INPLASY PROTOCOL

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Conflicts of interest:
None.

Oral herbal medicine on chemoradiotherapy- induced gastrointestinal side effects in patients with colorectal cancer: a systematic review and meta-analysis

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Review question / Objective: **P: Adult patients with colorectal cancer undergoing chemoradiotherapy, regardless gender or race. I: Oral herbal medicine (single herb, compound recipe or patent medicine). C: Addition of oral herbal medicine during chemoradiotherapy versus chemoradiotherapy alone or with placebo. O: Response Rate (RR), Karnofsky performance scale score (KPS). S: Randomized or quasi- randomized trials regardless of blinding.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 20 January 2021 and was last updated on 20 January 2021 (registration number INPLASY202110074).

INTRODUCTION

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Condition being studied: **Due to the considerable changes in lifestyle and diet, colorectal cancer (CRC) ranks fourth in terms of incidence and fifth in terms of cancer-related mortality in China. It is**

predicted that colorectal cancer will become the main tumor classification threatening the health of Chinese people in the next decade. Chemoradiotherapy, as one of the main means of comprehensive treatment for colorectal cancer, is still widely used in clinic. Adjuvant chemoradiotherapy can improve the radical rate of early to medium-stage colorectal cancer, and palliative chemotherapy can prolong the overall survival of advanced cancer patients. However, chemoradiotherapy-induced gastrointestinal side effects are one of the main reasons for patients to reject chemoradiotherapy, which seriously affect the quality of life of patients undergoing chemoradiotherapy. In order to manage the discomfort during chemoradiotherapy, many patients choose to use traditional Chinese medicine(TCM) in China. Studies have shown that TCM treatment has positive effectiveness reducing chemoradiotherapy-related gastrointestinal side effects, and improve the quality of life of patients.

METHODS

Participant or population: Adult patients with colorectal cancer (pathologically diagnosis of any tumor stage) undergoing chemoradiotherapy, regardless gender or race.

Intervention: Oral herbal medicine during chemoradiotherapy treatment included single herb, compound recipe and Chinese patent medicine during chemoradiotherapy treatment. Dosage forms include but are not limited to decoctions, pills, powders, oral liquids, tablets, capsules, etc.

Comparator: Addition of oral herbal medicine during chemoradiotherapy versus chemoradiotherapy alone or with placebo.

Study designs to be included: Randomized or quasi-randomized trials will be considered regardless of blinding.

Eligibility criteria: The study meets the requirements of PICOS, and has at least one of the outcomes. No region and language restrictions.

Information sources: 1. Electronic searching: Using Cochrane Colorectal Cancer Group search strategy to retrieve primary trials from the Cochrane Library, EMBASE, Pubmed, Web of science , CNKI (Chinese National Knowledge Infrastructure), Wanfang, CBM(China BioMedical Literature) and VIP(Chongqing VIP Information Resource Integration Service Platform) database from their establishment to December 2020. The Clinicaltrials.gov, the WHO International Clinical Trials Registry Platform (ICTRP) and the Chinese clinical trials registry website will also be searched for new relevant to the topic. 2. Manual searches for studies included in previous relevant systematic reviews and meta-analysis will be performed. Furthermore, unpublished trial reports from academic conferences, and theses of postgraduates are included in the range of manual searching.

Main outcome(s): The main outcomes are Response Rate（RR） of gastrointestinal side effects symptoms and Karnofsky performance scale score（KPS）to assess quality of life.

Quality assessment / Risk of bias analysis: According to the Cochrane risk of bias tool (Cochrane Handbook for Systematic Reviews of Interventions, version 5.1.0), the included studies are examined in 6 aspects by two independent investigators. Discrepancies were resolved either by consensus or through adjudication by a third investigator. The quality evaluation items of each trial included selection bias (random sequence generation and allocation concealment), performance bias (blinding of participants and personnel), detection bias (blinding of outcome assessment), attrition bias (incomplete outcome data), reporting bias (selective reporting), and other bias. These items were scored as low, high, or unclear risk of bias.

Strategy of data synthesis: 1.Quantitative data synthesis. We will use Revman 5.4 software to conduct Meta-analysis. Meta-analysis with available trials will be performed by Response Rate (RR) in dichotomous data and weighted mean difference in continuous variance data, both expressed by the 95% confidence interval (CI). 2. Assessment of heterogeneity. Heterogeneity among trials will be identified by Chi-square test and reported as I2. When P>0.1 and I275%, it is considered that there is statistics heterogeneity between the studies. 3. Assessment of publication bias. Publication bias will be assessed by the symmetry of the funnel chart when at least 10 trials are included.

Subgroup analysis: Subgroup sensitivity analysis will be conducted to explore potential sources of heterogeneity. When possible and appropriate, subgroup analysis including clinical stage(stageI-III and stage IV) and therapeutic methods (chemoradiotherapy and chemotherapy alone).

Sensibility analysis: Sensitivity analysis will be performed by sequentially omitting each study to examine the robustness of the primary outcome.

Country(ies) involved: China.

Keywords: herbal medicine, chemotherapy, colorectal cancer, gastrointestinal side effects, meta-analysis.

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