was used for statistical analysis. For continuous variable data, 95% confidence intervals (CIs) were calculated for each effect size. If the source of heterogeneity needs to be explored, subgroup analysis will be used.Heterogeneity among the studies was evaluated using the heterogeneity index I2. If the included studies were homogenous (I2 50%),the random effect model (REM) was used to analyze the heterogeneity of sources and data distribution. When the result is the inverted funnel symmetric distribution on the ordinate, there is no bias. When the results are inverted funnel asymmetry distribution on the ordinate, there is publication bias. To ensure the stability and accuracy of the meta-analysis results. $P < 0.05$ was considered statistically significant.

Subgroup analysis: We performed several subgroup analyses to test interactions according to daily dose equivalent,number of rats,the species of rat(SD rat and Wistar rat)and age of rats.

Sensitivity analysis: Sensitivity analyses were assessed by removing each study separately and re-analyzing the data.

Country(ies) involved: China (Nanjing University of Chinese Medicine).

Keywords: Total flavone of epimedium; Bone mineral density; Postmenopausal osteoporosis;Animal experiments;Meta-analysis.

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