INPLASY PROTOCOL

To cite: Xie et al. The efficacy and safety of Xiaochaihu decoction adjuvant chemotherapy for breast cancer: a systematic review and meta-analysis protocol. Inplasy protocol 202180033. doi: 10.37766/inplasy2021.8.0033

Received: 09 August 2021

Published: 09 August 2021

Corresponding author:
Li Luo

3533075590@qq.com

Author Affiliation:
Guizhou University of Traditional Chinese Medicine; The First Affiliated Hospital of Guizhou University of Chinese Medicine; Guihang Guiyang Hospital.

Support: **No:GZS [2016]08; No. [2016]4032.**

Review Stage at time of this submission: **The review has not yet started.**

Conflicts of interest:
None declared.

The efficacy and safety of Xiaochaihu decoction adjuvant chemotherapy for breast cancer: a systematic review and meta-analysis protocol

Xie, Z[1]; Zhu, X[2]; Liu, J[3]; Chen, J[4]; Ke, L[5]; Tian, S[6]; Luo, L[7]; Yang, Z[8]; Tang, D[9].

Review question / Objective: **Is Xiaochaihu decoction effective and safe in adjuvant chemotherapy treatment of breast cancer?**
Condition being studied: **Breast cancer(BRCA).**
Information sources: **Literature databases: CNKI (China National Knowledge Infrastructure), VIP (Chinese Scientific Journals Database), Wanfang database, Sinomed, PubMed, EMBASE, Cochrane library and Web of Science; Trial registry: Clinicaltrials.gov, and Chinese Clinical Trial Registry; Source of grey literature: reference lists of relevant reviews.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 09 August 2021 and was last updated on 09 August 2021 (registration number INPLASY202180033).

INTRODUCTION

Review question / Objective: **Is Xiaochaihu decoction effective and safe in adjuvant chemotherapy treatment of breast cancer?**

Rationale: **Breast cancer(BRCA) is a malignant tumor occurring in the lobular and ductal epithelium of the breast , which ranked first among female malignant tumors , and mainly concentrated in women aged 40 to 60 years. BRCA is a**

refractory malignancy that causes death in women . At present, intravenous chemotherapy is still the main measures for the treatment of BRCA, while exert anticancer effect to produce certain damage to normal tissue organs, some patients unable to bear the side effects of chemotherapy drugs cause to give up treatment, even by immune suppression and died of secondary infection, therefore, explore new anticancer drugs has important clinical significance. In recent years, Chinese herbal medicine has been used and studied by many medical workers because of its obvious anticancer effect and few adverse reactions. Xiaochaihu decoction (XD) was compound prescription consisting of Chaihu, Huangqin, Banxia, Shengjiang, Renshen, Dazao, and Gancao.Many studies have demonstrated, Xiaochaihu decoction adjuvant chemotherapy can effectively inhibit the growth of tumor, promote the transformation of lymphocytes, induce cells to further secrete interferon, increase the levels of CD3+, CD4+, IgG, IgA, IgM, inhibit the expression of CD8 +, reduce the secretion and synthesis of tumor markers CEA, CA125, CA153, IGF-1, sEC and inhibit the formation of tumor blood vessels of VEGFA, VEGFB, with good safety. But, there is no systematic review and meta-analysis to evaluate its efficacy and safety at present. Therefore, the purpose of this study is to explore the efficacy and safety of Xiaochaihu decoction as adjuvant chemotherapy treatment for BRCA by pooling the current randomized controlled trials.

Condition being studied: Breast cancer (BRCA).

METHODS

Search strategy: We will systematically search 8 major databases including CNKI (China National Knowledge Infrastructure), VIP (Chinese Scientific Journals Database), Wanfang database, Sinomed, PubMed, EMBASE, Cochrane library and Web of Science and collect the RCTs of Xiaochaihu decocotion adjuvant chemotherapy treatment of BRCA. The time range of the search will be from the database to July 31, 2021. We will use a combination of medical subject words and free words to search for terms such as "Xiaochaihu decocotion", "Xiaochaihu decocotion adjuvant chemotherapy", "Xiaochaihu decocotion chemotherapy", and "breast cancer", "breast tumor", "breast oncology", "breast carcinoma", "breast neoplasm", "breast malignant neoplasm", "breast malignant tumor", a search strategy in PubMed was listed in table1. For including more studies, we will also search the two trial registration platforms ClinicalTrials.gov and Chinese Clinic Trials.gov, as well as references from related reviews.

Participant or population: Patients with BRCA, without restrictions on age, gender, course of disease and severity.

Intervention: Xiaochaihu decoction adjuvant chemotherapy, Xiaochaihu decoction, 2 ~ 3 times a day.

Comparator: The comparator should be the same chemotherapy regimens as the intervention group

Study designs to be included: Randomized controlled trials (RCTs).

Eligibility criteria: We will include patients according to the diagnostic criteria of Guidelines and norms for diagnosis and treatment of breast cancer of Chinese anticancer association (2019 edition) for BRCA. We will include patients according to the diagnostic criteria of Guidelines and norms for diagnosis and treatment of breast cancer of Chinese anticancer association (2019 edition) for BRCA

Information sources: Literature databases: CNKI (China National Knowledge Infrastructure), VIP (Chinese Scientific Journals Database), Wanfang database, Sinomed, PubMed, EMBASE, Cochrane library and Web of Science; Trial registry: Clinicaltrials.gov, and Chinese Clinical Trial Registry; Source of grey literature: reference lists of relevant reviews.

Main outcome(s): Total effective rate.

Additional outcome(s): Immunoglobulin A(IgA), Immunoglobulin G(IgG), Immunoglobulin M(IgM), total number of T lymphocytes(CD3+), T lymphocyte subsets (CD4+ , CD8+, CD4+/ CD8+), Carbohydrate Antigen 125(CA125), Carbohydrate Antigen 153(CA153), Carcinoembryonic Antigen(CEA), insulin growth factor 1(IGF-1), soluble e-cadherinin (sEC), vascular endothelial generating factor A (VEGFA), vascular endothelial generating factor B (VEGFB), soluble vascular endothelial growth factor receptor 1(sFlt-1), and the rate of adverse reactions.

Data management: Two reviewers will independently and repeatedly screen the literatures and extract relevant information, and will cross-check the results. Disagreements will be determined by a third reviewer. The reviewers will first exclude irrelevant literatures by reading the titles and abstracts, then read the full texts to determine the final included RCTs. The data extraction will cover the following data:1) Publishing features: title, first author, establishments, journals, and publication date; 2) patients and treatment: sex, age, sample size, with or without blinding, chemotherapy regimens, Xiaochaihu decoction usage, duration of treatment, adverse reactions, adverse events, follow-up time, loss rate and reasons; 3) outcome data: baseline and follow-up measurement of each index.

Quality assessment / Risk of bias analysis: Two reviewers will independently and repeatedly assess the risk of bias in the included studies and cross-check the results. The disagreement will be determined by a third reviewer. The risk of bias will be assessed using the risk assessment tool for randomized controlled trial recommended in the Cochrane handbook 5.1.0. It includes 7 items: 1) random list generation method; 2) allocation concealment; 3) blinding of patients and clinicians; 4) blinding of outcome evaluator; 5) data completeness; 6) selective reporting; 7) other bias sources. Each item will be rated as low, high, or uncertain risk of bias.

Strategy of data synthesis: 1) Meta-analysis for continuous outcomes: weighted mean difference or standardized mean difference and 95% confidence intervals (CIs) will be used as the effect measures and the inverse variance method will be used to combine the data; 2) Meta-analysis for dichotomous outcomes: relative risks and 95% CIs will use as the effect measures and the data will be combined using the Mantel-Haenszel method. Cochran's Q test and I2 statistics will be used to evaluate the heterogeneity among studies in the meta-analysis.

Subgroup analysis: Based on the experience of Xiaochaihu decoction and chemotherapy therapy in clinical application, when there is obvious heterogeneity in the analysis results, we will analyze the source of the heterogeneity from the following subgroups: 1) Subgroup analysis by chemotherapy regimens types: We will compare different chemotherapy regimens. 2) Subgroup analysis by treatment course: We will compare randomized controlled trials with a course of treatment > 3 months and ≤3 months. The former is expected to have a better effect.

Sensitivity analysis: In order to verify the robustness of the meta- analysis results, we will conduct the following two sets of sensitivity analyses: 1) excluding studies with high risk of bias; 2) using a fixed-effects model to collect the data from the meta- analysis.

Language: No restrictions.

Country(ies) involved: China.

Keywords: Xiaochaihu decoction, chemotherapy, breast cancer, protocol, systematic review, meta-analysis.

Contributions of each author:
Author 1 - Zhenming Xie.
Author 2 - Xianming Zhu.
Author 3 - Jie Liu.

Author 4 - Jie Chen.
Author 5 - Longzhu Ke.
Author 6 - Shengxia Tian.
Author 7 - Zhu Yang.
Author 8 - Li Luo.
Author 9 - Dongxin Tang.