INPLASY PROTOCOL

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Review Stage at time of this submission: Preliminary searches.

Conflicts of interest: None.

The effect of oral Chinese herbal medicine on Oxaliplatin-induced Peripheral Neuropathy in patients with advanced colorectal cancer treated with FOLFOX: A Systematic Review and Meta-analysis

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Review question / Objective: P: Any patients with advanced colorectal cancer diagnosed by imaging and pathology, and any gender, any profession or ethnicity, and any age≥18, will be included. I: Oral Chinese herbal medicine + FOLFOX chemotherapy regimen. C: The same FOLFOX alone and no use of Chinese medicine preparations and methods. O: Primary events: The instances of acute, cumulative, or total neurotoxicity; Secondary events: Response rate (RR); Karnofsky performance scale score. S: randomised controlled trials (RCTs).

Condition being studied: Oral Chinese Herbal Medicine (OCHM) used in the treatment of advanced colorectal cancer have been widely implemented in clinical practice, but the effect of which in FOLFOX chemotherapy regimen on Oxaliplatin-induced Peripheral Neuropathy (OIPN) remain unclear. This paper aims to evaluate the efficacy of OCHM combined with FOLFOX regimen on OIPN in the treatment of advanced colorectal cancer.

INTRODUCTION

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METHODS

Search strategy: Literature searches are conducted to identify reports of RCTs involving OCHM in combination with FOLFOX for advanced advanced colorectal Cancer in the following electronic databases: Chinese National Knowledge Infrastructure (CNKI), Wanfang Database, China BioMedical Literature (CBM), Cqvip Database, EMBASE, Cochrane Library Pubmed, and from inception to December 2020. Manual searches for studies included in previous relevant systematic reviews and meta-analysis will be performed. No restrictions on languages and regions. The following key words or phrases and their abbreviations or derivatives are utilized singly or in combination: "Chinese herbal medicine" or "traditional Chinese" or "classical Chinese herbal formulas" or "Chinese herb" or "Chinese herb therapy" or "herbal medicin" or "herbal remedy" or "herb therapy" or "nature plant" or "decoction" and "FOLFOX" and "colon neoplasm" or "colon carcinoma" or "colon cancer" or " colon tumor" or "colonic neoplasm" or "colonic carcinoma" or "colonic cancer" or "colonic tumor" or "colorectal neoplasm" or "colorectal carcinoma" or "colorectal cancer" or "colorectal tumor". Search terms will be adapted according to the search

capabilities of each particular database.Search terms appropriately according to the situation to adapt to different databases. Searching work will be done by two reviewers independently. Searching results will be cross-checked for accuracy.

Participant or population: Any patients with advanced colorectal cancer diagnosed by imaging and pathology, and any gender, any profession or ethnicity, and any age≥18, will be included. Advanced cancer is defined as stage IIB, III, or IV. Staging followed criteria of the American Joint Commission on Cancer Manual for Staging of Cancer. Research sample size is not less than 30 people.

Intervention: Oral Chinese herbal medicine(OCHM) combined with FOLFOX chemotherapy regimen. OCHM included self-modified herbal formula and oral Chinese patent medicine. Dosage forms include but are not limited to decoctions, pills, powders, oral liquids, tablets, capsules, etc. Any dosage of OCHM form administrated intravenously, intramuscularly, or subcutaneously will be removed. Studies involving co-interventions of Traditional Chinese Non-medicinal therapies such as acupuncture, cupping, or point application will be removed.

Comparator: The same FOLFOX alone and no use of Chinese medicine preparations and methods.

Study designs to be included: All randomised controlled trials (RCTs) will be included, regardless of blinding, and regions. Excluding pseudo-randomized controlled trials grouped by hospitalization date, hospitalization number, outpatient number, visit order, birthday date, etc.

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

Information sources: Literature searches are conducted to identify reports of RCTs

involving OCHM in combination with FOLFOX for advanced advanced colorectal Cancer in the following electronic databases: Chinese National Knowledge Infrastructure (CNKI), Wanfang Database, China BioMedical Literature (CBM), Cqvip Database, EMBASE, Cochrane Library Pubmed, and from inception to December 2020. Manual searches for studies included in previous relevant systematic reviews and meta-analysis will be performed.

Main outcome(s): The primary outcomes are the incidence of acute, cumulative, or total neuroicicality.

Additional outcome(s): The secondary outcomes measures are response rate (RR) and Karnofsky performance scale (KPS).

Quality assessment / Risk of bias analysis: The included studies are evaluated in 7 aspects by the assessment tool recommended by Cochrane, including random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting and other bias. The risk of bias is divided into "low risk", "uncertain" and "high risk" levels in evaluating the included studies. This work is independently carried out and cross checked by two researchers.

Strategy of data synthesis: Two researchers independently screen the articles and extract the data. Firstly, we remove duplicate pieces of literature by Endnote X9. Secondly, we exclude artical that do not meet the inclusion criteria by reviewing the titles and abstracts. Thirdly, we re-screen the literature's full text that may meet the inclusion criteria to determine whether it is finally included or not, and cross-checked them.To compare titles and author information to delete duplicate documents based on pre-designated inclusion criteria, and preliminarily screen by reading titles and abstracts to exclude documents that do not meet the standards. For documents that cannot be determined whether they meet the inclusion or exclusion criteria, the full text is read and judged. The above steps strictly implement screening based on the criteria. If two searchers cannot agree on a disagreement, the third review researcher will joint discussion, and make a final decision. The 2 researchers independently extract the data and cross-checked them. Excel 2016 literature information database is established to extract data including the first author, year of publication, sample size, type of OIPN, the treatment time of OCHM, the total dose of Oxaliplatin, sex, age, intervention measures, course of treatment, outcomes, etc. For missing information studies, contact the author when needed. Otherwise, the concerned study would be be removed.In case of disagreement, the issue is discussed and resolved with a third researcher.

Subgroup analysis: If there is significant heterogeneity, subgroup sensitivity analyses will be conducted to explore potential sources of heterogeneity. When possible and appropriate, planning subgroup analyses included type of OIPN (acute, cumulative, or total neurotoxicity), total dose of oxaliplatin and the treatment time of OCHM.

Sensibility analysis: The sensitivity analysis of single study will be conducted to test the stability of the meta-analysis results. When needed, sensitivity analysis also will be used to assess the quality of the included studies based on sample size, statistical method, and missing data.

Language: No restriction.

Country(ies) involved: China.

Keywords: Oral Chinese Herbal Medicine; Advanced Colorectal Cancer; FOLFOX Chemotherapy; Oxaliplatin-induced peripheral neuropathy; Meta-Analysis; Systematic Review.

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