INPLASY PROTOCOL

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Corresponding author:
Wenbin Hou

bucmhwb@163.com

Author Affiliation:
Beijing University of Chinese Medicine

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None declared.

Five-Flavor Sophora Flavescens Enteric-Coated Capsules for Ulcerative Colitis: A Systematic Review and Meta-Analysis of Randomized Clinical Trials

Hou, WB[1]; Sun, WJ[2]; Zhang, XW[3]; Li, YX[4]; Zheng, YY[5]; Sun, YX[6]; Liu, JP[7]; Liu, ZL[8].

Review question / Objective: **We aimed to assess the effectiveness and safety of FSEC for UC to provide reference for clinical practice and further studies on the mechanism of drug action.**
Main outcome(s): **Primary outcomes were clinical effective rate (defined as the improvement of clinical symptoms, colonoscopy results and stool examination results) and colonoscopy curative effect; secondary outcome were disease activity index (DAI), effective rate of Chinese medicine syndromes (Clinically controlled: clinical symptoms and physical signs disappeared or basically disappeared, with the decrement of scores (DS) 90%; Markedly effective: obvious improvement of clinical symptoms and physical signs, with DS 70% but <90%; Effective: clinical symptoms and physical signs were improved to some degree, with DS 30% but <70%; Ineffective: no improvement or even aggravation of clinical symptoms and physical signs, with DS <30%. The sum of the first three items constituted the total effective rate), cytokines and adverse events.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 18 May 2021 and was last updated on 18 May 2021 (registration number INPLASY202150068).

INTRODUCTION

Review question / Objective: **We aimed to assess the effectiveness and safety of FSEC for UC to provide reference for clinical practice and further studies on the mechanism of drug action.**

Condition being studied: **Ulcerative colitis (UC) is a chronic inflammatory bowel disease (IBD) that mainly affects the mucosa and submucosa of the rectum and colon. The main clinical manifestations are abdominal pain, diarrhea and mucopurulent bloody stool. UC has the characteristics of**

long course, difficult to cure, easy to relapse, and high risk of cancer, which seriously affects the quality of life of patients . It has been listed as one of the intractable diseases by the World Health Organization and became a hotspot and difficulty in research of digestive disease recently. Epidemiological studies showed that the incidence and prevalence of IBD were higher in western countries, but the overall trend was stable. In the past 20 years, the incidence and prevalence of IBD in eastern countries had increased rapidly, and IBD has gradually become a global disease . Studies have shown that China is currently one of the countries with the highest incidence of UC in Asia, with an incidence of about 3.44 per 100,000. With economic development and urbanization, the incidence of UC in China may increase rapidly . Due to the long course and easy recurrence of UC, it brought a serious disease burden to patients. It was estimated that the costs associated with UC are about 12.5 to 29 billions , including 1 billion Euros per year in Europe, and about 8.1 to 14.9 billions U.S. dollars per year in the United States. A German study showed that the average annual treatment cost for patients with UC was 8772.03 Euros, and the number of absentee days due to UC was about 16.1 days . At present, conventional treatment of UC is mainly based on 5-aminosalicylic acid preparations, glucocorticoids, immunosuppressive agents and biological preparations, but there are limitations such as poor efficacy for some patients, and lower tolerance of patients due to adverse reactions . For a long time, Chinese medicine has been widely used in the treatment of UC. Studies have proved that Chinese medicine may control the symptoms of UC patients, accelerate the repair of intestinal mucosa, regulate immunity, and improve the quality of life . Chinese patent medicine has the characteristics of being convenient to carry and easy to take. Five-flavor Sophora flavescens enteric-coated capsules (FSEC) is a Chinese patent medicine used for the treatment of UC by indication. There have been a certain number of clinical trials to evaluate the clinical effectiveness and safety of FSEC.

METHODS

Participant or population: Aged 18 years or older given the diagnosis of UC defined by clear diagnostic criteria. There was no limitation of gender, course of disease, and severity.

Intervention: FSEC or FSEC in combination with conventional medicine, with clear reporting of the method of medication, dosage and course of treatment.

Comparator: Conventional western medicine, with clear reporting of the method of medication, dosage and course of treatment.

Study designs to be included: Only RCTs were included.

Eligibility criteria: (1) Study: only RCTs were included. (2) Participants: aged 18 years or older given the diagnosis of UC defined by clear diagnostic criteria. There was no limitation of gender, course of disease, and severity. (3) Interventions: FSEC or FSEC in combination with conventional medicine, with clear reporting of the method of medication, dosage and course of treatment. (4) Controls: conventional western medicine, with clear reporting of the method of medication, dosage and course of treatment. (5) Outcomes: primary outcomes were clinical effective rate (defined as the improvement of clinical symptoms, colonoscopy results and stool examination results) and colonoscopy curative effect; secondary outcome were disease activity index (DAI), effective rate of Chinese medicine syndromes (Clinically controlled: clinical symptoms and physical signs disappeared or basically disappeared, with the decrement of scores (DS) 90%; Markedly effective: obvious improvement of clinical symptoms and physical signs, with DS 70% but <90%; Effective: clinical symptoms and physical signs were improved to some degree, with DS 30% but <70%; Ineffective: no improvement or even aggravation of

clinical symptoms and physical signs, with DS <30%. The sum of the first three items constituted the total effective rate), cytokines and adverse events.

Information sources: PubMed, the Cochrane Library, Chinese SinoMed, China National Knowledge Infrastructure (CNKI), Chinese Scientific Journal Database (VIP), and Wanfang databases.

Main outcome(s): Primary outcomes were clinical effective rate (defined as the improvement of clinical symptoms, colonoscopy results and stool examination results) and colonoscopy curative effect; secondary outcome were disease activity index (DAI), effective rate of Chinese medicine syndromes (Clinically controlled: clinical symptoms and physical signs disappeared or basically disappeared, with the decrement of scores (DS) 90%; Markedly effective: obvious improvement of clinical symptoms and physical signs, with DS 70% but <90%; Effective: clinical symptoms and physical signs were improved to some degree, with DS 30% but <70%; Ineffective: no improvement or even aggravation of clinical symptoms and physical signs, with DS <30%. The sum of the first three items constituted the total effective rate), cytokines and adverse events.

Quality assessment / Risk of bias analysis: Two review authors in pairs independently used the Cochrane Risk of bias tool to determine the bias for each included trial. We resolved any disagreements by consensus or by consulting a third author. Risk ratings of “low”, “high” or “unclear” were assigned to the following items: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other biases.We used GRADE to assess the overall quality of evidence.

Strategy of data synthesis: We used RevMan 5.4 software for data analysis. For outcome measures, we presented as relative risk (RR) with 95% confidence interval (CI) (after-intervention values were used to calculate the effect estimate). Statistical analysis was performed according to the statistical guidelines cited in the latest Cochrane Handbook for Systematic Reviews of Interventions. We performed meta-analyses if the trials had good homogeneity on study design, participants, intervention, control, and outcomes. We performed meta-analyses using random effects model. The I2 statistic was used to calculate statistical heterogeneity. If the heterogeneity between studies was significant (I2>90%), we would not perform meta-analysis and the source of heterogeneity should be analyzed. When more than 10 RCTs were available to test the same outcome in one meta-analysis, we used funnel plots to intuitively assess publication bias.

Subgroup analysis: We performed subgroup analysis where different types of controls were used.

Sensitivity analysis: We performed a sensitivity analysis to assess the robustness of the meta-analysis.

Country(ies) involved: China.

Keywords: Five-flavor Sophora flavescens enteric-coated capsules, Ulcerative colitis, Systematic review, Meta-analysis, Randomized controlled trials, Clinical evidence.

Contributions of each author:
Author 1 - Wenbin Hou.
Author 2 - Weijia Sun.
Author 3 - Xiaowen Zhang.
Author 4 - Yuanxi Li.
Author 5 - Youyou Zheng.
Author 6 - Yuxin Sun.
Author 7 - Jianping Liu.
Author 8 - Zhaolan Liu.