

# Meta Analysis of Mesalazine Combined with Chinese Herbal Compound Enema in the Treatment of Ulcerative Colitis

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**Abstract:** To evaluate the clinical efficacy of mesalazine combined with Chinese herbal compound enema in the treatment of ulcerative colitis, we searched CNKI, Wangfang, VIP, CBM, The Cochrane Library, Pubmed, Web of Science and EMBASE databases. Randomized controlled trials (RCTs) about mesalazine combined with TCM compound enema for ulcerative colitis were randomized controlled trials (RCTs), all randomized controlled trials were conducted from database establishment to August 2022, in which control group received mesalazine treatment, and treatment group received TCM reenema on the basis of control group. The "risk bias assessment" tool provided by the Cochrane Reviewer's Handbook was used for literature quality assessment, and RevMan5.3 software was used for statistical analysis. Eleven literatures were finally included, all of which were randomized controlled trials with a total of 1029 patients. The results of meta-analysis showed that the clinical effective rate of the treatment group [RR=4.26, 95%CI (2.79,6.50),  $P<0.00001$ ] was higher than that of the control group. It can effectively reduce Baron score [MD=-0.98, 95%CI (-1.25, -0.71),  $P<0.00001$ ], DAI score [MD=-1.61, 95%CI (-1.81, -1.42),  $P<0.00001$ ], CRP value [MD=-6.61, 95%CI (-7.29, -5.93),  $P<0.00001$ ], the treatment group was more effective than the control group in relieving clinical symptoms, including abdominal pain [MD=-1.03, 95%CI (-1.99, -0.07),  $P = 0.03$ ], diarrhea (MD = 0.86, 95% CI (1.46, 0.25),  $P = 0.006$ ), and purulent blood [MD = 0.86, 95% CI (1.62, 0.09),  $P = 0.03$ ]. Funnel plot of clinical response rate showed obvious asymmetry between left and right, suggesting possible publication bias. Mesalazine combined with Chinese herbal compound enema has significant clinical efficacy in the treatment of ulcerative colitis, but the literature included is too few and the quality evaluation is not high, so it needs to be further confirmed by multiple books and high-quality RCT tests in the future.

**Keywords:** Mesalazine; Chinese herbal compound enema; Randomized control; Ulcerative colitis; Meta-analysis

## 1. Introduction

Ulcerative colitis is a kind of inflammatory bowel disease, which belongs to chronic non-specific intestinal inflammatory diseases, mainly involving continuous and diffuse inflammation of colorectal mucosa and submucosa and damage of intestinal wall [1]. The main clinical manifestations were diarrhea, mucous pus and blood stools and abdominal pain [2]. At present, the pathogenesis is generally followed as follows: In patients with UC genetic susceptibility, under specific environmental conditions, the intestinal microecology changes, the body's immune dysfunction, resulting in damage to the intestinal mucosal barrier, and further causing repeated inflammatory damage to the large intestine mucosa [3]. Epidemiology shows that the global incidence of UC is gradually increasing, and UC is classified as one of the refractory diseases by the World Health Organization [4,5]. Clinically, the goal of UC treatment is to maintain symptom relief and induce mucosal healing. Amino salicylic acid preparation is used as the first-line treatment drug, including 5-amino salicylic acid (5-ASA), such as mesalazine (MS) and sulfasopyridine (SASP). However, UC itself has repetitive and cancerous degeneration, which leads to a long drug taking cycle in Western medicine. Many adverse reactions, easy to relapse and many other inevitable problems.

In traditional Chinese medicine, UC is called "chronic dysentery", and the syndrome classification mentioned in Expert Consensus on TCM Diagnosis and Treatment of Ulcerative Colitis (2017) [6] is

widely used in domestic clinical practice. TCM has the characteristics of syndrome differentiation and treatment, which provides the exact treatment methods and prescriptions for the precise treatment of different types of UC. Based on the dialectical treatment of different prescriptions for different syndrome types, TCM compound enema further gives full play to the direct effect of the disease, maximizes the efficacy, avoids the first-pass effect of oral administration, reduces the burden on the liver, and reduces the damage to the spleen and stomach caused by long-term use of TCM. Besides, TCM is characterized by few side effects. In the treatment of UC and Western medicine has a complementary role. In recent years, many scholars have analyzed the advantages of integrated Chinese and Western medicine in the treatment of UC, but rarely analyzed the effectiveness of simple TCM compound enema combined with Western medicine in the treatment of UC. Therefore, this meta-analysis was conducted in order to provide a reliable basis for the adjuvant treatment of UC with TCM compound enema in the future.

## **2. Data and methods**

### **2.1. Retrieval strategy**

Computer search Chinese databases: CNKI, Wanfang, VIP, China Biomedical Literature Service System (CBM), foreign language databases: The Cochrane Library, Pubmed, Web of Science, EMBase and other 8 databases. The Chinese search terms were "Mesalamine", "TCM compound enema" and "Ulcerative Colitis", the main search words were "Mesalamine and TCM compound enema and ulcerative colitis", while the foreign search words were "subject words add free words", and the foreign search words were "Mesalamine, Ulcerative Colitis", Chinese medicine " is the main inscription. Randomized controlled studies (RCTS) of mesalazine combined with TCM compound enema in the treatment of ulcerative colitis were retrieved from database establishment to August 2022.

### **2.2. Inclusion criteria**

(1) Study type: Randomized controlled clinical trial in Chinese or Chinese language. (2) Subjects: The disease diagnosis was in line with the reference standards of the Consensus Opinion on Diagnosis and Treatment of Inflammatory Bowel Disease (2012 • Guangzhou) [7]. (3) Intervention measures: the control group was mesalazine (without limiting the manufacturer, dosage and dosage); On the basis of the control group, the study group was added enema treatment with Chinese herbal compound (without restriction of Chinese herbal compound components). (4) "Clinical response rate" was the primary outcome indicator, and "colonoscopy Baron score, DAI score, CRP and clinical symptom score" were the secondary outcome indicators.

### **2.3. Exclusion criteria**

(1) Non-RCTs: retrospective studies, experience, case reports, reviews; (2) did not meet the diagnostic criteria of UC, such as infectious bowel disease, Crohn's disease and ischemic enteritis; (3) The control group did not use or did not use mesalazine, or the study group used other TCM therapies, such as oral decoction, acupuncture, etc. (4) Data is missing and key data is not given. (5) Select the one with comprehensive data and high quality of the repeatedly published literature.

### **2.4. Literature screening and data extraction**

The two researchers used NoteExpress software to independently complete the literature screening according to the inclusion and exclusion criteria, and completed the cross-check of the selected literature. In case of any difference or disagreement, the third party personnel would join in and make a decision together. The data were further proposed and Excel was used to develop a basic feature table, including the first author of the included literature, publication year, sample size, gender, age and other baseline data as well as intervention measures and outcome indicators.

### **2.5. Included literature quality assessment**

Two researchers applied the Cochrane Reviewer's Handbook [8]. The provided "risk bias assessment" tool evaluated the quality of the included literature from six aspects: sequence generation, allocation hiding, blind method, incomplete outcome data, selective outcome report and no other

sources of bias. The assessment level was divided into: At high risk, uncertain and low risk levels, cross-check will be made once the assessment is completed. If the results are different, the third party will negotiate to determine.

## 2.6. Statistical analysis

Meta-analysis was performed using RevMan 5.3 software of the Cochrane Collaboration network. Dichotomous variables, i.e., relative risk (RR), were used as effect values for counting data; continuous variables and measurement data, i.e., mean difference (MD), i.e., weighted mean difference (WMD) and standard mean difference (SMD), were used as counting data. Other indicators are measurement data. 95% confidence interval (CI) was used for both studies, and I<sup>2</sup> test was used to evaluate statistical heterogeneity. If there was good homogeneity among studies ( $P > 0.05$ ,  $I^2 \leq 50\%$ ), fixed effects model was selected; if there was heterogeneity among studies,  $P < 0.05$ ,  $I^2 > 50\%$ , random effects model was selected. The sources of heterogeneity were analyzed by sensitivity analysis or subgroup analysis. The funnel plot of total clinical efficiency was drawn to determine whether there was publication bias.

## 3. Results

### 3.1. Literature screening results

A total of 2149 literatures were preliminarily searched: CNKI638 article, Wanfang1047 VIP219 article, CBM245, did not retrieve the relevant foreign language, for 1240 after rechecking, further removed by eliminating standard documents, eventually into 11 RCTs literature [9-19]. The literature screening process is shown in Figure 1.

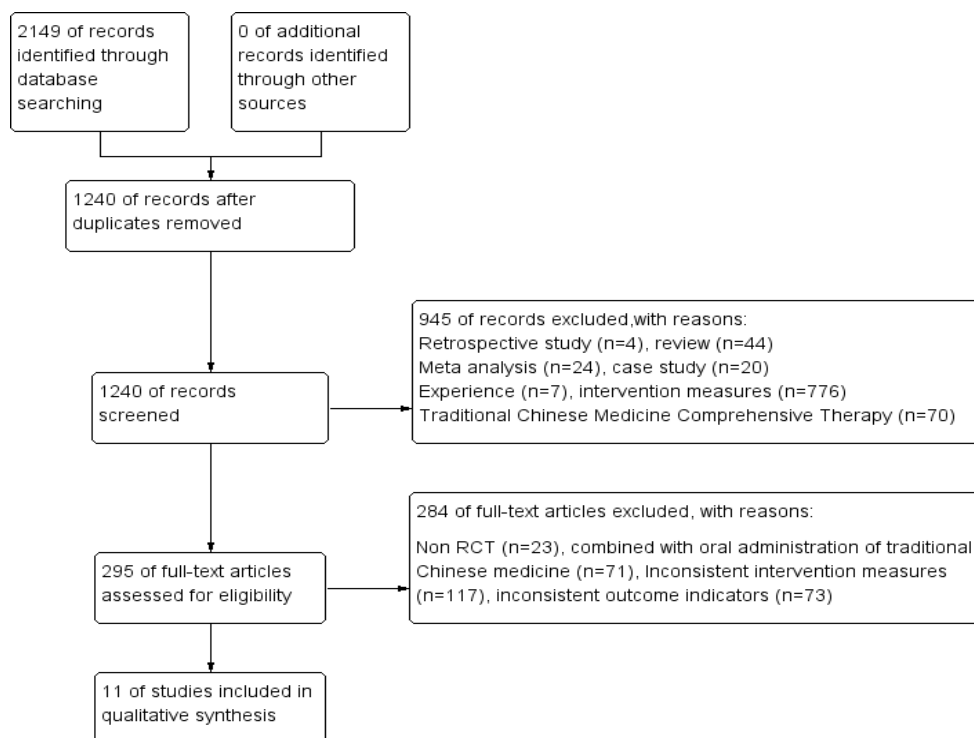


Figure 1: Literature screening process

### 3.2. Basic features of the included literature

A total of 1029 patients were included in this study, including 516 patients in the experimental group and 513 patients in the control group. There was no statistically significant difference in baseline data such as age and gender between the included control group and the treatment group ( $P > 0.05$ ). The basic characteristics are shown in Table 1 and Table 2.

Table 1: Basic characteristics of included RCTs

Researcher	Time	Number of cases		Age (years)		Gender (male/female)		Course of treatment (d)	Outcome indicators
		T	C	T	C	T	C		
Li Xuejun	2017	24	24	23~55 (34.83±8.67)	24~54 (34.81±8.43)	13/11	10/14	60	(1)(3)
Dong Ying	2011	28	28	20~59(45.2±9.8)	21~57 (44.8±9.2)	12/16	11/17	60	(1)(4)
Huo Hong	2018	30	30	19~78 (50.01±13.21)	18~75 (51.31±12.58)	17/13	15/15	30	(1)(3)
Zheng Xiaotao	2014	48	48	25~52(36.7±11.2)	27~53 (35.2±10.9)	23/25	21/27	4weeks	(1)(2)(4)(5)
Yang Lei	2017	30	29	37.12±8.22	39.23±7.90	16/14	15/14	6weeks	(1)(4)
Huang Juan	2017	90	90	38.48±4.11	39.41±4.28	60/30	53/37	4weeks	(1)(4)
Liu Xuejin	2017	56	56	25~58 (39.34±2.56)	27~55 (38.79±2.31)	27/27	26/28	21	(3)(5)
Xie Liusong	2015	69	67	22~65(44.3±9.6)	21~64 (43.9±8.6)	35/34	34/33	60/4weeks(T/C)	(1)(4)
Fan Yufeng	2015	49	49	16~5(36.4±2.1)	15~56 (35.2±2.5)	27/22	26/23	4weeks	(1)(2)
Ning Yufeng	2015	60	60	22~65(41.4±7.5)	25~63 (43.9±8.2)	33/27	39/21	4weeks	(1)(2)(4)(5)
Zhang Juan	2012	32	32	—	—	15/17	14/18	15	(1)(5)

Note: T= experimental group, C= control group; - Indicates that there is no relevant data. (1) Clinical response rate (2) Sutherland DAI score (3) C-reactive protein (4) Colonoscopy Baron score (5) Clinical symptom score

Table 2: Continued—Basic characteristics of included RCTs

Researcher	Time	Intervention measures	
		T	C
Li Xuejun	2017	Traditional Chinese Medicine Compound Enema (Spleen Stomach Peiyuan Enema Formula, Concentrated decoction 150mL, 1 dose/d)	
Dong Ying	2011	C+Traditional Chinese Medicine Compound Enema (self-made Kui Sukang Tang, concentrated decoction of 150 mL, liquid temperature of 40°C -42°C, try to drain all feces before enema, raise the buttocks 30° after enema, keep it for a long time, once a day)	Oral administration of mesalazine enteric coated tablets (active phase: 3 times per day, 3 tablets per dose; remission phase: 3 times per day, 2 tablets per dose)
Huo Hong	2018	C+Traditional Chinese Medicine Compound Enema (Zi'ai Tang, decoction with 150 mL of water, temperature maintained at around 37 °C. After defecation, take a knee chest position for retention enema before going to bed. After enema, take an arm high, head low, and buttocks and pad them up by 10cm for about 30 minutes. The retention time of the enema solution in the intestine is >4 hours. If the retention time is not good, add 20mL of 2% lidocaine hydrochloride into the enema solution to extend the retention time, and enema once a night.)	Oral administration of mesalazine enteric coated tablets (specification 0.25g/tablet, initial dosage 4 times/day, 1g (4 tablets) each time)
Zheng Xiaotao	2014	C+Traditional Chinese Medicine Compound Enema (self formulated Kuijie Formula, decoction twice with water, mix to 300ml, empty stool before bedtime, take the knee chest lying position, pour in the medicine, and keep the medicine for at least 20min)	Oral administration of mesalazine enteric coated tablets (1g daily, 3 times a day)
Yang Lei	2017	C+Chinese herbal compound enema (Qingbai enema solution, 300mL each time, enema before bedtime)	Oral administration of mesalazine orally (1g each time, 4 times daily)
Huang Juan	2017	C+Chinese herbal compound enema (Qingbai enema solution, 200mL per bag, 200mL per time, once a day)	Mesalazine enema solution enema (4g per tube, 4g per time, twice daily)
Liu Xuejin	2017	C+Traditional Chinese Medicine Compound Enema (Qingchang Yuyang Tang, concentrated in 200ml, temperature at 37 °C, enema before bedtime and after defecation every night, taken in a prone position, with the medicine juice retained for 20-30 minutes, qd)	Oral administration of mesalazine enteric coated tablets (1g/dose, tid)
Xie Liusong	2015	C+Traditional Chinese Medicine Compound Enema (Yuyang Tang, concentrated decoction, extract 200ml of juice, medicine temperature 37-42 °C, advise to keep the medicine liquid for a long time, twice a day, one in the morning and one in the evening)	Oral administration of mesalazine enteric coated tablets (4 times daily, 1g each time)
Fan Yufeng	2015	C+Traditional Chinese Medicine Compound Enema (Self-made Jiedu Liangxue Tang, boiled twice in water, mixed and concentrated into 300ml, once a day)	Mesalazine intestinal suppository (1g/piece, 2 pieces each time)
Ning Yufeng	2015	C+Traditional Chinese Medicine Compound Enema (Yuchang decoction, concentrate the liquid to 120ml, keep the enema, once a day, continuously for 5 days per week, rest for 2 days, and then proceed to the next treatment course)	Oral administration of mesalazine enteric coated tablets (swallow without chewing, 1g/time, 4 times/day)
Zhang Juan	2012	C+Traditional Chinese Medicine Compound Enema (Qingchang Yuyang Tang, boiled twice in water, mixed and concentrated into 200ml, once a day, enema before bedtime and after defecation every night, with a retention time of at least 20min)	Oral administration of mesalazine enteric coated tablets (1g/time, 4 times/day)

### 3.3. Results of literature quality assessment

The quality of the 11 included articles should be assessed using the Cochrane "bias risk assessment" tool: In one of the included literatures [10], it was mentioned that patients were randomized according to the order number of their visits, which may have risk bias, and were assessed as high risk. Five literatures [11-13,18,19] used the number table randomization method, and one [6] used the central stratified randomization method, so all the six studies were assessed as low risk. The remaining 4 literatures [9,15-17]. Only mentioned random grouping without specific methods, so they were assessed as uncertain risks. Among all the 11 literatures, only one [6] mentioned that the distribution hiding method was sealed opaque envelope and double-blind was used, so the two items in this paper were assessed as low risks, while the others were not mentioned and assessed as uncertain risks. All 11 literatures have clear outcome indicators, so quality assessment is low risk; all studies have unknown other bias, so they are assessed as uncertain risk; all literatures have complete data reports, and there is no selective outcome, so they are assessed as low risk (Figure 2, 3).

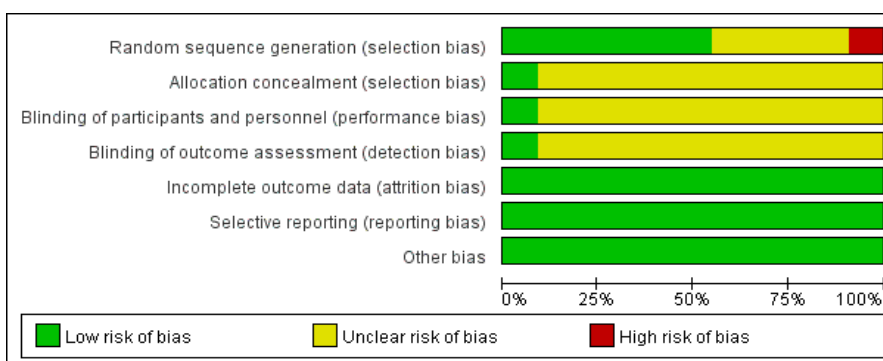


Figure 2: Percentage of included RCTs with the risk of bias

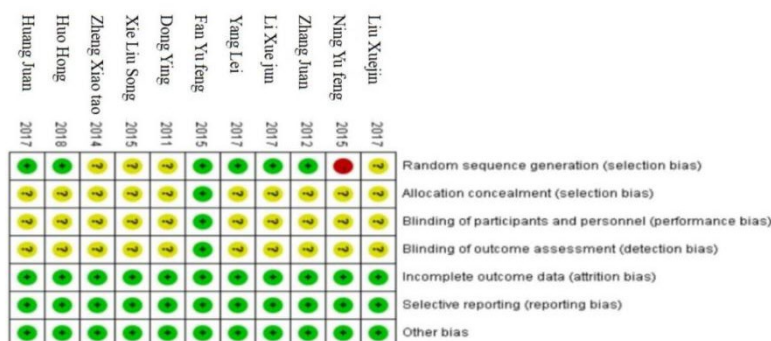


Figure 3: Distribution of risk of bias of included RCTs

### 3.4. Meta-result analysis

#### 3.4.1. Clinical effective rate

Included in the study reports the clinical effective rate, the treatment group 460 examples, the control group of 457 cases [9-19]. There was good homogeneity among all studies ( $P=0.88$ ,  $I^2=0\%$ ), so fixed effect model was adopted. Meta-analysis showed that  $[RR=4.26, 95\%CI (2.79, 6.50), P<0.00001]$ , the difference between the treatment group and the control group was statistically significant, indicating that TCM compound enema combined with mesalazine was more effective than mesalazine alone, as shown in Figure 4.

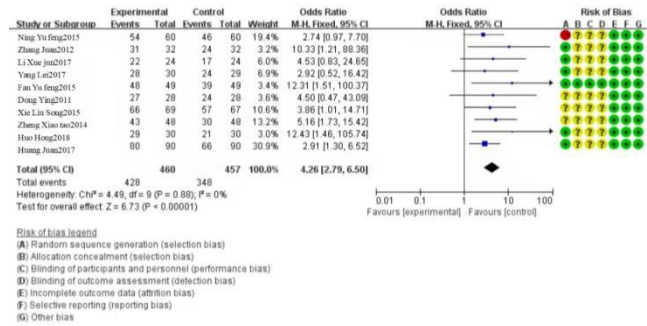


Figure 4: Meta-analysis of clinical effective rates

3.4.2. Colonoscopy Baron score

Six of the included studies reported colonoscopy Baron scores, including 325 in the treatment group and 322 in the control group [10-14,16,18]. The random effects model was adopted because of the large heterogeneity among studies (P<0.00001, I<sup>2</sup>=84%). Meta-analysis showed that [MD= -0.98, 95%CI (-1.25, -0.71), P<0.00001], the difference between the treatment group and the control group was statistically significant, indicating that TCM compound enema combined with mesalazine could better reduce the colonoscopy Baron score, as shown in Figure 5.

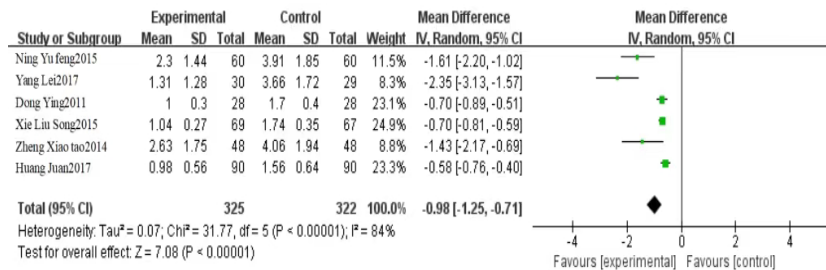


Figure 5: Meta-analysis of Baron score of enteroscopy

Heterogeneity exists among various studies. The source of heterogeneity was analyzed by sensitivity, and the paper by paper exclusion method was applied. After the two studies of Ning Yufeng and Yang Lei were excluded [13,18], the heterogeneity was I<sup>2</sup>=44%, P=0.15 (Figure 6). Considering these two studies as sources of heterogeneity, further meta-analysis was conducted on the remaining four literatures, and the fixed-effect model was adopted. The results were as follows: [MD = -0.68, 95%CI (-0.76, -0.60), P<0.00001], the difference between the treatment group and the control group was statistically significant, indicating that TCM compound enema combined with mesalazine could better reduce the colonoscopy Baron score.

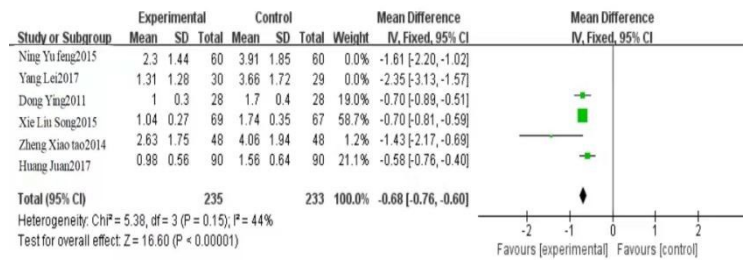


Figure 6: Baron score of enteroscopy after sensitivity analysis

3.4.3. DAI integral

DAI scores were reported in three included studies, 157 in the treatment group and 157 in the control group [12,17,18]. There was no significant heterogeneity among the studies (P<0.00001, I<sup>2</sup>=50%), so fixed effect model was adopted. Meta-analysis showed that [MD= -1.61, 95%CI (-1.81, -1.42), P<0.00001], the difference between the treatment group and the control group was statistically significant, indicating that TCM compound enema combined with mesalazine could better reduce DAI score, as shown in Figure 7.

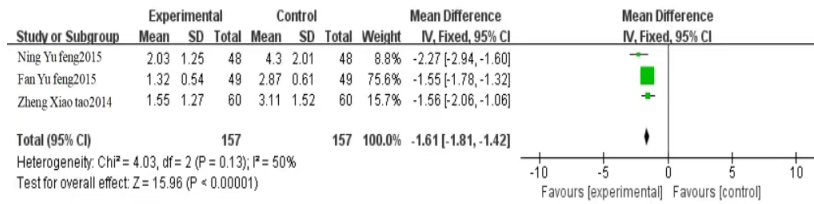


Figure 7: Meta-analysis of DAI integral

3.4.4. CRP

CRP scores were reported in 3 included studies, 110 in the treatment group and 110 in the control group [9,11,15]. The random effects model was adopted because of the large heterogeneity among studies (P<0.00001, I<sup>2</sup>=98%). Meta-analysis showed that [MD= -6.61, 95%CI (-7.29.56, -5.93), P<0.00001], the difference between the treatment group and the control group was statistically significant, indicating that TCM compound enema combined with mesalazine could more effectively reduce inflammation, as shown in Figure 8. Heterogeneity exists among various studies. Literature review shows that the average age of inclusion in Huo Hong's study is relatively large, so it may be considered as a factor leading to heterogeneity. However, due to the small number of literature articles involved, subgroup analysis was not conducted.

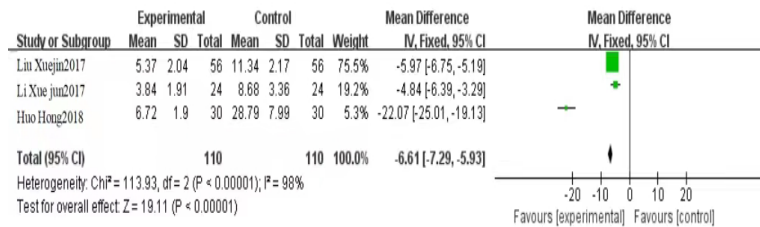


Figure 8: Meta-analysis of CRP

3.4.5. Clinical symptom score

Clinical symptom scores (abdominal pain, diarrhea, pus and blood stools) were reported in 4 included studies, including 196 cases in the treatment group and 196 cases in the control group [12,15,18,19]. There was significant heterogeneity among all studies (P<0.00001, I<sup>2</sup>=100% or I<sup>2</sup>=99%), so random effects model was adopted. Meta-analysis showed that [abdominal pain: MD=-1.03, 95%CI (-1.99,-0.07), P=0.03; diarrhea: MD= -0.86, 95%CI (-1.46, -0.25), P=0.006; pus, blood and stool: MD= -0.86, 95%CI (-1.62, -0.09), P=0.03], the difference between the treatment group and the control group was statistically significant, indicating that TCM compound enema combined with mesalazine could more effectively relieve clinical symptoms, as shown in Figure 9-11. There is great heterogeneity among all studies. Combined with the actual situation of each study, it can be found that there is a lack of unified standards for clinical symptom score, which may lead to great heterogeneity of results.

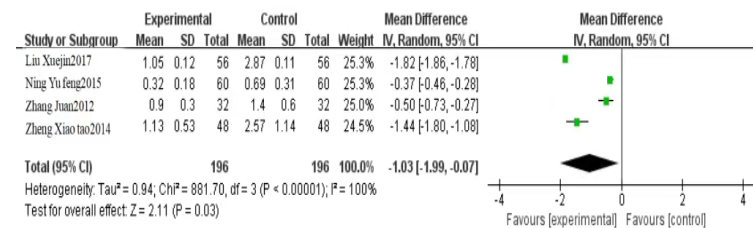


Figure 9: Meta-analysis of Abdominal pain

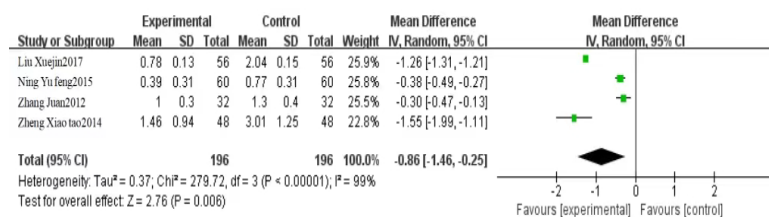


Figure 10: Meta-analysis of Diarrhea

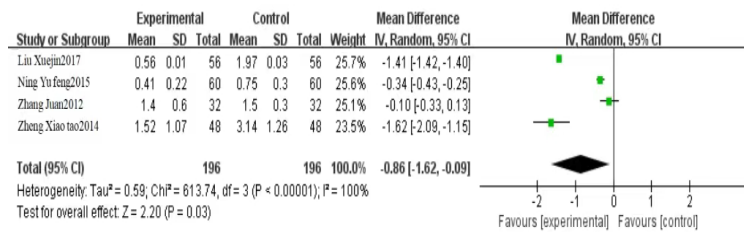


Figure 11: Meta-analysis of Purulent and bloody stool

### 3.5. Risk bias analysis

Funnel plots were drawn for the studies with more than 10 papers combined with outcome indicators, and the funnel plots of clinical effectiveness were obviously asymmetrical (Figure 12), indicating the existence of publication bias in the included studies.

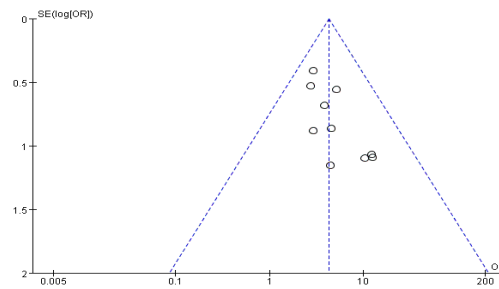


Figure 12: Published bias funnel plot of clinical effective rates

## 4. Discussions

### 4.1. Meta-result analysis

In this paper, a comprehensive search of RCTS meeting the inclusion criteria was conducted, and finally 11 literatures were included. Through data collation, a meta-analysis was conducted on 4 outcome indicators of UC treatment. According to the main indicators, it was concluded that the clinical effective rate of TCM compound enema combined with mesalazine was higher than that of mesalazine alone. Wei's team also mentioned at the 2020 American Digestive Disease Week [20]. By regulating Treg/ Th17-related immune factors, TCM can reduce the score of disease activity index and alleviate the damage of intestinal mucosa. TCM compound enema can also direct drugs to the disease site, effectively reduce the score of disease syndrome and regulate intestinal flora to a certain extent [21]. The team also further innovated TCM compound enema technology and applied TET tube in TCM enema, effectively solving the problems of tube folding, blockage and single tube administration in the practical operation of TCM compound enema, providing technical support for better clinical application of TCM compound enema [22]. At present, colonoscopy is the most direct and accurate examination means for the diagnosis and differentiation of UC, also known as the extension of TCM observation, which is very crucial in the integrated diagnosis and treatment of traditional Chinese and Western medicine. Now more and more scholars are committed to studying the correlation between mucosal signs under colonoscopy and TCM syndrome types, in order to provide objective basis for TCM syndrome differentiation and treatment [23-26]. It can be seen that the colonoscopy score is crucial in the diagnosis and treatment of UC, so it is necessary to conduct a meta-analysis of the colonoscopy Baron score of TCM compound enema in the treatment of UC. In this paper, a meta-analysis of intestinal Baron on secondary indexes showed that TCM compound enema combined with mesalazine could effectively reduce intestinal Baron and DAI scores. Liu Qiong et al. also concluded by discussing the progress of TCM treatment of UC that single TCM or TCM classic compound can effectively improve the intestinal mucosal injury of UC patients [27]. Zhao Hongbo et al. effectively reduced the mucosal score of patients with mild and moderate UC by injecting flavorful Radix Paeoniae decoction into the intestine [28]. Han Ying et al. found that Zhenzhen Zang Nourishing decoction can effectively slow down the development of inflammation by reducing the level of serum inflammatory factors, and its DAI score index was significantly reduced. In conclusion, Baron and DAI scores can effectively evaluate the changes of TCM compounds on the intestinal mucosa of patients with UC. Ulcerative



colitis is a chronic inflammatory disease. It is of great clinical significance to evaluate the effectiveness of drugs in treating inflammation using CRP [29]. This study conducted a meta-analysis of CRP values in three studies by Li Xuejun, Huo Hong and Liu Xuejin, and found that TCM compound enema could more effectively reduce CRP index. Zhu Leilei et al. mined the data of oral and enema treatment of UC with traditional Chinese medicine, summarized and analyzed the prescription rules, and concluded that *Coptis coptis* with the highest frequency was the medicine flavor, and the main component of *Coptis* was berberine hydrochloride [30]. Gan Jingang et al. confirmed through research that Berberine hydrochloride can regulate the imbalance of intestinal immunity by reducing the levels of inflammatory factors such as IL-8, IL-6 and TNF- $\alpha$  in serum, and effectively reduce the damage degree of large intestine mucosa [31]. This study also conducted a meta-analysis of its clinical symptoms (abdominal pain, diarrhea, and abscess and blood stools), and the results suggested that TCM compound enema combined with mesalazine could effectively alleviate the above clinical symptoms. However, due to the large subjectivity of various research literatures on clinical symptoms, the research results were not persuasive and scientific, so the study results were only used as a reference. A more comprehensive and standard assessment of this index should be made in future meta-analyses.

#### 4.2. Methodological quality

A large number of RCTS with high quality methodology is a necessary requirement to obtain high quality system evaluation [32]. According to the quality assessment maps obtained by the "bias risk assessment" tool provided by Cochrane, it can be determined that there are some methodological quality problems in this meta-analysis: (1) There is a certain gap in the sample size of the included literature, a certain imbalance in the age of patients, different treatment duration, complex composition of TCM compounds, and inconsistent dosage, which will lead to excessive heterogeneity in the final meta-analysis and reduce the universality of clinical application. (2) A total of 11 literatures were included in this study, of which only 1 used the central random allocation method of stratified block and double-blind method, and 6 used the random number table method. The other literatures only mentioned the random method, but did not specify the specific implementation method, and lacked certain standardization. (3) Several studies on the adverse reactions of this test and whether there is a shedding report are too simple and do not describe their situation in detail. (4) The limited number of included literatures may lead to certain limitations in the final results. To solve the above problems, the author has the following suggestions: (1) Further subgroup analysis of baseline data was made to comprehensively consider the causes of heterogeneity, in order to provide a basis for human-based treatment in clinical practice. (2) To improve the reliability of the test results, the method of stratified block central random assignment and double-blind method were adopted as far as possible. (3) Further detailed description of adverse reactions and shedding, increased follow-up, in order to guide clinical drug selection. (4) Refer to the criteria proposed by CONSORT [33]. Focus on improving the quality of RCTS.

This study focuses on the analysis of the effectiveness of simple TCM compound enema combined with Western medicine on UC, which is different from previous TCM comprehensive treatment studies and provides a clear direction for the future clinical selection of TCM compound enema. Although the results of this study show that: TCM compound enema combined with mesalazine can be more effective in the treatment of UC. However, due to the poor quality of the methodology, funnel plot showed certain publication bias, so more standardized, multi-center, large-sample and low-bias RCT evidence is still needed in the future.

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(2) Research Project of Shaanxi University of Traditional Chinese Medicine Affiliated Hospital (2020XZ001).

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