

INPLASY PROTOCOL

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None declared.

Effectiveness and Safety of Chinese Patent Medicine for Functional Constipation: A Systematic Review and Network-Meta Analysis

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Review question / Objective: To evaluate the effectiveness and safety of Chinese patent medicine in treatment of functional constipation by using the Network Meta-Analysis. **1. Types of participants:** participants diagnosed as functional constipation according to Rome III, Rome IV or other published criteria or guidelines. No limitation on types of FC, age, sex, and nation. Children and pregnant women were excluded. Participants who had other constipation-related diseases including irritable bowel syndrome, functional defecation disorders and opioid-induced constipation were excluded. **2 Types of Interventions.** Chinese patent medicine which have been registered with the approval batch number beginning with "Z," approved by Chinese National Medical Product Administration (NMPA), used alone or in combination with Polyethylene Glycol, Lactulose, Bisacodyl, Prucalopride Succinate, probiotic, or Mosapride which recommended by latest clinical guidelines released by authorized organizations. The dosage, formulation, and route of administration of Chinese patent medicine were not limited. **3 Types of control.** Registered Chinese patent medicines used alone, Polyethylene Glycol, Lactulose, Bisacodyl, Prucalopride Succinate, probiotic, Mosapride which recommended by latest clinical guidelines released by authorized organizations or placebo were eligible. **4 Types of outcomes.** Primary outcomes were the clinical effect, score of dyschezia and defecation time. Secondary outcomes were adverse events and recurrence rate. **5 Types of study design.** Parallel randomized controlled trials (RCTs) were included. Conference abstracts were excluded if full articles were not available.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 09 May 2022 and was last updated on 09 May 2022 (registration number INPLASY202250049).

INTRODUCTION

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constipation according to Rome III, Rome IV or other published criteria or guidelines. No limitation on types of FC, age, sex, and nation. Children and pregnant women were excluded. Participants who had other constipation-related diseases including irritable bowel syndrome, functional defecation disorders and opioid-induced constipation were excluded. 2 Types of Interventions. Chinese patent medicine which have been registered with the approval batch number beginning with “Z,” approved by Chinese National Medical Product Administration (NMPA), used alone or in combination with Polyethylene Glycol, Lactulose, Bisacodyl, Prucalopride Succinate, probiotic, or Mosapride which recommended by latest clinical guidelines released by authorized organizations. The dosage, formulation, and route of administration of Chinese patent medicine were not limited. 3 Types of control. Registered Chinese patent medicines used alone, Polyethylene Glycol, Lactulose, Bisacodyl, Prucalopride Succinate, probiotic, Mosapride which recommended by latest clinical guidelines released by authorized organizations or placebo were eligible. 4 Types of outcomes. Primary outcomes were the clinical effect, score of dyschezia and defecation time. Secondary outcomes were adverse events and recurrence rate. 5 Types of study design. Parallel randomized controlled trials (RCTs) were included. Conference abstracts were excluded if full articles were not available.

Rationale: In the treatment of functional constipation, patients prefer the use of Chinese patent medicine due to its convenience and efficiency. It is reported that the use of Chinese patent medicine has increased in recent years under supportive policies. Unlike the modification of herbal decoction in response to patients with differentiated syndromes, more chances were provided to develop specific Chinese patent medicine for accurate Chinese medicine syndrome. Considering the value of Chinese patent medicine for FC, it is necessary to provide suggestions for the users to choose from the available large amount of Chinese patent medicine. Although two meta-analyses have been

published to explore the effectiveness of Chinese patent medicine for functional constipation, not all Chinese patent medicine available are covered, and evidence on head-to-head comparisons is absent. Therefore, indirect comparisons are planned in this paper with the method of network meta-analysis (NMA) to compare the effectiveness and safety of multiple Chinese patent medicine simultaneously in single analysis.

Condition being studied: Two meta-analyses have been published to explore the effectiveness of Chinese patent medicine for functional constipation, not all Chinese patent medicine available are covered, and evidence on head-to-head comparisons is absent.

METHODS

Search strategy: PubMed, Cochrane library, Embase, SinoMed, CNKI, Wanfang, and Cqvip databases were searched from their inception dates to February, 2022. The searching words included “Constipation”, “Functional Constipation”, “Functional chronic constipation”, “Chronic Constipation”, “Chronic Functional constipation”, “chronic idiopathic constipation”, “FC”, “CFC”, “Chinese proprietary medicine”, “Chinese proprietary medicine”, “Chinese patent medicine”, “Chinese patent medicine”, “Marenwan”, “Marenrunchangwan”, “Simotang”, “Qirongrunchangkoufuye”, “Liuweinengixaowan”, “Zhishidaozhiwan”, “Liuweianxiaosan”, “Wumeiwan”, “Tongbianling Capsule”, “Tongbianling Pill”, “Xinfufangluhui Capsule”, “Biantong Pill”, “Congrongtongbiankoufuye”, “Marenzipiwan”, “Houbobaiqiheji”, “Muxiangbinlang Pill”, “Huanglianshangqingwan”, “Dangguilonghuiwan”, “Qizhiweitong Pill”, “Xinqingning Pill”, “Sanhuang Pill”, “Dahuangtongbian Pill”, “Jiangzhitongbian Capsule”, “Sanhuanggao”, “Bimayou”, “Changshutongshuan”, “Yangyintongmi Capsule”, “Yiqitongbian Capsule”, “Bianmitong”, “Ziyinrunchangkoufuye”, “Qingchangtongbian Capsule”, “Tongle Granules”, “Mojiqingning”,

“Wurenrunchangwan”, “Muxiangliqi”, “Banliuwan”, “randomized controlled trial”, “randomly”.

Participant or population: Participants diagnosed as functional constipation according to Rome III, Rome IV or other published criteria or guidelines. No limitation on types of FC, age, sex, and nation. Children and pregnant women were excluded. Participants who had other constipation-related diseases including irritable bowel syndrome, functional defecation disorders and opioid-induced constipation were excluded.

Intervention: Chinese patent medicine which have been registered with the approval batch number beginning with “Z,” approved by Chinese National Medical Product Administration (NMPA), used alone or in combination with Polyethylene Glycol, Lactulose, Bisacodyl, Prucalopride Succinate, probiotic, or Mosapride which recommended by latest clinical guidelines released by authorized organizations. The dosage, formulation, and route of administration of Chinese patent medicine were not limited.

Comparator: Registered Chinese patent medicines used alone, Polyethylene Glycol, Lactulose, Bisacodyl, Prucalopride Succinate, probiotic, Mosapride which recommended by latest clinical guidelines released by authorized organizations or placebo were eligible.

Study designs to be included: Parallel randomized controlled trials (RCTs) were included. Conference abstracts were excluded if full articles were not available.

Eligibility criteria: To evaluate the effectiveness and safety of Chinese patent medicine in treatment of functional constipation by using the Network Meta-Analysis.1. Types of participants: participants diagnosed as functional constipation according to Rome III, Rome IV or other published criteria or guidelines. No limitation on types of FC, age, sex, and nation. Children and pregnant women were excluded. Participants who had other

constipation-related diseases including irritable bowel syndrome, functional defecation disorders and opioid-induced constipation were excluded. 2 Types of Interventions. Chinese patent medicine which have been registered with the approval batch number beginning with “Z,” approved by Chinese National Medical Product Administration (NMPA), used alone or in combination with Polyethylene Glycol, Lactulose, Bisacodyl, Prucalopride Succinate, probiotic, or Mosapride which recommended by latest clinical guidelines released by authorized organizations. The dosage, formulation, and route of administration of Chinese patent medicine were not limited.3 Types of control. Registered Chinese patent medicines used alone, Polyethylene Glycol, Lactulose, Bisacodyl, Prucalopride Succinate, probiotic, Mosapride which recommended by latest clinical guidelines released by authorized organizations or placebo were eligible. 4 Types of outcomes. Primary outcomes were the clinical effect, score of dyschezia and defecation time. Secondary outcomes were adverse events and recurrence rate.5 Types of study design. Parallel randomized controlled trials (RCTs) were included. Conference abstracts were excluded if full articles were not available.

Information sources: PubMed, Cochrane library, Embase, SinoMed, CNKI, Wanfang, Cqvip databases.

Main outcome(s): Primary outcomes were the clinical effect, spontaneous bowel movement frequency, score of dyschezia and defecation time.

Additional outcome(s): Secondary outcomes were adverse events and recurrence rate.

Data management: NoteExpress will be used to manage the included studies. Data chart designed by Excel 2016 to manage the extracted data.

Quality assessment / Risk of bias analysis: Risk of bias (ROB1.0) from Cochrane will be used to perform the quality assessment.

Strategy of data synthesis: The analysis will be completed by network meta-analysis and standard pairwise comparisons. Statistical heterogeneity, inconsistencies, and ranking probability will be evaluated. ADDIS 1.16.6, Review Manager 5.4 and Stata 13 will be used for data analysis.

Subgroup analysis: In the outcome clinical effect, the subgroup will be set among their different criteria.

Sensitivity analysis: If necessary, the sensitivity analysis will be performed by metan module of stata 16.0.

Language: Chinese & English.

Country(ies) involved: China.

Keywords: Chinese patent medicine; traditional Chinese medicine; functional constipation; systematic review; network meta-analysis.

Contributions of each author:

Author 1 - You-you Zheng - Main author who complete the research protocol, study searching, data extraction, data analysis, paper writing and submission.

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