Effectiveness of jianpibushen Herbal Medicine for myelosuppression Induced by adjuvant Chemotherapy in Adults with Colorectal Cancer: A Systematic Review and Meta-analysis

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Review question / Objective: “The aim of this systematic review is to compare jianpibushen Herbal Medicine in combination with adjuvant Chemotherapy and adjuvant Chemotherapy in terms of efficacy and acceptability in the myelosuppression Induced by adjuvant Chemotherapy to better inform clinical practice. To this end, the proposed systematic review will address the following question: Which is the best choice to reduce myelosuppression Induced by adjuvant Chemotherapy in Colorectal Cancer, jianpibushen Herbal Medicine in combination with adjuvant Chemotherapy or adjuvant Chemotherapy?”.

Condition being studied: Jianpibushen Herbal Medicine in combination with adjuvant Chemotherapy; Colorectal Cancer; myelosuppression Induced by adjuvant Chemotherapy.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 18 May 2022 and was last updated on 18 May 2022 (registration number INPLASY202250117).

INTRODUCTION

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METHODS

Search strategy: #13 #9 AND #12 #10 OR #11 #11 (chinese medicine[Title/Abstract]) OR (Chinese herb[Title/Abstract]) OR (traditional Chinese medicine[Title/Abstract]) OR (Chinese herbal medicine[Title/Abstract]) OR (Chinese Herbs[Title/Abstract]) OR (herbal medicine[Title/Abstract]) OR (herbal[Title/Abstract]) #10 “Medicine, Chinese Traditional”[Mesh] #9 #7 AND #8 #8 (bone marrow suppression[Title/Abstract]) OR (Marrow depression[Title/Abstract]) OR (Myelosuppression[Title/Abstract]) OR (medulla suppressed[Title/Abstract]) OR (hematotoxicity[Title/Abstract]) OR (leukopenia[Title/Abstract]) OR (leukocytopenia[Title/Abstract]) OR (aleukocytosis[Title/Abstract]) OR (oligoleukocytos[Title/Abstract]) OR (neutropenia[Title/Abstract]) OR (neutrocytopenia[Title/Abstract]) OR (neuctrocytopenia[Title/Abstract]) #7 #5 AND #6 #6 chemotherapy[Title/Abstract] #5 #1 OR #2 OR #3 OR #4 (carcinoma of colon[Title/Abstract]) OR (colon cancer[Title/Abstract]) OR (rectal cancer[Title/Abstract]) OR (carcinoma of rectum[Title/Abstract]) OR (rectal carcinoma[Title/Abstract]) OR (colorectal cancer[Title/Abstract]) OR (CRC[Title/Abstract]) OR (Colorectal carcinoma[Title/Abstract]) #3 “Colorectal Neoplasms” [Mesh] #2 “Recta.”

Participant or population: “Colorectal cancer after radical resection with adjuvant chemotherapy will be eligible for this review, with no exclusions based on ethnicity or age.”

Intervention: jianpibushen Herbal Medicine in combination with adjuvant Chemotherapy; adjuvant Chemotherapy.

Comparator: Jianpibushen Herbal Medicine in combination with adjuvant Chemotherapy.

Study designs to be included: Randomized controlled study.

Eligibility criteria: Inclusion and Exclusion Criteria for Articles. Inclusion criteria. Studies in accordance with all the following were included. (1) Participants diagnosed with CRC and receiving chemotherapy, aged ≥18 years, regardless of gender and race. (2) Intervention of the treatment group was oral CHM alone, with the components of the prescription and treatment courses. Comparison (control group) untreated or treated with placebo of CHM. (3) Outcome measurements included the incidence of leukopenia/neutropenia, the incidence of grade 3/4 leukopenia/neutropenia and the absolute count of leukocyte/neutropenia. (4) Types of studies: randomized controlled trials (RCTs) only. Exclusion criteria. Studies in accordance with the any of the following were excluded. (1) Information not available on the stage of the tumor, either TNM stage or Duke’s stage. (2) Chemotherapy scheme (both the agents and the dosage) not clarified. (3) Intraperitoneal infusion chemotherapy or oral chemotherapy drug alone. (4) Intervention combined with other types of Chinese Medicine, such as moxibustion, acupuncture, or enema. (5) Full-text not available.

Information sources: Pubmed, EMBASE, Web of Science, Cochrane Library, China National Knowledge Infrastructure (CNKI), Wanfang, Chongqing VIP (CQVIP), and China Biology Medicine disc (CBM).

Main outcome(s): Incidence of grade I/II/III/IV leukopenia; incidence of grade I/II/III/IV/V leukopenia; incidence of leukopenia; white blood count; (5) incidence of grade I/II/III/IV neutropenia; incidence of grade I/II/III/IV/V neutropenia; incidence of neutropenia; incidence of grade 0-II/III-IV neutropenia.
Additional outcome(s): Incidence of thrombocytopenia; grade I/II/III/IV thrombocytopenia; incidence of grade I/II/III/IV/V thrombocytopenia.

Data management: Two authors independently screened the articles for eligibility of trials, according to the criteria demonstrated above. Any inconsistency in this process was resolved by the third party. For the included studies, 2 reviewers extracted the following information: study ID, sequence generation, sample size, mean age, gender ratio, tumor stages, basic chemotherapy regimens, duration of treatment, treatment of the experimental/control groups, and outcomes. For papers with information not available, the correspondence authors were contacted by e-mail.

Quality assessment / Risk of bias analysis: The risk of bias of individual studies was assessed by 2 reviewers following the Cochrane Handbook for Systematic Review of Interventions whose main items are: random sequence of generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete data addressed, and selective reporting. Other bias was defined as the imbalance of baseline and for-profit bias.

Strategy of data synthesis: Meta-analysis was performed by RevMan 5.4 software. For continuous data (white blood count and neutrophil count), mean difference (MD) and its 95% confidence intervals (CIs) were used to represent the effect measures, while the relative risk (RR) with 95% CI were applied for the dichotomous outcomes, such as incidence of grade I/II/III/IV leukopenia/neutropenia, incidence of leukopenia/neutropenia, incidence of grade I/II/III/IV/V leukopenia/neutropenia, and incidence of grade III/IV neutropenia.

Subgroup analysis: Clinical case staging; Duration of Taking Chinese medicine.
Sensitivity analysis: Heterogeneity was tested with the chi-squared ($\chi^2$) test and I$^2$ statistic. A fixed-effects model was used when I$^2$<50%, otherwise a random-effects model was applied. We performed subgroup analyses and sensitivity analysis to investigate the factors of heterogeneity and the robustness of the finding, respectively.

Language: In both Chinese and English.

Country(ies) involved: China.

Keywords: jianpibushen Herbal Medicine; yelosuppression Induced by adjuvant Chemotherapy; Colorectal Cancer; Systematic Review.

Contributions of each author:
Author 1 - Wu Na - onceiving the review; designing the review; coordinating the review; data collection; data management; analysis of data; interpretation data; writing the protocol or review.
Author 2 - Tang Mo.
Author 3 - Sun Lingyun.
Author 4 - Yan Yunzi.
Author 5 - Ning Chunhui.
Author 6 - Yang Yufei.