

# INPLASY PROTOCOL

To cite: Wang et al. External Application of traditional Chinese Medicine in Combination with Three-Step Analgesics for Cancer-induced Bone Pain: A Systematic Review and Meta-analysis. Inplasy protocol 202180004. doi: 10.37766/inplasy2021.8.0004

Received: 02 August 2021

Published: 02 August 2021

**Corresponding author:**  
Wang Fei

1158251432@qq.com

**Author Affiliation:**  
Hunan University of Chinese Medicine

**Support:** 2018SK2127.

**Review Stage at time of this submission:** Data analysis.

**Conflicts of interest:**  
None declared.

## INTRODUCTION

**Review question / Objective:** Cancer-induced bone pain (CIBP) is one major symptom of primary and metastatic bone tumors, and the prolonged painful state will affect patients physically and psychologically to varying degrees. External application of traditional Chinese medicine (EA-TCM) has the characteristics

## External Application of traditional Chinese Medicine in Combination with Three-Step Analgesics for Cancer-induced Bone Pain: A Systematic Review and Meta-analysis

Wang, F<sup>1</sup>; Lai, GH<sup>2</sup>; Zhou, F<sup>3</sup>; Nie, DR<sup>4</sup>; Cheng, XT<sup>5</sup>; Wang, Y<sup>6</sup>; Cao, JX<sup>7</sup>.

**Review question / Objective:** Cancer-induced bone pain (CIBP) is one major symptom of primary and metastatic bone tumors, and the prolonged painful state will affect patients physically and psychologically to varying degrees. External application of traditional Chinese medicine (EA-TCM) has the characteristics of simple operation, rapid effect, green and safe, and has been widely used as an adjuvant therapy for CIBP in clinic. There is no systematic review and meta-analysis to assess the efficacy of EA-TCM combined with three-step analgesic drugs for CIBP. Thus, this study aimed to summarize the effect of EA-TCM combined with three-step analgesic drugs for CIBP.

**Information sources:** EMBASE, PubMed, Cochrane Library, Web of Science, Scopus, Chinese National Knowledge Infrastructure (CNKI), China Science and Technology Journal Database (VIP), Chinese Biomedical Literature Service System (SinoMed) and WanFang database

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 02 August 2021 and was last updated on 06 May 2024 (registration number INPLASY202180004).

of simple operation, rapid effect, green and safe, and has been widely used as an adjuvant therapy for CIBP in clinic. There is no systematic review and meta-analysis to assess the efficacy of EA-TCM combined with three-step analgesic drugs for CIBP. Thus, this study aimed to summarize the effect of EA-TCM combined with three-step analgesic drugs for CIBP.

**Condition being studied:** Cancer-induced bone pain.

## METHODS

**Search Strategy:** Two investigators independently searched databases EMBASE, Web of Science, PubMed, Scopus, Cochrane Library, Chinese National Knowledge Infrastructure (CNKI), Chinese Biomedical Literature Service System (SinoMed), China Science and Technology Journal Database (VIP) and WanFang from their inception to 31 December, 2023, using the MeSH Terms ("external treatment" OR "external use" OR "external application" OR "powder" OR "paste" OR "cream" OR "patch" OR "traditional Chinese medicine" OR "Chinese medicine" OR "TCM") AND ("bone cancer pain" OR "cancer induced bone pain" OR "bone metastatic cancer pain" OR "bone metastatic pain") AND ("clinical" OR "random").

**Participant or population:** CIBP patients.

**Intervention:** The treatment group was treated with EA-TCM in combination with three-step analgesic drugs.

**Comparator:** The control group were treated by three-step analgesic drugs alone or in combination with placebo externally.

**Study designs to be included:** RCT.

**Eligibility criteria:** Types of Participants. patients with definite primary lesions, and bone metastases confirmed by imaging examination and presenting with symptoms of pain could be enrolled in this review. The study did not place limits on age, gender, or nationality.

Types of interventions. The treatment group was treated with EA-TCM in combination with three-step analgesic drugs, while patients in the control group were treated by three-step analgesic drugs alone or in combination with placebo externally. There is no limitation on the dosage form of EA-TCM, which can be powder, paste, or patch, etc..

Types of Outcome measures. Included studies had clear efficacy evaluation criteria with at least one of the following clinical indicators, such as pain relief rate, pain intensity, frequency of breakthrough pain, analgesic duration, quality of life, or incidence of side effects (including nausea, vomiting, constipation, drowsiness).

Types of studies. Included in this study were randomized controlled trials (RCTs) of EA-TCM in combination with three-step analgesic drugs for the treatment of CIBP.

**Information sources:** EMBASE, PubMed, Cochrane Library, Web of Science, Scopus, Chinese National Knowledge Infrastructure (CNKI), China Science and Technology Journal Database (VIP), Chinese Biomedical Literature Service System (SinoMed) and WanFang database.

**Main outcome(s):** Pain relief rate, pain intensity, frequency of breakthrough pain, analgesic duration, quality of life, or incidence of side effects (including nausea, vomiting, constipation, drowsiness).

**Quality assessment / Risk of bias analysis:** Two authors assessed the quality of included studies according to the grading of recommendation assessment, development and evaluation (GRADE) guidelines./Two investigators separately assessed the quality of included studies according to the Cochrane risk of bias tool, as "low risk," "unclear risk," and "high risk" based on six domains.

**Strategy of data synthesis:** The data analysis of dichotomous and continuous outcomes was performed with the Review Manager Software 5.4.1 (Nordic Cochran Center, Copenhagen, Denmark). Continuous outcomes were evaluated as weighted mean difference (WMD) or standardized mean difference (SMD) with 95% confidence intervals (CIs). Dichotomous outcomes were evaluated as risk ratio (RR) with 95% CIs. The heterogeneity was evaluated using inconsistency index (I<sup>2</sup>) statistics. We used a fixed effect model when the heterogeneity was not statistically significant ( $p \geq 0.05$  and  $I^2 < 50\%$ ). We used

---

a random effect model when the heterogeneity was high ( $I^2 \geq 50\%$  or  $p < 0.05$ ). A  $p$  value  $0.05$ .

**Subgroup analysis:** Subgroup analysis analyzed the source of heterogeneity.

**Sensitivity analysis:** Sensitivity analysis analyzed the source of heterogeneity.

**Country(ies) involved:** China.

**Keywords:** External application of traditional Chinese medicine, three-step analgesic drug, cancer-induced bone pain, systematic review, meta-analysis.

**Contributions of each author:**

Autor 1-Wang Fei.

Email:20163314@stu.hnucm.edu.cn

Author 2-Lai Guihua.

Email:20173249@stu.hnucm.edu.cn

Author 3-Zhou Fang.

Email:20192004@stu.hnucm.edu.cn

Author 4-Nie Duorui.

Email:ndrise@hotmail.com

Author 5-Cheng Xiongtao.

Email:kevincheng@stu.hnucm.edu.cn

Author 6-Wang Yue.

Email:yy1573221820@outlook.com

Author 7-Cao Jianxiong.

Email:003998@hnucm.edu.cn