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Meta-analysis of the regulatory effect of traditional Chinese medicine on intestinal flora in patients with constipation

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Keywords: Chinese medicine; Intestinal flora; Constipation; Meta-analysis

Abstract: **Objective:** To systematically evaluate the regulatory effect of traditional Chinese medicine on intestinal flora in patients with constipation. **Methods:** From PubMed, Embase, Web of Science and Cochrane Library to December 2022, the qualified research was screened in strict accordance with the nanofiltration standard. The Cochrane bias risk assessment method and the modified Jadad scale were used to evaluate the quality of literature, and the meta-analysis was carried out using stata 15.0 software. **Results:** 16 clinical randomized controlled trials were finally included, with a total of 1099 patients. Meta-analysis shows that Chinese medicine can effectively promote bifidobacteria (SMD=0.95, 95% CI (0.78-1.12), Z=10.79, P=0.000<0.05), lactobacillus (SMD=0.61, 95% CI (0.25 - 0.98), Z=3.26, P=0.001<0.05), lactobacillus (SMD=0.72, 95% CI (0.42 - 1.03), Z=4.68, P=0.000<0.05) and gram-positive bacilli (SMD=2.12, 95% CI (1.65, 2.59), Z=8.90, P=0.000<0.05) in the intestine of constipation patients), It can inhibit Escherichia coli (SMD=-0.46, 95% CI (-0.66, -0.27), Z=4.69, P=0.000<0.05), enterobacteria (SMD=-0.86, 95% CI (-1.08, -0.64), Z=7.67, P=0.000<0.05), enterococcus (SMD=-0.42, 95% CI (-0.62, -0.22), Z=4.14, P=0.000<0.05), yeast (SMD=-0.94, 95% CI (-1.28, -0.59), Z=5.32, P=0.000<0.05) and gram negative cocci (SMD=-0.68, 95% CI (-1.23, -0.15), Z=2.50, P=0.012<0.05). There is no significant difference between traditional Chinese medicine and western medicine in terms of gram-negative bacilli (SMD=-0.19, 95% CI (-0.56,0.18), Z=1.02, P=0.306>0.05), gram-positive cocci (SMD=-0.23, 95% CI (-0.60,0.13), Z=1.26, P=0.208>0.05), and cocci ratio (SMD=1.32, 95% CI (-0.22,1.16), Z=1.92, P=0.186>0.05). In addition, traditional Chinese medicine can reduce the intestinal PH value of constipation patients (SMD=-0.85, 95% CI (-1.11, -0.59), Z=6.38, P=0.000<0.05), and keep the intestinal micro-ecological environment in balance. **Conclusion:** Compared with western medicine, traditional Chinese medicine has more advantages in regulating intestinal flora of constipation patients.

1. Introduction

Constipation refers to a group of symptoms related to excretion disorders, mainly including reduced stool frequency, reduced stool volume, dry stool, delayed and laborious stool [1]. According to the presence or absence of organic diseases, constipation can be divided into functional constipation (FC) and organic constipation. FC is the most common type of constipation in clinical practice. Constipation is a serious threat to human physical and mental health. Long-term constipation will cause anorectal diseases, gastrointestinal nerve dysfunction, induce and aggravate various cardio-cerebrovascular diseases, and even induce colorectal cancer, hepatic encephalopathy, etc. [2].

Intestinal microflora is a huge micro-ecosystem in human intestines [3]. It is one of the main components of feces, accounting for about 1/3 of the dry weight of feces. Therefore, the change of host intestinal microflora is an important factor affecting the normal defecation function [4]. In recent years, the relationship between constipation and intestinal microecology has become more and more close, and more and more clinical studies have used microecological agents and microflora transplantation technology to treat constipation, and have achieved significant results. Compared with western medicine, traditional Chinese medicine has obvious advantages in the treatment of constipation and has been confirmed by extensive clinical and animal experiments. However, it is not clear whether traditional Chinese medicine is superior to probiotics or western medicine in regulating the intestinal flora of constipation patients. This study adopts a systematic evaluation method to conduct a meta-analysis of the previous clinical research literature to provide high-quality evidence-based medical evidence for clinical guidance.

2. Data and methods

2.1. Literature retrieval

Two researchers independently used the key words (subject words plus free words) to retrieve the research published on CNKI, Wanfang, VIP, PubMed, Embase, Web of Science and Cochrane Library from the establishment of the database to December 2022, The retrieval strategy takes Wanfang database as an example: subject: (traditional Chinese medicine or traditional Chinese medicine or traditional Chinese medicine) and subject: (constipation or dry stool or defecation disorder not incontinence) and subject: (intestinal flora or flora or gastrointestinal flora or intestinal flora or intestinal microecology).

2.2. Inclusion and exclusion criteria

The inclusion criteria are as follows:

(1) Study population: patients diagnosed as constipation in the recognized diagnostic criteria (such as Rome IV standard), age ≥ 18 years old, without gender, country, region and race restrictions.

(2) Intervention measures: the control group was treated with western medicine alone; The treatment group was treated with traditional Chinese medicine alone or combined with traditional Chinese medicine on the basis of the control group. There was no restriction on the specific drug type, dosage form, and route of administration.

(3) Outcome measures: changes in intestinal flora and fecal PH value.

(4) Research type: Randomized controlled trial (RCT), regardless of the allocation concealment method or blind method.

(5) Language: limited to Chinese and English documents.

Exclusion criteria:

(1) Subjects: studies that did not specifically describe the diagnostic criteria for constipation or did not meet the diagnostic criteria.

(2) Intervention measures: In the treatment group, there was no Chinese medicine treatment or other Chinese medicine treatment methods such as acupuncture and moxibustion, acupoint application, cupping, etc. were used; The treatment group used western medicine which was inconsistent with the control group; The control group used traditional Chinese medicine or non-drug treatment methods such as surgery and bacterial colony transplantation.

(3) Outcome indicators: there is no study on the change of intestinal flora or the outcome indicators cannot be extracted.

(4) Research type: research without random method or design.

(5) Sample size: research with sample size ≤ 20.

(6) In vitro experiments, animal experiments, comments, letters, guidelines, case reports, pathological mechanisms, conference summaries, reviews or systematic evaluations.

(7) Repetitive publications or studies lacking reliable data.

(8) Research on writing in other languages.

2.3. Literature screening and data extraction

Two researchers independently screened all articles identified by the database. First, use EndNote X 9.0 software to remove duplicate documents and exclude case reports, meeting summaries, letters and review articles. Then, screen the titles and abstracts of the remaining literature, exclude the research irrelevant to the subject, and review the full text of the remaining research to determine the eligible research. Finally, we manually searched the review articles, meta-analysis and the list of references of the included studies related to this study. Any differences encountered in the course of this study were resolved through discussion with the third researcher.

The two researchers independently extracted the following data from studies that met the inclusion criteria: (1) General data: first author, year of publication, diagnostic criteria and efficacy criteria; (2) Study object characteristics: sample size, gender, age and course of disease; (3) Intervention measures: drug type, dosage form, dose, frequency, mode of administration, course of treatment and follow-up time. (4) Observation index: changes of intestinal flora and PH value. (5) Study design: random allocation method, allocation concealment and blind method.

2.4. Quality assessment

The quality of the study was evaluated with reference to Cochrane's bias risk assessment method and the modified Jadad scale [5]. It mainly includes random sequence generation, allocation concealment, use of blind method, data integrity, selective reporting and other bias, as shown in the figure. The score of the modified Jadad scale [6] is considered as low quality between 1-3 and high quality between 4-7, as shown in the figure below.

2.5. Statistical analysis

Meta-analysis is conducted by using the software Stata 15.0. The relative risk (OR) is used to represent the general measure of the effect value of the binary variable, and the weighted mean difference (WMD) is used to represent the statistical measure of the effect value of the continuous variable. If the observation indicator unit is not uniform, the standardized mean difference (SMD) is used. All effects are expressed with 95% confidence interval (CI). For the judgment of heterogeneity, refer to the P value and I2 value of Q test at the same time. If $P>0.1$ and $I2<50\%$, it

means that there is little or no heterogeneity among the studies, and the fixed effect model can be used to calculate the effect amount; On the contrary, it is believed that there is heterogeneity among the studies, and the random effect model is used to combine the effect quantity. At the same time, it is necessary to further explore the source of heterogeneity through sensitivity analysis and subgroup analysis. Finally, the publication bias is visually presented by funnel graph, and Egg's test and Egg's test are used for statistical test. If the funnel graph is symmetrical, the Begg test P>0.05 and Egg's test P>0.05, which means that there is no publication bias in the literature selected in this study; On the contrary, it is believed that the included literature may have publication bias.

3. Results

3.1. Literature search results

According to the retrieval strategy, 892 articles were retrieved and 4 were supplemented by other means. 75 duplicate articles were removed. Then read the title and abstract of the literature according to the Napier criteria, and 762 articles were excluded. The remaining 59 articles were initially included. Through reading the full text and analysis, 43 articles were excluded, mainly because the intervention measures were inconsistent and the data could not be extracted. Finally, 16 articles were included in the meta-analysis, and the literature screening process is shown in Fig.1.

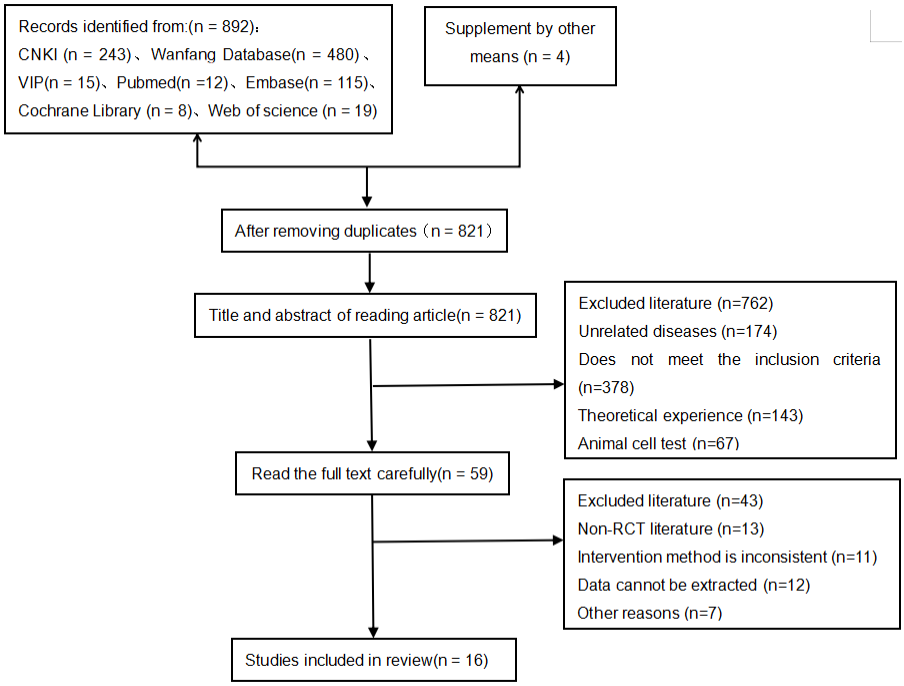

Figure 1: Screening process of literature

3.2. Basic characteristics of included documents

A total of 16 [7-22] studies were included, all of which were single-center studies published in China from 2007 to 2022. A total of 1099 patients were involved. The number of men and women was 507 (46.13%) and 592 (53.87%), respectively. The number of experimental group and control group was 551 and 548, respectively. There was no statistical difference in the general data between the patient groups (P>0.05), which was comparable. The results are shown in Table 1.

Table 1: Basic features of the included literature

Study	Cases(n)	Age		Interventions		Course of treatment	Outcome indicators	Jadad (scores)
	T/C	T	C	T	C			
Zhu Yeshan 2022[7]	36/36	55.43±5.95	54.21±5.76	Dispelling Turbidity, Detoxicating and Runchang Formula	Compound polyethylene glycol electrolyte powder (IV)	4 weeks	(1)(3)(4)	5
Zhang Desheng 2021[8]	63/63	61.39±11.57	61.24±11.86	Shengxue Tongbian Granules, Polycurate Sodium Tablets	Sodium docurate tablets	2 weeks	(1)(2)(5)	3
Li Jie 2021[9]	29/28	41.72±9.39	41.11±10.36	Jiezhuo Jiedu Tongbian Granules	Macrogol 4000 Powders	4 weeks	(1)(2)(5)(6)	4
He Yu 2021[10]	30/30	56.73±8.5	56.66±7.7	Modified Huangqi Decoction, Compound Lactobacillus acidophilus tablets	Compound lactobacillus acidophilus tablets	4 weeks	(1)(3)(4)(6)	3
Zhang Guiying 2020[11]	30/30	56±12.6	58±10.2	Self-made Zhipu Jieyu Decoction and Compound Polyethylene Glycol Electrolyte Powder (IV)	Compound polyethylene glycol electrolyte powder (IV)	1 month	(1)(2)(3)	1
Yang Feng 2020[12]	50/49	65.8±9.2	66.0±8.8	Yuan Xingshi's empirical prescription "Jichuan Yanshou Cream", lactulose oral solution, domperidone tablets	Lactulose oral solution, domperidone tablets	4 weeks	(1)(2)(3)	4
Ma Yan 2020[13]	30/30	38.9±12.54	40.23±15.19	Hospital preparation Linggu mixture	mosapride citrate tablets	3 weeks	(1)(2)(3)(6)(12)(13)	4
Zhang Huan 2019[14]	30/30	67.62±8.45	65.14±7.63	Flavored Xiaojianzhong Soup, Cisapli	Sishabili	10 days	(1)(2)(3)(5)	3
Li Beiting 2019[15]	36/36	42.78±9.68	43.92±9.09	Intestinal Runfang	Macrogol 4000 Powders	4 weeks	(1)(2)(3)(6)(12)(13)	4
Zhang Shuangxi 2018[16]	59/59	68.3±4.7	67.8±4.2	Jichuan decoction, prukaspiride succinate tablets	Prukapril succinate tablets	1 month	(1)(4)(5)(7)	4
Yu Shaolei 2015[17]	30/30	39.0±10.7	40.6±9.5	Huangqi Runchang Pill	Cisapride Tablets	4 weeks	(8)(9)(10)(11)(12)	1
Pan Yan 2007[18]	26/27	65.69±10.83	63.70±14.20	Yiqi Yangyin Tongbian Decoction	Macrogol 4000 Powders	3 weeks	(1)(2)(5)(6)(7)(12)	3
Li Yaqi 2020[19]	28/29	44.89±7.86	44.45±7.48	Self-made Shugan Xingqi Decoction	Compound polyethylene glycol electrolyte powder (IV)	4 weeks	(8)(9)(10)(11)(13)	2
Xiao Changfang 2019[20]	29/26	63.79±14.28	57.5±17.55	Yiqi Kaiji Recipe, Clostridium butyricum viable tablets	Clostridium butyricum viable tablets	4 weeks	(8)(9)(10)(11)	4
Duan Xiaoxin 2022[21]	30/30	48.47±11.19	47.40±8.20	Prescription for invigorating qi, invigorating spleen and relieving constipation	Prukapril succinate tablets	4 weeks	(1)(2)(5)(6)(7)(12)(13)	4
Tianjun 2021[22]	15/15	65.6±12.1	66.7±10.9	Yiqi Yangyin Tongbian Decoction	Macrogol 4000 Powders	3 weeks	(1)(2)(5)(6)	4

Note: T: Test group C: Control group (1) Bifidobacterium (2) Lactobacillus (3) Escherichia coli (4) Lactobacillus (5) Enterobacterium (6) Enterococcus (7) Yeast (8) Gram-positive bacilli (9) Gram-negative bacilli (10) Gram-positive cocci (11) Gram-negative cocci (12) Corynecoccus ratio (13) Fecal pH value

3.3. Quality evaluation of inclusion research methodology

All 16 papers mentioned random grouping, among which 1 paper [17] described the wrong random grouping method (odd and even number grouping according to the outpatient visit date), 2 papers [11, 19] did not specifically describe the random grouping method, and the other 13 papers described the random number table method; Two papers [7,15] reported the method of allocation concealment, one study [17] adopted the single-blind method, and 10 papers [7,9,12,13,16,17,19-22]

described the number of missing cases, causes and treatment methods. The missing data were small and basically balanced between groups, which did not affect the true value of the results; All the literatures reported the designed observation indicators, and it is unclear whether there are other sources of bias. The results are shown in Figure 2 and Figure 3. The quality of literature was evaluated according to the improved Jadad scale, and the literature with score ≥ 1 could be included in this study. Among them, 2 papers [11, 17] scored 1 point, and 9 papers [7,9,12,13,15-16,20-22] scored ≥ 4 points. See Table 1 for the results.

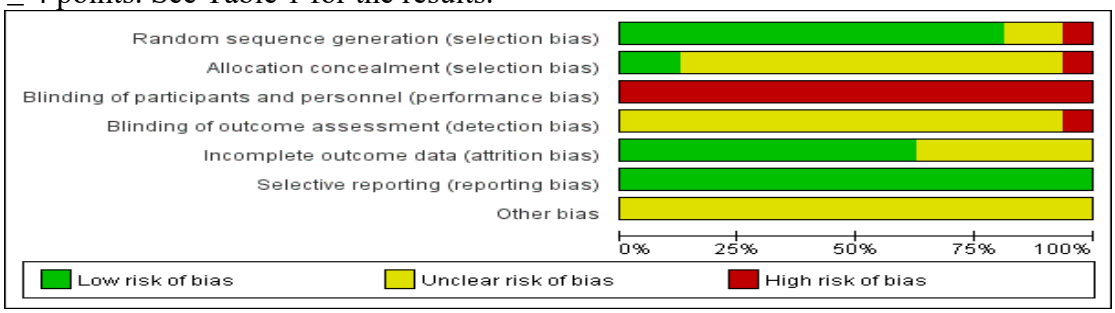

Figure 2: Bias risk map

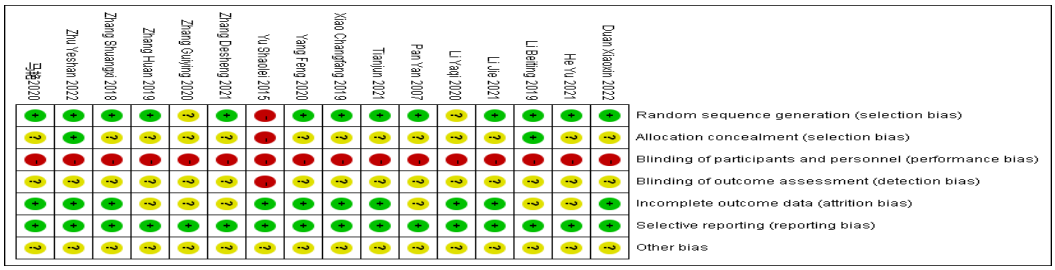

Figure 3: Included study bias risk assessment diagram

3.4. Meta-analysis results

3.4.1. Variation of bifidobacteria

Thirteen papers [7-16,18,21-22] reported the change of bifidobacteria. Through the heterogeneity test, it was suggested that there was high heterogeneity among the selected papers in this study (I2=94.3%>50%, P=0.000<0.1). In order to ensure the accuracy and stability of the study, the sensitivity analysis was continued. It was found that the research of Zhang Guiying [11], Zhu Yeshan [7], Zhang Desheng [8] and Zhang Huan [13] had a great impact on the heterogeneity, as shown in Figure 4. After removing four documents, the heterogeneity test was conducted again, and the results showed that the remaining nine documents were less heterogeneous (I2=41.4%>50%, P=0.091<0.1). The fixed effect was used for the meta-analysis. The results were statistically significant (SMD=0.95, 95% CI (0.78-1.12), Z=10.79, P=0.000<0.05). It is suggested that traditional Chinese medicine is better than western medicine in promoting the growth of bifidobacteria in the intestine of constipation patients, as shown in Figure 5.

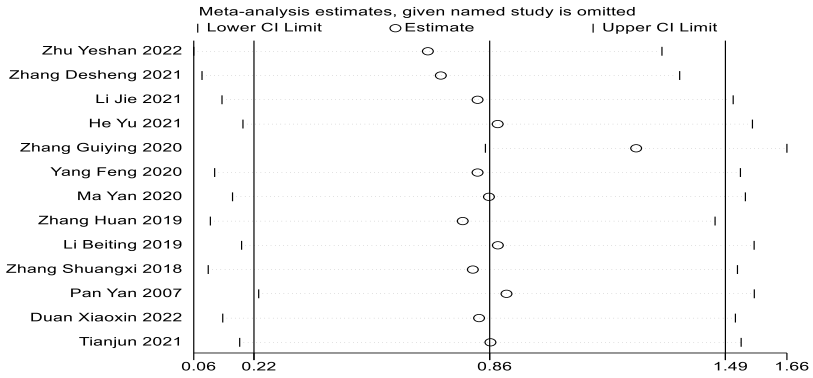

Figure 4: Sensitivity analysis of changes in bifidobacteria

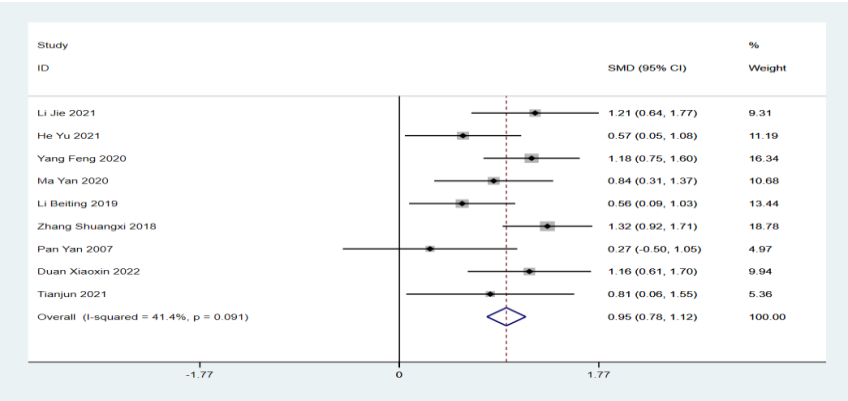

Figure 5: Forest map of quantitative quantity of bifidobacteria

3.4.2. Change amount of lactobacillus

Ten papers [8-15, 18, 21-22] reported the change of lactobacillus. Through the heterogeneity test, it was suggested that there was a high heterogeneity among the papers selected in this study (I2=95.6%>50%, P=0.000<0.1). In order to ensure the accuracy and stability of the study, sensitivity analysis was continued. It was found that the study of Zhang Desheng [8] and Zhang Guiying [11] had a significant impact on heterogeneity. After removing two studies, the heterogeneity test was conducted again. The results showed that the heterogeneity was significantly lower than before (I2=72.5%>50%, P=0.001<0.1). The results of meta-analysis using random effects were statistically significant (SMD=0.61, 95% CI (0.25 - 0.98), Z=3.26, P=0.001<0.05). It is suggested that traditional Chinese medicine has significant advantages in promoting the growth of lactobacillus in the intestine of constipation patients. See Figure 6 for details.

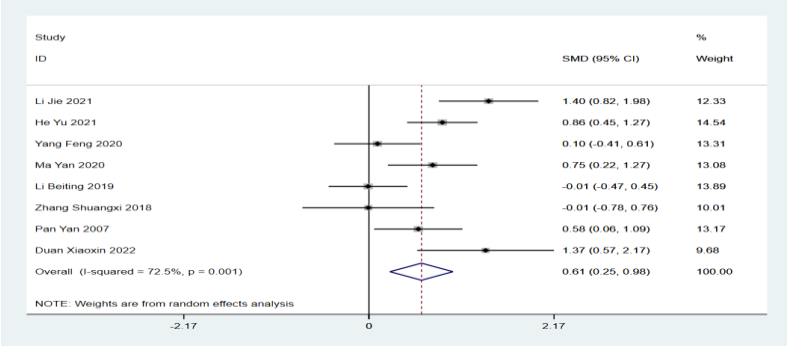

Figure 6: Forest map of lactobacillus change

3.4.3. Change of Escherichia coli

Seven papers [7, 10-15] reported the change of Escherichia coli. Through the heterogeneity test, it was suggested that there was high heterogeneity among the papers selected in this study (I2=84%>50%, P=0.000<0.1). In order to ensure the accuracy and stability of the study, sensitivity analysis was continued. It was found that the study of Zhang Guiying [11] had a great impact on heterogeneity. After removing the study, the heterogeneity test was conducted again. The results showed that the remaining six articles had a small heterogeneity (I2=35.4%<50%, P=0.171>0.1). The results of meta-analysis using fixed effects were statistically significant (SMD=-0.46, 95% CI (-0.66, -0.27), Z=4.69, P=0.000<0.05). It is suggested that traditional Chinese medicine can effectively inhibit the growth of Escherichia coli in the intestine of constipation patients, and the effect is better than that of western medicine group. As shown in Figure 7.

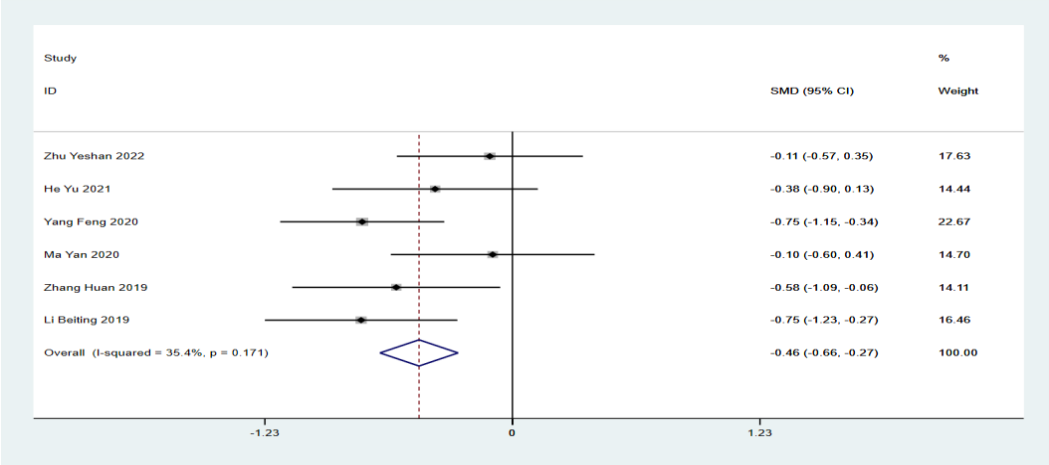

Figure 7: Change of Escherichia coli in forest

3.4.4. Change amount of lactobacillus

Three papers [7, 10, 16] reported the change of lactobacillus. The heterogeneity test showed that there was significant heterogeneity between the selected papers in this study (I2=59.8%>50%, P=0.083<0.1). It was found that after removing the study of Zhu Yeshan [7], there was no heterogeneity in the remaining two articles (I2=0%<50%, P=0.428>0.1). The results of meta-analysis using fixed effects were statistically significant (SMD=0.72, 95% CI (0.42 - 1.03), Z=4.68, P=0.000<0.05). It is suggested that traditional Chinese medicine has significant advantages in promoting the growth of lactobacillus in the intestine of constipation patients.

3.4.5. Change of Enterobacteriaceae

Seven papers [8,9,14,16,18,21-22] reported the change of Enterobacteriaceae. Through the heterogeneity test, it was suggested that there was a high heterogeneity among the papers selected in this study (I2=89.7%>50%, P=0.000<0.1). In order to ensure the accuracy and stability of the study, sensitivity analysis was continued. It was found that the research of Zhang Desheng [8] had a great impact on heterogeneity. After removing the research, the heterogeneity test was carried out again. The results showed that the remaining six articles had low heterogeneity (I2=37.1%<50%, P=0.159>0.1). The results of meta-analysis using fixed effects were statistically significant (SMD=-0.86, 95% CI (-1.08, -0.64), Z=7.67, P=0.000<0.05). It is suggested that traditional Chinese medicine can effectively inhibit the growth of intestinal enterobacteria in constipation patients, and the effect is better than that of western medicine group. As shown in Figure 8.

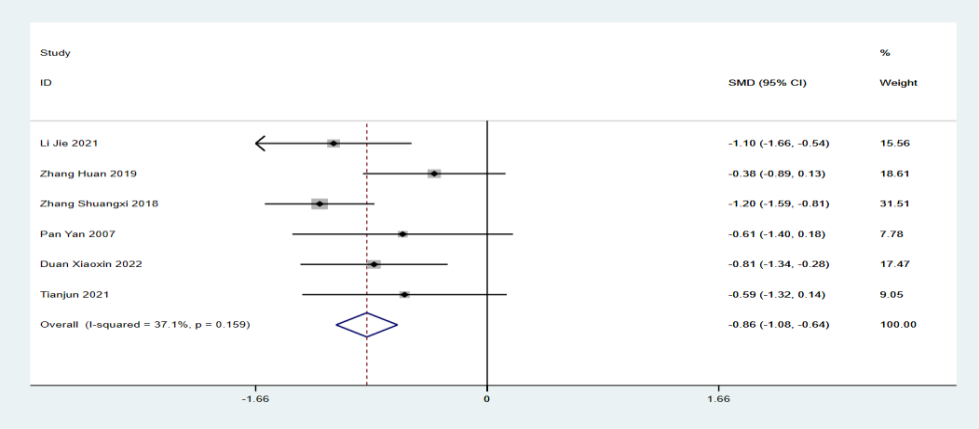

Figure 8: Change of Enterobacteriaceae

3.4.6. Change amount of enterococcus

Eight papers [9,10,13-15,18,21-22] reported the change of enterococcus. After the heterogeneity test, I2=42.4%<50%, but the Q test P=0.096<0.1, suggesting that there is heterogeneity between the selected papers in this study. In order to ensure the accuracy and stability of the study, sensitivity analysis was continued. It was found that Tian Jun's research [22] had a great impact on heterogeneity. After removing the research, the heterogeneity test was conducted again. The results showed that the remaining seven articles had no heterogeneity (I2=0.0%<50%, P=0.913>0.1). The results of meta-analysis using fixed effects were statistically significant (SMD=-0.42, 95% CI (-0.62, -0.22), Z=4.14, P=0.000<0.05). It is suggested that traditional Chinese medicine can effectively inhibit the growth of enterococcus in the intestine of constipation patients, and the effect is better than that of western medicine group. As shown in Figure 9.

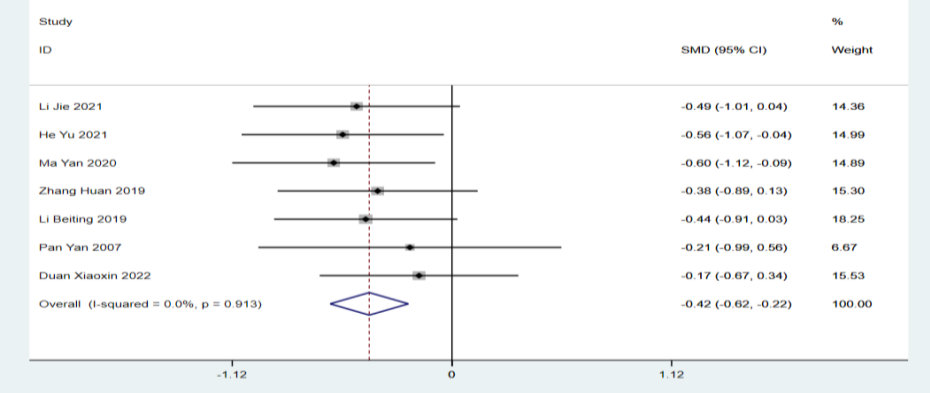

Figure 9: Change of enterococcus forest

3.4.7. Variation of yeast

Two papers [16,18] reported the variation of yeast. Through the heterogeneity test, it was suggested that the heterogeneity between the papers selected in this study was low (I2=4.3%<50%, P=0.307>0.1). The fixed effect was used for meta-analysis. The results were statistically significant (SMD=-0.94, 95% CI (-1.28, -0.59), Z=5.32, P=0.000<0.05). It is suggested that traditional Chinese medicine can effectively inhibit the growth of yeast in the intestine of constipation patients, and the effect is better than that of western medicine group.

3.4.8. Gram-positive bacilli

Three papers [17,19-20] reported the change of Gram-positive (G+) bacilli. Through the heterogeneity test, it was suggested that there was a high heterogeneity among the papers selected in this study (I2=87.3%>50%, P=0.000<0.1). Yu Shaolei's [17] study used the wrong randomized control method, which may be the source of heterogeneity. After removing this article, the remaining two articles have no heterogeneity (I2=0.0%<50%, P=0.458>0.1). The results of meta-analysis using fixed effects are statistically significant (SMD=2.12, 95% CI (1.65, 2.59), Z=8.90, P=0.000<0.05). It is suggested that traditional Chinese medicine has significant advantages in promoting the growth of G+bacilli in the intestines of constipation patients.

3.4.9. Gram-negative bacilli

Three papers [17,19-20] reported the change of Gram-negative (G -) bacilli. Through the heterogeneity test, it was suggested that there was high heterogeneity among the selected papers in this study (I2=83.5%>50%, P=0.002<0.1). After Li Yaqi's [19] study was removed, the remaining two papers were less heterogeneous (I2=37.3%<50%, P=0.207>0.1). The results of meta-analysis using fixed effects showed no statistical significance (SMD=-0.19, 95% CI (-0.56,0.18), Z=1.02, P=0.306>0.05), suggesting that there was no difference between the effects of traditional Chinese medicine and western medicine on the change of Gram-negative bacilli in the intestine of constipation patients. A lot of research is needed to prove it in the future.

3.4.10. Gram-positive cocci

Three papers [17,19-20] reported the change of Gram-positive cocci. The heterogeneity test showed that there was high heterogeneity among the selected papers in this study (I2=85.9%>50%, P=0.001<0.1). After removing Xiao Changfang's [20] study, there was no heterogeneity between the remaining two articles (I2=0.0%<50%, P=0.943>0.1). The results of meta-analysis using fixed effects showed no statistical significance (SMD=-0.23, 95% CI (-0.60,0.13), Z=1.26, P=0.208>0.05). It is suggested that there is no difference in the influence of traditional Chinese medicine and western medicine on the change of Gram-positive cocci in the intestine of constipation patients.

3.4.11. Gram-negative cocci

Three papers [17,19-20] reported the change of Gram-negative cocci. Through the heterogeneity test, it was suggested that there was a high heterogeneity among the papers selected in this study (I2=92.6%>50%, P=0.000<0.1). When Xiao Changfang [20]'s study was removed, the heterogeneity was significantly reduced (I2=51.7%>50%, P=0.150>0.1). The results of meta-analysis using random effects were statistically significant (SMD=-0.68, 95% CI (-1.23, -0.15), Z=2.50, P=0.012<0.05). It is suggested that traditional Chinese medicine can effectively inhibit the growth of gram-negative cocci in the intestine of constipation patients, and the effect is better than that of western medicine group.

3.4.12. Corynecoccus ratio

Five papers [13,15,17-18,21] reported the ratio of cocci, and the heterogeneity test showed that the heterogeneity between the selected papers in this study was high (I2=88.6%>50%, P=0.000<0.1). In order to ensure the stability and accuracy of the study, sensitivity analysis was continued. It is found that the heterogeneity is caused by multiple documents, and the heterogeneity is still significant after deleting one or several of them. The results of meta-analysis of random

effects were not statistically significant (SMD=1.32, 95% CI (-0.22,1.16), Z=1.92, P=0.186>0.05). It is suggested that there is no difference in the effect of traditional Chinese medicine and western medicine on the ratio of enterococci in constipation patients.

3.4.13. PH value of stool

Four papers [13,15,19,21] reported the PH value of feces, and the heterogeneity test showed that there was no heterogeneity between the papers selected in this study (I2=0%<50%, P=0.813>0.1). The fixed effect was selected for meta-analysis, and the results were statistically significant (SMD=-0.85, 95% CI (-1.11, -0.59), Z=6.38, P=0.000<0.05). It is suggested that traditional Chinese medicine can effectively reduce the PH value of the intestine of constipation patients, and the effect is better than that of western medicine group.

3.5. Publication bias

The publication bias was evaluated for the change of bifidobacteria. The funnel graph showed that the left and right sides were basically symmetrical, as shown in Figure 10. The Begg test (P=0.502>0.05) and Egger test (P=0.109>0.05) were continued, and the results showed that there was no publication bias.

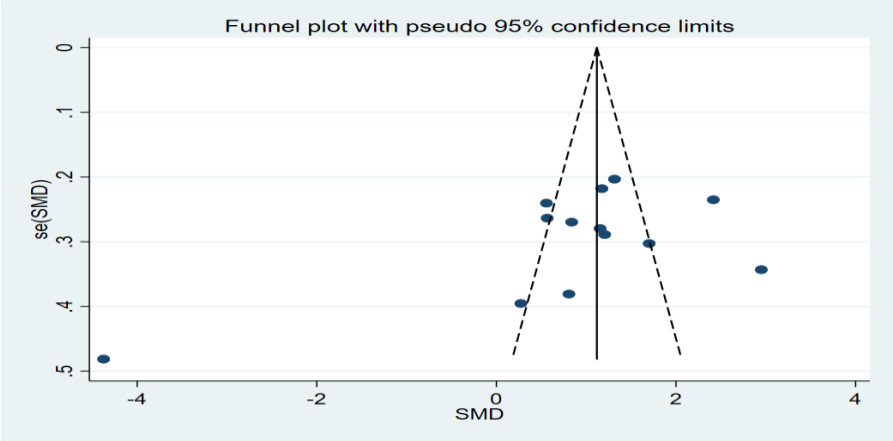

Figure 10: Funnel diagram of publication bias

4. Discussion

Traditional Chinese medicine can regulate the intestinal microecosystem by improving the richness and diversity of intestinal microflora in patients with constipation. According to the current research, the influence of traditional Chinese medicine prescription on intestinal flora is mainly reflected in the contrast between the growth and decline of anaerobic bacteria and aerobic bacteria [23]. For example, Runchang prescription can promote the proliferation of bacteroides, bifidobacteria and lactobacillus in the intestine of constipation patients, and can inhibit the growth of pathogenic bacteria such as Escherichia coli and enterococcus [24]. In addition, many animal experimental studies have also proved the regulatory effect of traditional Chinese medicine on intestinal microflora. For example, Tongfu Jiangzhuo Formula can increase the abundance of intestinal microflora in constipation model rats. After treatment, the abnormal microflora structure can almost recover to the level of normal group [25]. Zhuyang Tongbian Ointment maintains the homeostasis of intestinal flora by regulating the intestinal bacteria of constipation rats, and improves constipation symptoms by regulating water and electrolyte permeability [26].

Stable intestinal pH is an important factor to maintain the stability of the intestinal

microenvironment. On the contrary, the disturbance of intestinal flora will also affect the intestinal pH, and different intestinal flora also have relative selectivity to the range of environmental pH. This study shows that traditional Chinese medicine can effectively reduce the intestinal PH value of constipation patients, and make the intestinal micro-ecological environment more in line with the requirements of beneficial bacteria reproduction. Bifidobacterium will produce a large amount of lactic acid and acetic acid in the process of metabolism, which has the effect of reducing the pH value of the intestinal tract and maintaining the intestinal tract in a weak acidic environment [27]. When the intestinal microflora is unbalanced, the anaerobic bacteria will significantly reduce, the acid-producing capacity will be reduced, and the intestinal tract will be full of a large amount of oxygen, resulting in an increase in the pH value [28].

Based on the comprehensive analysis of previous relevant literature, the meta-analysis results of various outcome indicators show that traditional Chinese medicine has a better effect on promoting the growth and reproduction of bifidobacteria, lactobacillus, lactobacillus and G+bacilli than the western medicine group, and can effectively inhibit the growth of Escherichia coli, enterobacteria, enterococcus, yeast and G-cocci, effectively reduce the pH value of the intestine, and provide a suitable growth environment for beneficial bacteria in the intestine. There is no significant difference between traditional Chinese medicine and western medicine in the change of the ratio of G-bacilli, G+cocci, and cocci in the intestine of constipation patients.

This study has certain advantages. First of all, we have included larger sample studies, which is the first systematic review to compare the regulatory effects of traditional Chinese medicine and western medicine on intestinal flora of constipation patients. Secondly, there is no significant publication bias in this study. However, our research also has some limitations: (1) This study includes a small number of low-quality documents, which may affect the accuracy of the research report. (2) Different bacterial count units used in the included literature may increase the heterogeneity of the results. (3) The variation of the ratio of G+bacilli, G - bacilli, G+cocci, G - cocci and rodcoccus in the outcome indicators included in this study is characterized by a large range of microbiota and unclear names, which may increase the heterogeneity of the research results.

To sum up, traditional Chinese medicine is significantly better than western medicine in regulating the intestinal flora of constipation patients, which can effectively promote the growth of beneficial bacteria and inhibit the proliferation of harmful or potential pathogenic bacteria. In the future, more high-quality, large-sample, multi-center clinical research, animal experimental research and molecular biological research are needed to enrich the evidence resources of evidence-based medicine, and make the mechanism of TCM in regulating diseases clearer and more convenient to guide clinical medication.

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