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Comparison of Traditional Chinese Medicine with Trimebutine Maleate in the Treatment of Diarrhea-type Irritable Bowel Syndrome: A Meta-analysis

Mengyao Tan*, Yongju Wang, Qian Yang

Changchun University, Changchun, Jilin, China.

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***Corresponding author:** Mengyao Tan, Changchun University, Changchun, Jilin, China.

Abstract

Objective: To compare the clinical efficacy of traditional Chinese medicine with trimebutine maleate in the treatment of diarrheal irritable bowel syndrome (liver stagnation and spleen deficiency type). **Methods:** The computer searched CNKI, Wangfang Data, VIP, Chinese Medical Database, web of science, PubMed, and The Cochrane Library for clinical randomized controlled trials of traditional Chinese medicine versus trimebutine maleate in the treatment of IBS-D, and analyzed the data with RevMan and Stata software. **Results:** A total of 20 RCTs with a total of 2,496 subjects were included, with 1,270 in the treatment group and 1,226 in the control group. The results of the meta-analysis revealed that traditional Chinese medicine outperforms trimebutine in terms of total effective rate of treatment, abdominal pain score, diarrhea score, bloating score, defecation satisfaction score, defecation frequency score, stool trait score, irritability, adverse reactions, and recurrence rate, and the difference is statistically significant ($P<0.05$). **Conclusion:** Traditional Chinese medicine has definite efficacy in the treatment of IBS-D, and the effect is superior to trimebutine maleate, making it suitable for clinical promotion and application.

Keywords

Traditional Chinese medicine, Trimebutin, Diarrhea-predominant irritable bowel syndrome, Meta-analysis

The irritable bowel syndrome (IBS) is a chronic gastrointestinal disorder that is most common in digestive diseases and has a serious impact on patients' quality of life and work efficiency. It is characterized by recurrent abdominal pain and various changes in the stool. IBS is classified into four subtypes based on the Rome IV diagnostic criteria: constipation (IBS-C), diarrhea (IBS-D), mixed (IBS-M), and amorphous (IBS-A) (IBS-U). The diarrheal type is the most common among them. Epidemiological studies have revealed that the incidence of IBS-D is related to age and gender, with the prevalence being higher in people under the age of 50, and the incidence in women being slightly higher, at around 11.2% globally [1]. The prevalence varies greatly between different regions, and IBS-D is the most common in IBS patients in China [2]. Most researchers believe that it is the result of a combination of circumstances; these factors may be strongly related to aberrant brain-gut axis control, intestinal dysbacteriosis, and visceral hypersensitivity. Its pathophysiology is quite complex, and it is still unknown. There is no set course of treatment; clinical therapy is currently focused primarily on relieving symptoms. Western medicine tends

to use drug therapy, but this has many side effects, is expensive, and has poor efficacy. Traditional Chinese medicine, on the other hand, has the advantages of being multi-component, multi-channel, and multi-target, as well as having good curative effects and fewer side effects. There have been numerous publications in recent years on the use of traditional Chinese medicine in the treatment of IBS-D, but there are few pertinent systematic reviews. In order to provide an evidence-based medical foundation for clinical treatment, this article collects randomized controlled trials that compare traditional Chinese medicine with western medicine in the treatment of IBS-D.

1. Information and approach

1.1 Literature search

Computer search for randomized controlled trials (RCTs) of traditional Chinese medicines versuswestern drug trimebutine maleate for the treatment of diarrhea-type irritable bowel syndrome in 7 databases: CNKI, Wanfang Database, Weipu Database, Chinese Medical Database, web of science, PubMed, and The Cochrane Library .Terms include:“Chinese medicine”, “trimebutine”, “trimebutine maleate”, “irritable bowel syndrome”, “intestinal irritable syndrome”, “IBS”, “IBS-D”. The search period was from the beginning of the establishment of the library to January 3, 2023. In order to avoid omissions, it is also combined with manual search.

1.2 Inclusion criteria

(1) RCTs published only in Chinese and English; (2) Research subjects: patients with a valid case of IBS-D (hepatic depression and spleen deficiency type), with no limit on gender, age and course of the disease; (3) Interventions: Traditional Chinese medicine was mostly employed for the treatment group (referring to the use of traditional Chinese medicine only, which can be a combination of prescriptions). Trimebutine maleate was provided to the control group; (4) The efficacy is clear, and there are detailed treatment plans and outcome reports. The above four items need to be met at the same time.

1.3 Literature exclusion criteria

(1) Non-Chinese and English literature totally unconnected to controlled clinical studies, such as reviews, conference papers, or laboratory studies; (2) The treatment group was treated with non-simple traditional Chinese medicine or the control group was treated with a combination of western medicine; (3) Other types other than IBS-D; (4) Chinese medicine formulas adopt non-internal administration methods, such as enemas, umbilical compresses, etc. It can be removed if the aforementioned condition is met.

1.4 Data Extraction

The two researchers freely screened the summarized literature and used Excel to produce a table which contains data such as basic literature information, sample size, intervention, course of treatment, and outcome indicators. If there is disagreement, a third researcher steps in to make a decision.

1.5 Risk of bias assessment

Risk of bias was mapped using the risk of bias assessment tool recommended by the Cochrane Handbook, and assessed by two investigators independently to make "low", "unclear" and "high" judgments for each bias. When the results diverge, a third investigator makes the decision.

1.6 Statistical Methods

For the purpose of this research's data analysis, RevMan 5.4 and Stata software have been used. With 95% confidence intervals, effect sizes were expressed as odds ratios (OR) for dichotomous outcomes and mean differences (MD) and standardised mean differences (SMDs) for effect sizes. When the $p<0.1$, $I^2<50\%$, it suggested that the heterogeneity between the study's results was small, and the fixed-effect model was handpicked for analysis. When $p>0.1$ and I^2 were greater than 50%, indicating a high difference between studies, the random-effects hypothesis was selected for analysis. To determine publication bias, funnels were drawn.

2. Results

2.1 Literature search and screening process

A preliminary search of 375 articles was found, 196 articles were excluded after de-duplicate using NoteExpress,

and 159 articles were excluded after reading the title, abstract and full text, and finally a total of 20 articles were included in this study. See Figure 1 for details.

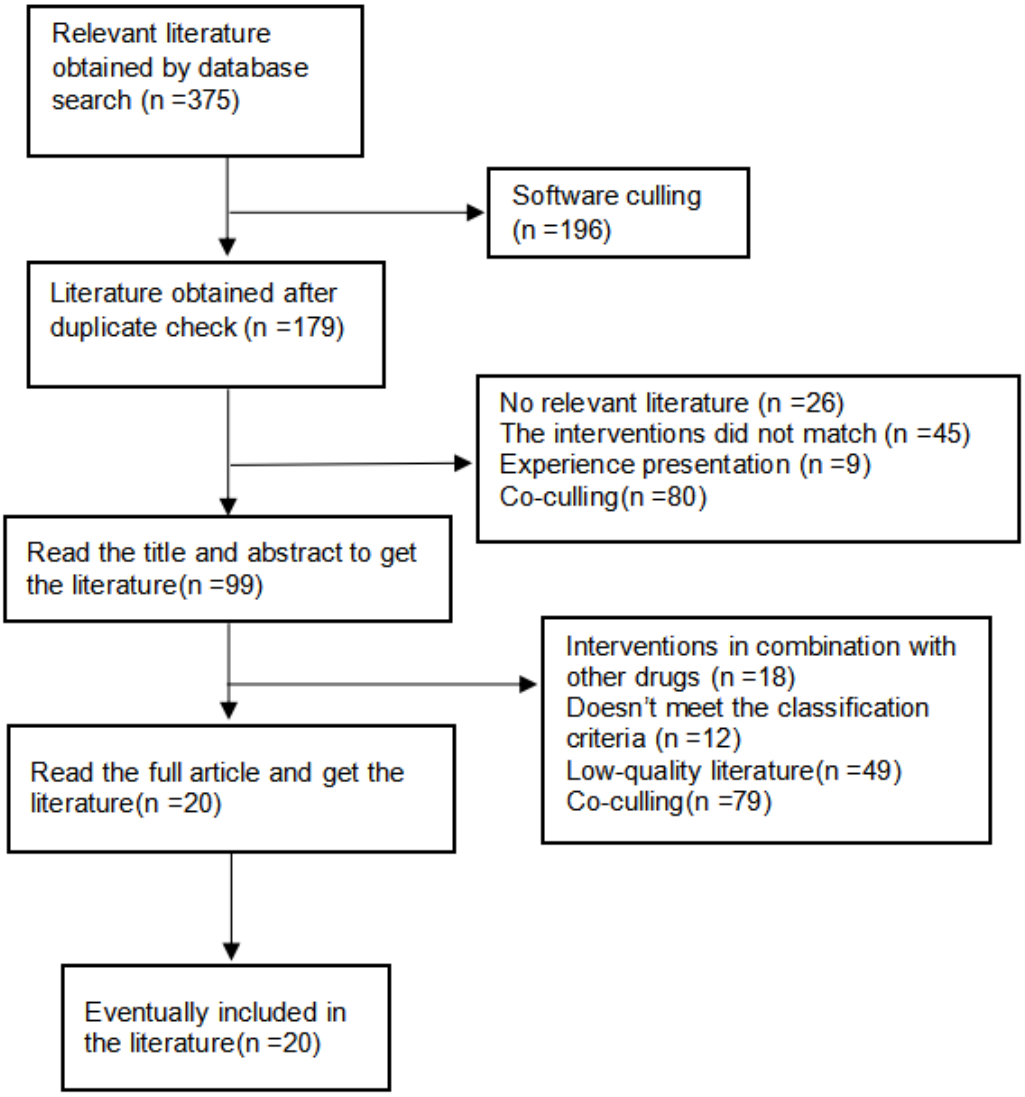

Figure 1. Literature screening process and results.

2.2 General information on inclusion

This study eventually included 20 RCTs with a total of 2,496 participants, including 1,270 in the treatment group and 1,226 in the control group. Its basic characteristics are shown in Table 1.

2.3 Risk of bias assessment was included in the studies

The 20 included studies are RCTs:(1) Stochastic method: Eight studies [3, 5-6, 10, 12, 15, 19-20] were grouped using a random number table and seven studies [7-9, 14, 17, 21-22] were randomised in order of presentation, Four studies [4, 13, 16, 18] had only the word 'random' in the method of grouping, and one study [11] didn't mention the method of grouping; (2) Assignment hiding: One study [15] mentioned and none of the rest; (3) Blinding: Seven studies [3, 5-6, 9-12] were assessed as high risk; One study [15] was judged to be low risk; None of the remaining 12 studies [4, 7-8, 13-22] stated. None of the outcome assessments mentioned whether blinding was used except in one study [15]. (4) Incomplete data outcomes: Two studies [4-5] were rated as high risk; The remaining 18 studies [3, 6-22] had no cases of dropout. (5) Selective reporting: all are announced. (6) Other biases: none were clear. The results of the risk assessment of the quality of the included literature are shown in Figures 2.

Table 1. Basic characteristics of the included studies

Included in the literature	Sample size(n)		Interventions		Course	Outcome measures
	Treatment group	Control group	Treatment group	Control group ①		
CAO Yujun [1] 2014	40	40	Tongxie Yaofang	T	2w	Total efficiency, Clinical symptom scores, Adverse reactions
Guo Shuo [2] 2019	85	85	Hehuanxiao granules	T	4w	Total efficiency, Treatment improvement rate, Clinical symptom scores, security
Huang Ming-han [3] 2016	43	40	The method of regulating the function of liver and spleen	T	4w	Total efficiency, Clinical symptom scores, Adverse reactions
Huang Qun [4] 2016	39	39	Plum Pill Decoction	T	30d	Total efficiency, Clinical symptom scores, Adverse reactions
Ji Yu [5] 2014	197	190	Self-Formulated Jian Chang No1 decoction	T	4w	Total efficiency
Jiang Sheng [6] 2019	30	30	Bowel prescription	T	4w	Total efficiency, IBS - SSS scale integrals, Adverse reactions
Kang Genghua [7] 2016	70	70	liver thinning and spleen strengthening Decoction	T	4w	Total efficiency, SF-36 scale integrals
Lu Min [8] 2015	43	42	Bowel prescription	T	4w	Total efficiency, Clinical symptom scores
Ma Mei [9] 2017	61	61	Xifeng Huashi Decoction	T	4w	Total efficiency, 5-HT②level, TNF-α, IL-6, IL-10③level
Su Qiang [10] 2014	100	100	Intestinal analgesic group	T	4w	Total efficiency, BSS scale integrals④, Adverse reactions
Wang Bing [11] 2014	48	34	liver relief and spleen decoction	T	6w	Total efficiency, Clinical symptom scores, Adverse reactions
Wang Enyuan [12] 2010	54	54	Solid intestine decoction	T	60d	Total efficiency, Clinical symptom scores
Wang Jidong [13] 2017	81	81	liver-dispersing,spleen-invigorating,kidney reinforcing and intestine-strengthening	T	4w	Total efficiency, Clinical symptom scores, Badge points, BSS scale integrals, Follow
Xi Zhaohong [14] 2015	83	82	Xifeng Huashi Decoction	T	4w	Total efficiency, Clinical symptom scores, 5-HT level
Yu Huiyao [15] 2012	55	51	Irritable decoction	T	4w	Total efficiency
Yue Yan [16] 2010	30	30	Cleansing the heart and awakening the spleen decoction	T	4w	Total efficiency, VIP⑤level, SP⑥level
Zhao Xiaodan [17] 2020	81	81	Enhance the spleen and strengthen the intestines decoction	T	4w	Total efficiency, IBS-SSS scale integrals, Clinical symptom scores, Chinese medicine badge points
Zheng Fengmin [18] 2008	56	56	Chaiyu Kezi Decoction	T	8w	Total efficiency, Clinical symptom scores
Zhou Yuwen [19] 2011	37	30	Liver thinning and spleen decoction	T	14d	Total efficiency
Zhou Zhenghua [20] 2010	37	30	Tongxie Yaofang and reasonable pills	T	2w	Total efficiency

Caution: ① T: trimebutine; ② 5-HT: 5-hydroxytryptamine; ③ TNF-α, IL-6, IL-10: Intestinal mucosal cytokines; ④ BSS scales: Beck Scale for Suicide Ideation; ⑤ VIP: vasoactive intestinal peptide; ⑥ SP: Human serum substance P.

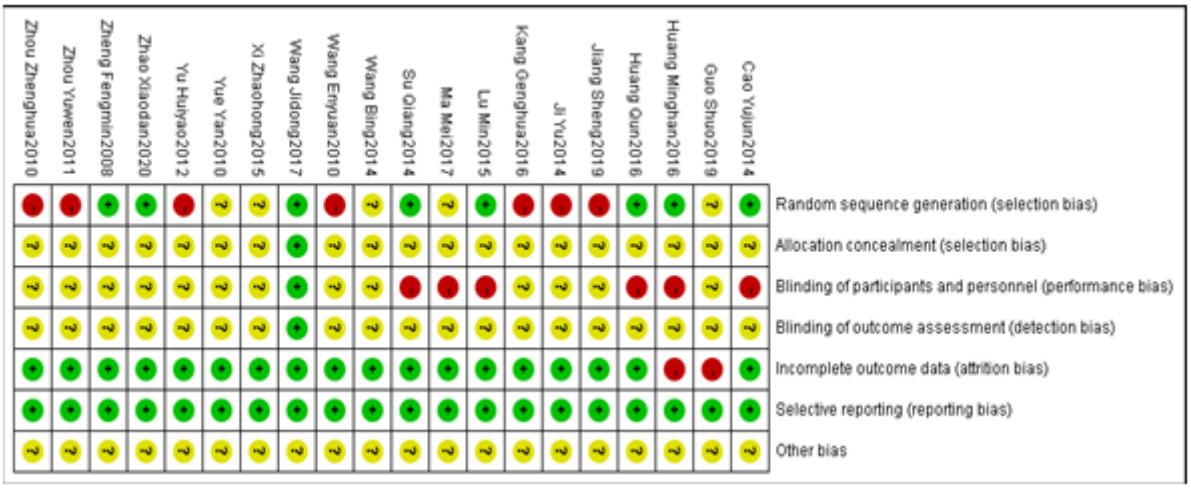

Figure 2. Summary of risk of bias of included studies.

2.4 Results of meta-analysis

2.4.1 Total Efficiency

Total response rates were reported in 20 studies, and meta-analysis showed significant heterogeneity between studies ($I^2 = 52.5\%$).

Therefore, the sensitivity analysis was carried out, it was found that the studies of Ji Yu [7] and Lu Min [10] had a great impact on the heterogeneity between the results. The two studies were removed and tested again, as shown in Figure 3: P=0.973, I^2=0%, indicating that there was no heterogeneity between the results, [OR=2.97, 95%CI (2.31, 3.82)], the difference was statistically significant, indicating that the effective rate of traditional Chinese medicine in the treatment of IBS-D (liver depression and spleen deficiency) was better than that of trimebutine.

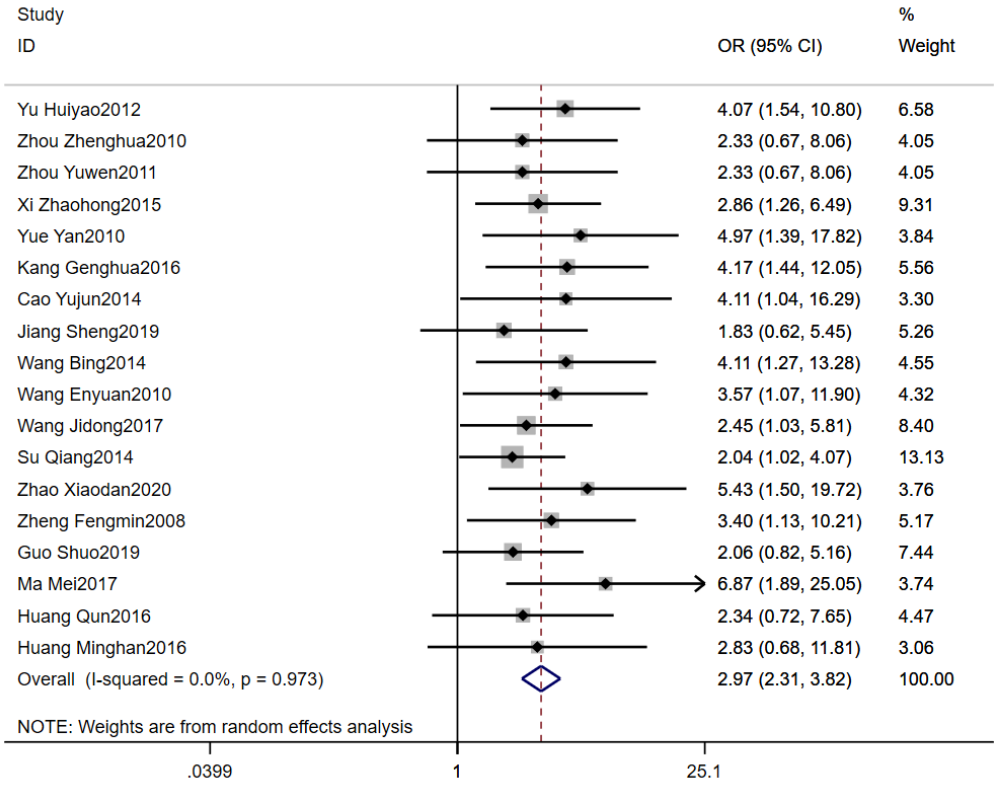

Figure 3. Total effective forest plot after sensitivity analysis.

2.4.2 Abdominal pain

Thirteen studies [3-6, 8, 10, 12-16, 19-20] reported abdominal pain before and after treatment, enrolling a total of 1,547 patients. The results showed high heterogeneity (I^2=91%).

After sensitivity analysis, it was found that after excluding five studies, Cao Yujun [3], Guo Shuo [4], Huang Qun [6], Wang Jidong [15], and Zhao Xiaodan [19],There was no significant heterogeneity between the results of the remaining eight studies [5, 8, 10, 12-14, 16, 20] (I^2=14%), and the results showed that the abdominal pain score of the patients in the treatment group was significantly lower than that of the control group, and the difference was statistically significant (SMD=-0.31, 95% CI [-0.44 to -0.18], P<0.05). See Figure 4.

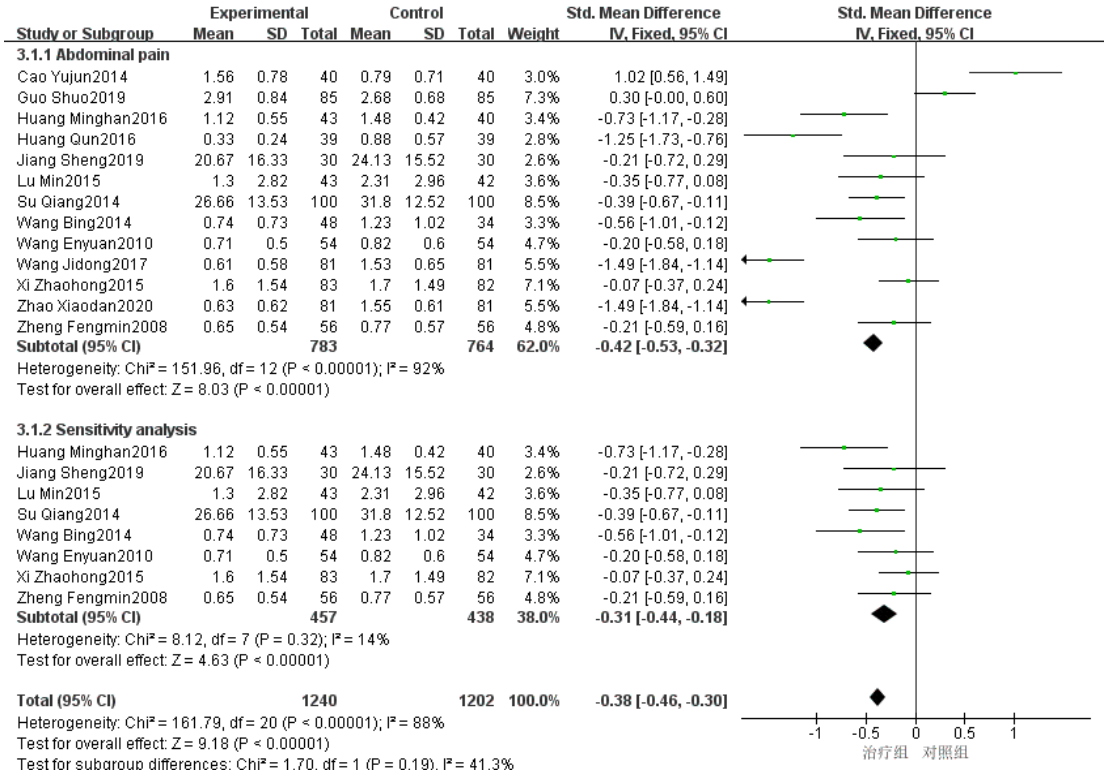

Figure 4. Forest plot of abdominal pain points.

2.4.3 Diarrhea

Eight studies [3-6, 10, 13, 15, 19] reported on diarrhoea in participants before and after treatment, with a total of 1010 patients. The results showed large heterogeneity (I^2=96%). After sensitivity analysis, four items [3, 6, 15, 19] were excluded, and the remaining four studies [4-5, 10, 13] showed less heterogeneity (I^2=28%), as shown in Figure 5, the results showed that the diarrhea score of patients in the treatment group was significantly lower than that in the control group, and the difference was statistically significant (SMD = -0.45, 95% CI [-0.65 to -0.26], P<0.05).

2.4.4 Abdominal distention

Eight studies [5, 8, 10, 12-13, 15, 19-20] reported on abdominal distension in participants before and after treatment, with a total of 946 patients. The results showed large heterogeneity (I^2=92%).

Therefore, after sensitivity analysis, excluding 2 items [15, 19], the remaining 6 studies [5, 8, 10, 12-13, 20] showed less heterogeneity (I^2=8%), indicating that the improvement of abdominal distension in traditional Chinese medicine for IBS-D with hepatic depression and spleen deficiency was better than that of trimebutine, and the difference was statistically significant (SMD = -0.26, 95% CI[-0.41 to -0.10], P<0.05) (see Figure 6).

2.4.5 Fecal satisfaction score

Four studies [8, 12, 15, 19] were reported. The results of heterogeneity analysis showed that the heterogeneity was large (I^2=95%). After sensitivity analysis, they were divided into two groups, and the results showed that the defecation satisfaction score of patients in the treatment group was significantly lower than that of the control group, indicating that the improvement of defecation satisfaction by traditional Chinese medicine was better than that of

trimebutine, and the difference was statistically significant, as shown in Figure 7.

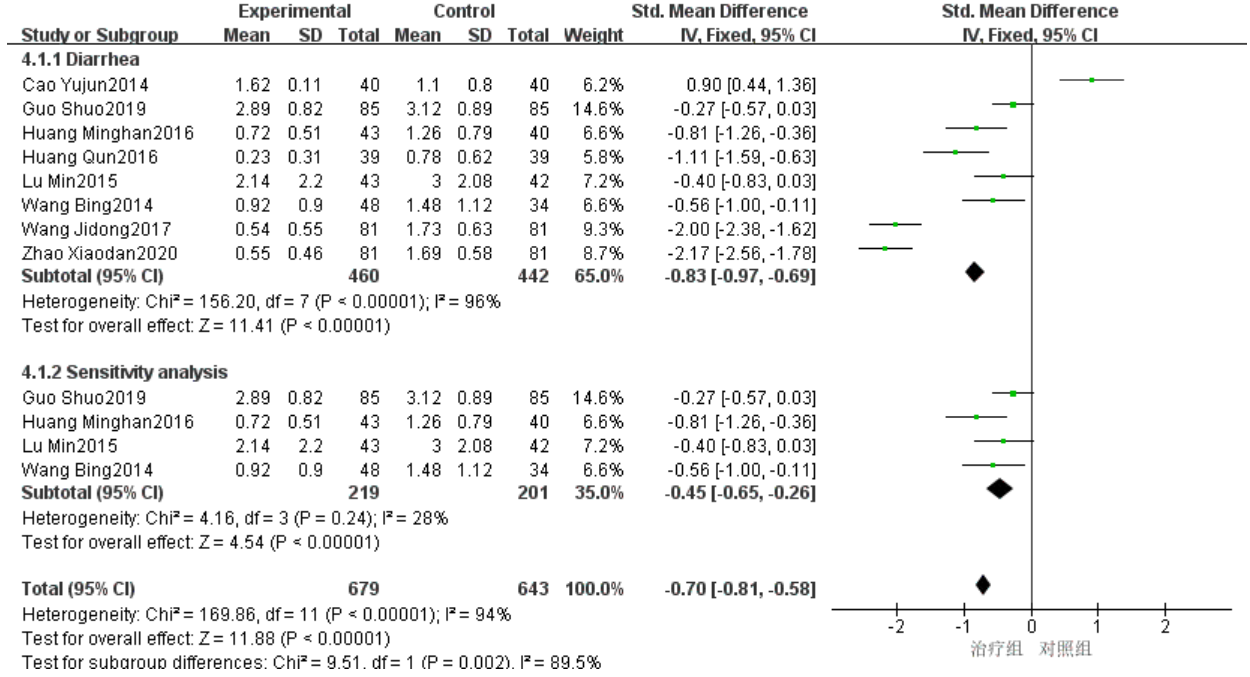

Figure 5. Forest plot of diarrhea points.

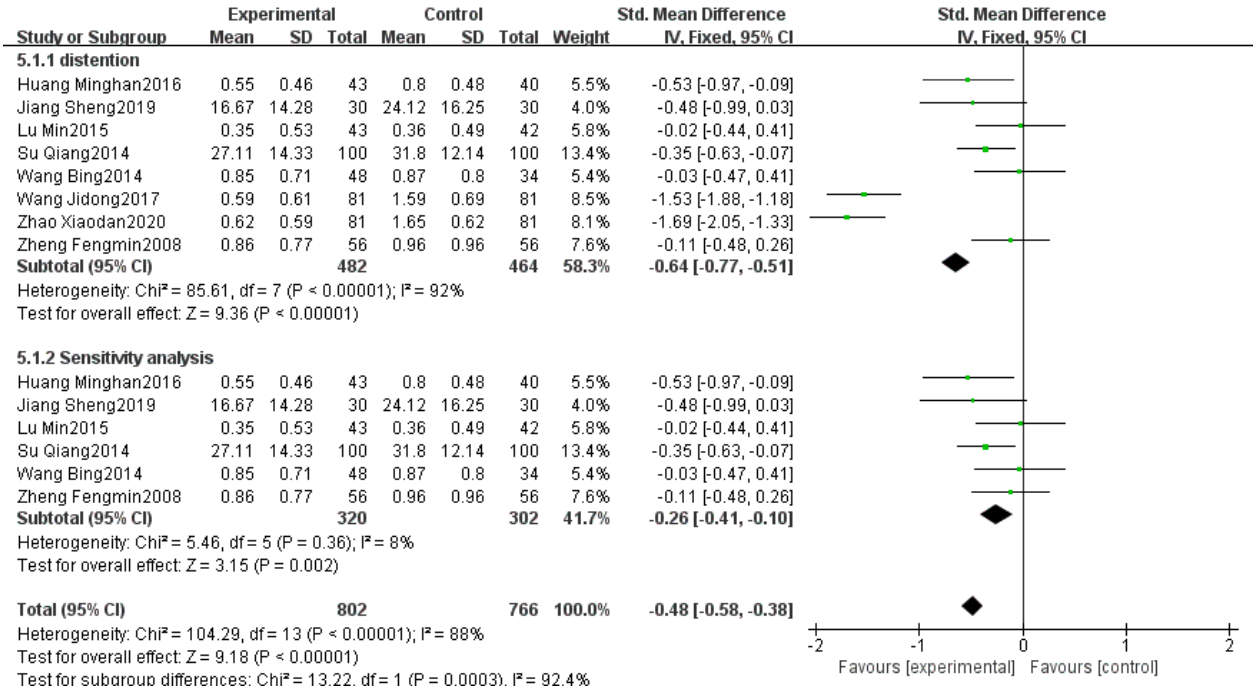

Figure 6. Forest plot of abdominal distention integral.

2.4.6 Impatience and irritability

Four studies [3-4, 10, 16] counted participants with impatience and irritability before and after treatment, with a total of 440 patients. The results of heterogeneity showed significant heterogeneity between studies (I^2=67%), so heterogeneity was searched. The sensitivity analysis showed that when the studies of Cao Yujun [3] and Xi Zhaohong [16] were excluded, there was no heterogeneity(I^2=0%), and the results showed that the irritability score of the treatment group was significantly lower than that of the control group, indicating that the improvement of the symptoms of irritability of patients by traditional Chinese medicine was better than that of trimebutine, and the dif-

ference was statistically significant (MD=-0.30, 95% CI [-0.51 to -0.10], P<0.05).

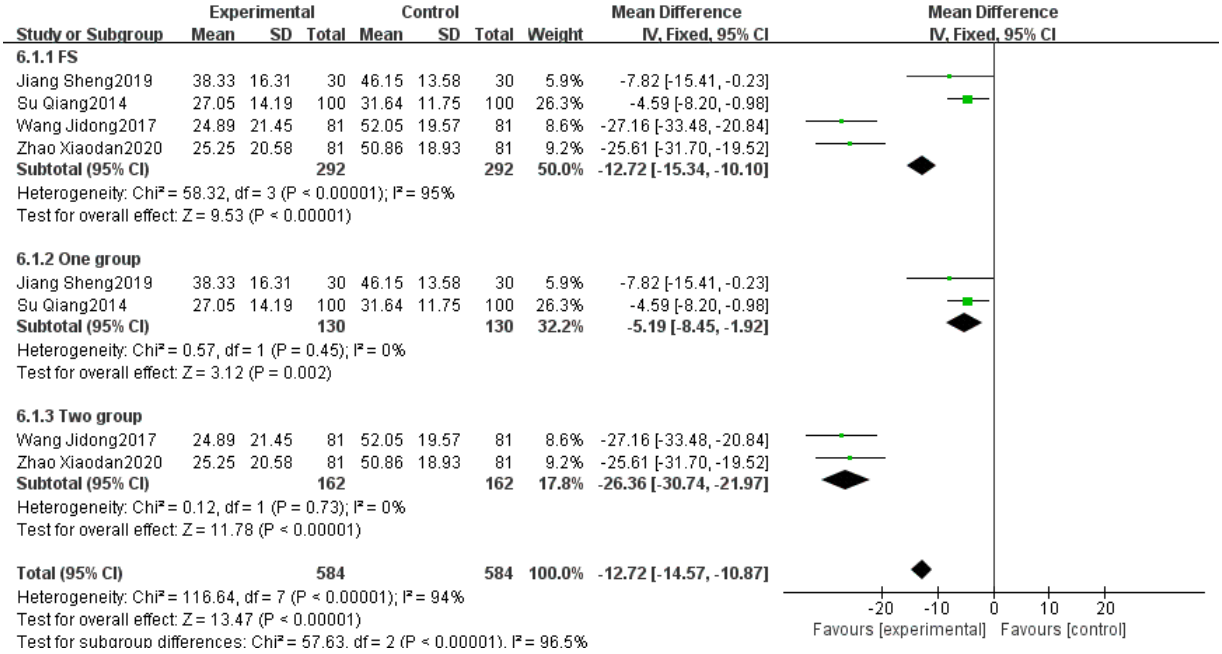

Figure 7. Forest plot of fecal satisfaction.

2.4.7 Adverse reactions

Adverse reactions were reported in 6 studies [3, 5-6, 8, 12-13], among which none of the enrolled cases in the studies of Cao Yujun [3], Jiang Sheng [8] and Su Qiang [12] had adverse events, and no abnormalities in blood, urine, stool routine, liver and kidney function.

In Wang Bing's study [13], 2 patients in the treatment group had no abdominal distention, mild abdominal distension and discomfort during the course of taking the drug, and the symptoms disappeared after continuing to take the drug; In the control group, 2 patients had mild elevation of alanine aminotransferase, and 2 patients had aggravated abdominal pain. No abnormalities were seen in other observers.

In Huang Minghan's study [5], one patient in the treatment group experienced mild dizziness on the fourth day of medication, and one patient in the control group experienced mild epigastric pain after one week of medication, both of which were relieved by themselves without severe adverse reactions.

In the study of Huang Qun [6], no obvious adverse reactions occurred in the treatment group, and 2 patients in the control group experienced dizziness, occasional drowsiness and other symptoms, which disappeared after stopping the drug.

2.4.8 Publication bias

The "funnel chart" of the total efficacy of the 20 included studies was plotted to observe publication bias, the distribution of points in the funnel plot was not completely symmetrical, and the analysis may be related to the inconsistency of the course of treatment, prescription and evaluation criteria of each study.

3. Conclusion

There is no "IBS-D" disease name in traditional Chinese medicine, modern according to clinical manifestations of it classified as "abdominal pain", "diarrhea" and other categories of traditional Chinese medicine, more common abdominal pain is diarrhea, post-diarrheal pain reduction, each due to emotional changes occur or aggravate, seriously reduce the quality of life of patients and negatively increase the emotional burden, and eventually form a vicious circle, so the key to treatment is to improve symptoms. Traditional Chinese medicine believes that the main causes and pathogenesis are poor mood, fatigue, mental depression, or spleen and stomach deficiency, poor diet, long-term illness leads to loss of spleen and healthy luck, large intestine conduction loss, that is, venting diarrhea, lingering and difficult to heal. As mentioned in the "Medical Formulae Investigations": "The spleen of laxative responsibility, the liver of pain, the reality of liver responsibility, the deficiency of spleen responsibility, the liver and spleen deficiency, so it makes pain diarrhea", liver depression and spleen deficiency often affect each other, so for

liver depression and spleen deficiency IBS-D should be treated to replenish the spleen and suppress the liver, dispel dampness and stop diarrhea.

A meta-analysis was used in this study to systematically compare the efficacy and safety of traditional Chinese medicine versus trimebutine maleate in the diagnosis of IBS-D with hepatic depression and spleen deficiency, and finally 20 studies with such a total of 2,496 patients were included. The results showed that the treatment group's effective outcome rate and clinical symptom improvement rate were considerably higher than those in the control group. In terms of safety, there were no serious adverse events either in that group, indicating a good safety profile; however, the incidence of adverse reactions was significantly lower in the treatment group than in the control group, and the recurrence rate was lower.

The shortcomings of this study are: (1) the included trials are not completely consistent in the dosage form, dosage and duration of traditional Chinese medicine in the treatment process, which may have a certain impact on the results; (2) The interventions were not uniform, although the control group was the same Western medicine, the treatment group was not uniform, which could only reflect the overall advantages of traditional Chinese medicine in the treatment of IBS-D; (3) The outcome indicators and evaluation criteria were inconsistent and uniform, and there was a lack of standardized and unified clinical symptom evaluation standards; (4) the course of treatment of each study was not completely uniform; (5) Adverse reactions and recurrence rates were reported less, and long-term follow-up data were lacking.

In summary, traditional Chinese medicine outshines trimebutine in terms of total effective rate, abdominal pain, diarrhea, abdominal distension, stool frequency, stool characteristics, and safety, indicating that the effect of traditional Chinese medicine in the treatment of IBS-D (liver depression and spleen deficiency) is advantageous to trimebutine, and the drug's safety is high, trying to make it worthy of wide - spread promotion.

References

[1] Canavan C, West J, Card T R. The epidemiology of irritable bowel syndrome [J]. Clinical Epidemiology, 2014, 6(1):71-80.

[2] Han Yafei, Wang Yunliang, LI Junxiang. Pathogenesis of Diarrhea-predominant Irritable Bowel Syndrome and Its Research Progress of Intervention with Chinese Medicine [J]. Journal of Liaoning University of Chinese Medicine, 2018, 20(1):114-117.

[3] Cao Yujun, He Changsheng. Clinical Observation of Modified Tongxie Yaofang Treating 40 Cases of IBS with the Dirrahea of Liver Depression and Spleen Deficiency Syndrome [J]. JETCM., 2014, 23(10):1816-1818.

[4] Guo Shuo, Liu Qiquan, Wang Zhikun, Xu Xiangjiang, Zhao Yongqiang, Ma Hongxiang, Li Yongxia. Clinical study of Hehuanxiao granules in the treatment of diarrheal irritable bowel syndrome and liver depression and spleen deficiency [J]. Lishizhen Medicine and Materia Medica Research, 2019, VOL.30, NO.11

[5] Huang Minghan, Chen Qin, Huang Jian, Li Sihan, Wang Wenrong, Wang Xin, Lin Ping, Huang Hengqing. Observation of curative effect of the method of regulating the function of liver and spleen on diarrhea-predominate irritable bowel syndrome [J]. Modern Journal of Integrated Traditional Chinese and Western Medicine, 2016 Aug, 25(22).

[6] Huang Qun, Leng Yujie. Effect of Plum Pill Decoction on Diarrhea Type Irritable Bowel Syndrome and Meaning of Chinese Materia Medica Guardianship [J]. Journal of Liaoning University of TCM, Vol. 18, No. 9, Sep. 2016.

[7] Ji Yu, Dai Haifeng, Mei Li, Jing Yali. 197 cases of irritable bowel syndrome were treated by Self-Formulated Jian Chang No 1. [J]. Chin J Integr Trad West Med Dig., Vol. 22, No. 3, P. 166, Mar 2014.

[8] Jiang Sheng, Lu Min. Clinical study of bowel prescription for the treatment of diarrhea-type irritable bowel syndrome [J]. Shaanxi Journal of Traditional Chinese Medicine, 2019, 40(03):331-334.

[9] Kang Genghua. Effects of liver thinning and spleen strengthening on clinical efficacy and quality of life in patients with diarrheal irritable bowel syndrome [J]. Guiding Journal of Traditional Chinese Medicine and Pharmacy, 2016, 22(21):74-76.

[10] Lu Min, Xie Hui, Fan Xinyu, Hua Yongzhi, Zhang Wei. A clinical study of 43 cases of "bowel prescription" in the treatment of diarrhea-type irritable bowel syndrome [J]. Jiangsu Journal of Traditional Chinese Medicine, 2015, 47(11):27-29.

[11] Mei Ma, Wei Xiang, Zhong-de Zeng. Effect of Xifeng Huashi Decoction on diarrhea predominant irritable bowel syndrome [J]. China Journal of Modern Medicine, 2017, 27(20):69-72.

[12] Su Qiang, Liu Zhenwei, Niu Lijun, Niu Jiao. An intestinal analgesic group was prescribed to treat 100 cases of diarrhea-type irritable bowel syndrome [J]. Shaanxi Journal of Traditional Chinese Medicine, 2014, 35(01):14-16.

[13] Wang Bing. Clinical observation of liver relief and spleen decoction in the treatment of diarrhea-type irritable bowel syndrome [J]. Journal of Emergency in Traditional Chinese Medicine, Oct. 2014, Vol. 23, No.10.

[14] Wang Enyuan, Li Baiqun, Wei Darong. 54 cases of diarrheal irritable bowel syndrome were treated with solid intestine decoction [J]. Chinese Journal of Integrated Traditional and Western Medicine on Digestion, 2010, 18(02):122-123.

[15] Wang Ji-Dong, Yang Zhong-Ting, Qiu Xin-Ping, Niu Ke-Min, Shen Qing-Yan, Zhou Tao. Obervation of the therapeutic ef-

fects of methods of liver-dispersing, spleen-invigorating, kidney reinforcing and intestine-strengthening on diarrhea-predominant irritable bowel syndrome [J]. Beijing Journal of Traditional Chinese Medicine, August, 2017, Vol. 36, No. 8.

[16] Xi Zhaohong, Tian Yaozhou, Chen Xuan, Yan Rui. Clinical Observation of Xifenghuashi Fang in Treating Diarrhea Type of Irritable Bowel Syndrome [J]. Journal of Nanjing University of Traditional Chinese Medicine, 2015, 31(04):331-333.

[17] Yu Huiyao, Wen Xinli. Irritable decoction was used to treat irritable bowel syndrome and diarrhea in 55 cases [J]. Shaanxi Journal of Traditional Chinese Medicine, 2012, 33(09):1130-1132.

[18] Yue Yan, Yang Qiang, Chen Daquan, Zhang Yanxia, Liu Xiangjin. Cleansing the heart and awakening the spleen decoction was used to treat 30 cases of irritable bowel syndrome with diarrhea [J]. Journal of Traditional Chinese Medicine, 2010, 51(01):56-57.

[19] Zhao Xiaodan, Wang Jidong, Tan Haicheng, Wu Chen, Zhang Lihong, Chen Lin, Gong Ran. Clinical study on the treatment of diarrhea-type irritable bowel syndrome and hepatic depression and spleen deficiency [J]. Shaanxi Journal of Traditional Chinese Medicine, 2020, 41(09):1245-1247+1261.

[20] Zheng Fengmin, Ji Haifeng. Clinical Observation on 56 Cases of Irritable Bowel Syndrome of Diarrhea Type Treated by Chaiyu Kezi Decoction [J]. Journal of Traditional Chinese Medicine, 2008(08):707-708.

[21] Zhou Yuwen, Zhang Zhijuan. Liver thinning and spleen decoction was used to treat diarrhea-type irritable bowel syndrome in 37 cases [J]. Shaanxi Journal of Traditional Chinese Medicine, 2011, 32(09):1142-1143.

[22] Zhou Zhenghua, Wang Wei, Wang Jing, Yao Peng, Liu Ying, Wu Yajing. 67 cases of irritable bowel syndrome (diarrhea type) were treated with Tongxie Yaofang and reasonable pills [J]. Liaoning Journal of Traditional Chinese Medicine, 2010, 37(10): 1989-1990.