Original Article

Overview of systematic evaluation of efficacy of Tongxie Yaofang in treating diarrhea-predominant irritable bowel syndrome

Xuan Chen[1,2]^, Xiaowen Yu[3], Yaxiang Shi[3], Hong Shen[4]

[1]First Clinical Medical College, Nanjing University of Chinese Medicine, Nanjing, China; [2]Department of Traditional Chinese Medicine, The Affiliated Suzhou Science and Technology Town Hospital of Nanjing Medical University, Suzhou, China; [3]Department of Gastroenterology, Zhenjiang Hospital Affiliated to Nanjing University of Chinese Medicine, Zhenjiang, China; [4]Department of Gastroenterology, Affiliated Hospital of Nanjing University of Chinese Medicine, Nanjing, China

Contributions: (I) Conception and design: H Shen; (II) Administrative support: H Shen, Y Shi; (III) Provision of study materials or patients: X Chen, X Yu; (IV) Collection and assembly of data: X Chen, X Yu; (V) Data analysis and interpretation: X Chen; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Hong Shen. Department of Gastroenterology, Affiliated Hospital of Nanjing University of Chinese Medicine, 155 Hanzhong Road, Nanjing 210029, China. Email: shenhong999@163.com.

Background: Tongxie Yaofang is commonly used in the treatment of IBS-D. Many systematic reviews have confirmed its efficacy and safety, but the methodology and quality of evidence need to be further evaluated.

Methods: The databases of Chinese National Knowledge Infrastructure (CNKI), Chinese Biomedical Literature (CBM), Wanfang, VIP, Web of Science (SCI), PubMed, Cochrane Library, and Embase were searched to gather systematic evaluations of TXYF in treating IBS-D. The search time was from inception to January 2021. The search was performed independently by 2 researchers who screened the literature and extracted data. Methodological quality of the studies included in the systematic evaluation was evaluated by the A MeaSurement Tool to Assess systematic Reviews-2 (AMSTAR-2) scale. The Grading of Recommendations, Assessment, Development and Evaluations (GRADE) system was used to categorize the evidence quality of outcome indicators, and the curative effect evaluation was summarized.

Results: A total of 10 systematic evaluations were included, and the results of AMSTAR-2 evaluation showed that 6 reports were relatively complete, 4 reports were poor, and the overall quality was not high.

Discussion: It was revealed that TXYF can improve the total clinical effective rate and symptoms of patients with IBS-D, but the GRADE evaluation results showed that the quality of evidence was low to extremely low. It is suggested that further high-quality clinical research should be conducted to provide more reliable evidence-based medical evidence for the application of TXYF in the treatment of irritable bowel syndrome.

Keywords: Tongxie Yaofang (TXYF); diarrhea-predominant irritable bowel syndrome (IBS-D); re-evaluation of system evaluation; A MeaSurement Tool to Assess systematic Reviews-2 (AMSTAR-2); Grading of Recommendations, Assessment, Development and Evaluations (GRADE)

Submitted May 28, 2021. Accepted for publication Jul 19, 2021.
doi: 10.21037/apm-21-1612
View this article at: https://dx.doi.org/10.21037/apm-21-1612

^ ORCID: 0000-0003-4196-0553.

Introduction

Diarrhea-predominant irritable bowel syndrome (IBS-D) is a functional gastrointestinal disease characterized by abdominal pain, diarrhea, and relief of abdominal pain after defecation. It is the most common type of IBS, accounting for about 40–65% of IBS patients (1,2). At present, the pathogenesis of IBS-D is unclear, with Western medicine compartmentalizing the treatment of diarrhea, spasmolysis, and pain, regulation of intestinal flora, or addressing anxiety and depression; however, it lacks specific drugs for the treatment of IBS-D (3). Although there is no record of IBS-D in traditional Chinese medicine (TCM), it can be classified as "diarrhea" and "abdominal pain" according to its symptoms (4). There is a cloud in the "Medical Prescription Examination": "The spleen of diarrhea, the liver of pain, the reality of liver responsibility, and the deficiency of spleen responsibility; Spleen deficiency is solid, so it causes pain and diarrhea". Therefore, IBS-D is often treated with modified Tongxie Yaofang (TXYF), which soothes the liver and strengthens the spleen. Formerly known as Baizhu Shaoyao Powder, TXYF was derived from the Liu Caochuang prescription in the text Jing Yue Quan Shu, which was called "Tongxie Yaofang" by the herbalist Zhang Jingyue, and it has retained this name to date. Due to its wide clinical application, the number of clinical studies on TXYF is increasing, with several systematic evaluations already having been published. Results have shown that TXYF has significant efficacy and safety in treating IBS-D. However, systematic evaluation is commonly problematic, including research program design defects, incomplete retrieval, publication bias, low evidence of outcome evaluation indicators, and so on, which can not provide a good reference for clinical practice. Systematic evaluation and re-evaluation can provide more integrated and reliable documentation for those looking for quality evidence (5). However, systematic evaluation and re-evaluation of TXYF in treating IBS-D has not yet been performed. With this in mind, this study aimed to evaluate the quality of methodology and grade the evidence of outcome indicators for the related systematic evaluation of TXYF in treating IBS-D in order to provide more and more reliable evidence base for the clinical application of TXYF.

We present the following article in accordance with the PRISMA reporting checklist (available at https://dx.doi.org/10.21037/apm-21-1612).

Methods

Eligibility criteria

The inclusion criteria were as follows: (I) type of research: Chinese and English language meta-analysis or systematic evaluation based on randomized controlled trial (RCT) or quasi-RCT; (II) research subject: published systematic evaluation or meta-analysis on the efficacy and safety of TXYF in the treatment of IBS-D; (III) type of intervention: experimental group was treated with TXYF alone or in combination or with TXYF as the basic prescription, control group was given routine Western medicine, blank control, or placebo; (IV) type of outcome measures: the main outcome indicators were total effective rate, cure rate, recurrence rate, adverse reactions, and various symptom indicators.

The exclusion criteria were as follows: (I) duplicate literature; (II) conference papers, letters, and so on; (III) control group received treatment containing TXYF; (IV) documents with incomplete data, obvious errors, or there was inability to obtain data to be extracted.

Search strategy

The databases of Web of Science (SCI), PubMed, Embase, Cochrane Library, Chinese Biomedical Literature (CBM), Chinese National Knowledge Infrastructure (CNKI), VIP, Wanfang, and others, were searched online by 2 researchers in order to collect relevant systematic reviews of TXYF in treating IBS-D. The main search methods were combination of subject words and free words. The Chinese search words were Tongxie Yaofang, diarrhea irritable bowel syndrome, irritable bowel syndrome, systematic review, and meta-analysis. English search terms included Tongxieyaofang, Tong Xie Yao Fang, Tongxie Yaofang, TXYF, diarrhea preponderant irritable bowel syndrome, irritable bowel syndrome, IBS-D, systematic review, and meta-analysis. The search deadline was January 2021.

Selection process

Firstly, the 2 researchers collected articles according to their titles and abstracts, and then obtained the full text to ensure consistency with the literature. They then imported them into NoteExpress (Aegean Software, Beijing, China)

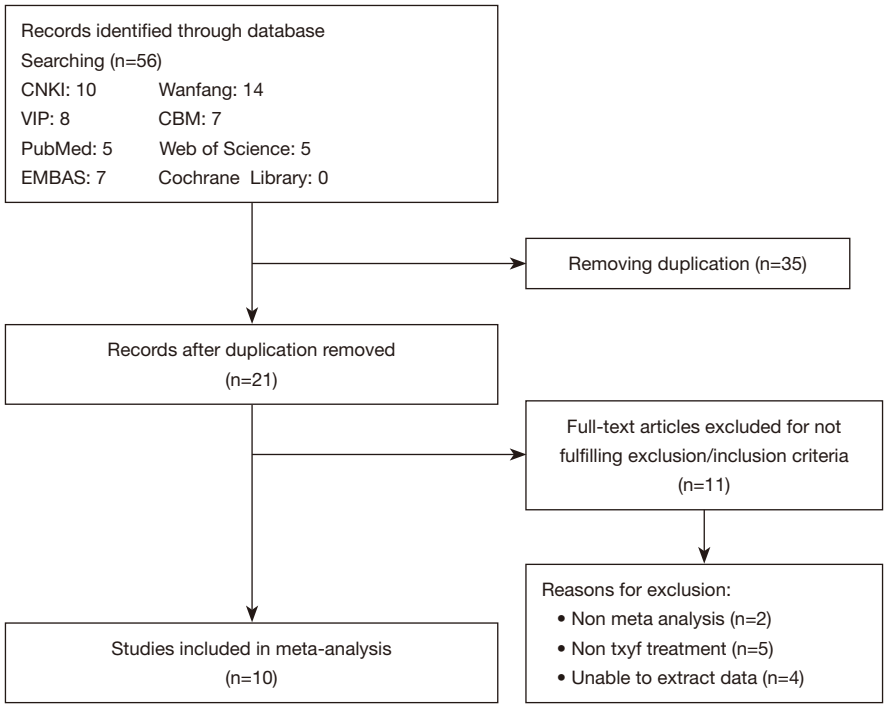

Figure 1 PRISMA 2009 flow diagram.

to eliminate duplicate literature according to the inclusion and exclusion criteria. Studies that met the inclusion criteria were selected and cross-checked. Next, the 2 researchers extracted and collated information included in the literature, and cross-checked them again. Any disagreements between the investigators were resolved through consultation with a third researcher.

Quality evaluation

Methodological quality evaluation

The 2 researchers applied the A MeaSurement Tool to Assess systematic Reviews-2 (AMSTAR-2) scale (6-8) to evaluate the methodological quality of the included studies. The AMSTAR-2 scale has a total of 16 items (the key items are 2, 4, 7, 9, 11, 13, and 15), which can be divided into "yes", "partial yes", and "no" according to the degree of satisfaction of evaluation criteria, and the methodological quality of systematic evaluation can be divided into high quality (none or only 1 non-critical item does not conform) and medium quality (more than 1 non-critical item does not conform), low quality (1 key item does not conform), and extremely low quality (more than 1 key item do not conform).

Evaluation of evidence quality

The 2 researchers used the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) scale (9,10) to grade the evidence quality of the outcome indicators included in the literature, and divided the evidence quality of systematic evaluation into 4 grades: high, medium, low, and extremely low.

Results

Description of the screening process

A total of 56 Chinese documents, 17 English documents, and 39 Chinese documents were obtained through the preliminary search. A total of 10 documents were finally included after removal of duplicates and exclusion of documents that did not meet the inclusion criteria (11-20). The document retrieval process is shown in *Figure 1*.

Study characteristics

All 10 of the included systematic reviews evaluated the methodology of the original studies, among which 6 documents were evaluated by the risk of bias (RoB) tool recommended by the Cochrane Collaboration, 2 were

evaluated by Jadad scale, 1 was evaluated by both Cochrane RoB and Jadad scale, and 1 was evaluated by the literature quality evaluation standard issued by the National Health Service (NHS). A total of 3 papers were funded by the National Natural Science Foundation of China, and the basic characteristics of the included studies are shown in *Table 1*.

Methodological quality evaluation

The AMSTAR-2 scale was used to evaluate the methodological quality of the included studies. The results showed that there were 5 items reported completely, which were item 1 (100%), item 3 (100%), item 11 (100%), item 13 (100%), and item 14 (100%). There were 5 items, namely, item 2 (10%), item 7 (0), item 10 (0), item 12 (0), and item 16 (2%), which were less completely reported, among which item 7 was the key item. The overall methodological quality included in the study was low, and the methodological quality evaluation was high and medium, with 0 systematic evaluations, 1 low (12), and 9 extremely low (11,13-20). A total of 10 papers did not mention the formulation of research scheme, 1 (12) paper was registered in PROSPERO (CRD42018105307), and the other nine papers did not mention a search test registry. There were 5 (11,14,18-20) documents that did not provide screening flow charts, 1 (17) document did not explain the reasons for excluding articles after reading of the full text, 10 documents did not provide a list of excluded documents, 1 (18) document did not provide a list of included research characteristics, and 3 (12,13,16) documents did not assess the bias of the original research. None of the 10 papers reported the source of funding for the included studies. Eight papers (11,14-20) did not describe whether there was a conflict of interest. See *Table 2*.

Evaluation of evidence quality

The quality of outcome indicators of the 10 included studies was evaluated by the GRADE system. In terms of total effective rate, 3 studies (12,17,19) were of low quality, and the rest were of extremely low quality. Another study (14) showed that the effective rate, ineffective rate, and recurrence rate were of low quality, and other indexes were of extremely low quality. All outcome indicators were degraded in the quality of included research methodology, and other degradation factors, such as inconsistency, inaccuracy, and publication bias, also had a great impact on the quality of research evidence. The GRADE quality grade evaluation is shown in *Table 3*.

Efficacy evaluation

A summary report of quantitative analysis results of 10 systematic evaluations is displayed in *Table 4*. Only 1 article (12) reported the incidence of adverse reactions, which was significantly lower than that of the control group (P=0.03).

Discussion

The etiology and pathogenesis of IBS have not been fully elucidated. Most academics (21-23) believe that the pathogenesis of IBS is mainly related to psychosocial factors, abnormal gastrointestinal motility, abnormal brain-intestinal axis function, visceral hypersensitivity, intestinal infection and inflammation, and destruction of intestinal mucosal barrier function. As IBS patients often display emotional disorders such as tension, anxiety, depression, and so on, the influence of psychological and mental disturbance on intestinal motor function and visceral sensitivity has been supported, upholding the modern medical belief that IBS-D is a psychosomatic disease (24). In TCM, it is held that the liver governs emotion, so IBS-D is closely related to liver. Dysfunction of liver-qi or stagnation of liver-qi, insult to the spleen, impaired temper, and disordered transportation and transformation result in abdominal pain and diarrhea. Therefore, liver stagnation and spleen deficiency is a common syndrome type of IBS-D, and TXYF is a common basic prescription for treating IBS-D. The TXYF prescription should be composed of Atractylodes macrocephala Koidz, Paeonia lactiflora Pall., Pericarpium Citri Reticulatae, and Saposhnikovia divaricate. Among the ingredients, Atractylodes macrocephala Koidz strengthens the spleen by taking advantage of imperial wood, and dries up dampness to stop diarrhea, white peony nourishes the blood and softens the liver, and relieves pain as a minister's medicine (the monarch and the minister match each other, which can “shed wood in the soil”). Dampness is easily generated in te presence of spleen deficiency, so it is an adjuvant medicine to use dried tangerine peel to regulate qi and dryness, invigorate the spleen and stomach; with the small amount of Saposhnikovia divaricata, one function is Xin San to regulate the liver, so that the liver qi can no longer invade the spleen; the second is to soothe the clear the spleen, and to overcome dampness and stop diarrhea. Saposhnikovia divaricata is also a medicine for inducing

Table 1 Basic characteristic of included studies

References	Document quantity	Sample size	Treatment group interventions	Control group intervention measures	Methodological quality evaluation tool	Funding
Bian *et al.* 2006 (11)	12	1,125	TXYF or TXYF-A	Conventional Western medicine treatment	Cochrane RoB	
Zhou *et al.* 2019 (12)	39	3,062	TXYF	Conventional Western medicine treatment or placebo	Cochrane RoB	
Dai *et al.* 2018 (13)	23	1,972	M-TXYF	Pividone bromide or pividone bromide + another drug	Cochrane RoB	National Natural Science Foundation of China (81373563), Guangzhou University of Traditional Chinese Medicine High-level University Construction Project (2016) No.64, Guangzhou University of Traditional Chinese Medicine Research Project Innovation Team Cultivation Project (2016KYTD07)
Xu *et al.* 2017 (14)	9	774	Modification of Shenling Baizhu Powder Combined with Tongxie Yaofang	Conventional Western medicine	Jadad scoring scale	
Guo *et al.* 2015 (15)	9	811	Modified Sijunzi Decoction and Tongxie Yaofang	Conventional Western medicine	Cochrane RoB	National Natural Science Foundation of China Youth Project (61301294), National University Innovation and Entrepreneurship Training Project (201510572007)
Yao 2016 (16)	12	1,778	Sini Powder Combined with Tongxie Yaofang + Western Medicine	Conventional Western medicine	Cochrane RoB	
Zhao *et al.* 2017 (17)	7	634	Modified Tongxie Yaofang	Conventional Western medicine	Jadad scoring scale	National Natural Science Foundation of China (81560754), Guangxi Natural Science Foundation of China (2015GXNSFAAI39199)
Su *et al.* 2009 (18)	22	2,347	Basic Prescription of Tongxie Yaofang	Western medicine or placebo	British national health Evaluation standard of literature quality issued by service center (NHS)	
Wang *et al.* 2017 (19)	26	2,694	Basic Prescription of Tongxie Yaofang	Conventional western medicine	Cochrane RoB	
Shi *et al.* 2007 (20)	23	1,997	Tongxie Yaofang or Modified Tongxie Yaofang	Western medicine or placebo or no treatment	Jadad rating scale and Cochrane RoB	

TXYF, Tongxie Yaofang; NHS, National Health Service; RoB, risk of bias.

Table 2 Methodological quality evaluation of AMSTAR-2

References	1	2	3	4	5	6	7	8	9	10	11	12	13	14	5	16	Quality evaluation
Bian *et al.* 2006 (11)	Y	N	Y	PY	Y	Y	N	PY	PY	N	Y	N	Y	Y	Y	N	Extremely low
Zhou *et al.* 2019 (12)	Y	PY	Y	PY	Y	Y	N	PY	PY	N	Y	N	Y	Y	Y	Y	Low
Dai *et al.* 2018 (13)	Y	N	Y	PY	Y	Y	N	PY	PY	Y	Y	N	Y	Y	Y	Y	Extremely low
Xu *et al.* 2017 (14)	Y	N	Y	PY	Y	N	N	PY	PY	N	Y	N	Y	Y	Y	N	Extremely low
Guo *et al.* 2015 (15)	Y	N	Y	PY	Y	Y	N	PY	PY	N	Y	N	Y	Y	Y	N	Extremely low
Yao 2016 (16)	Y	N	Y	PY	N	N	N	PY	PY	N	Y	N	Y	Y	N	N	Extremely low
Zhao *et al.* 2017 (17)	Y	N	Y	PY	Y	Y	N	PY	PY	N	Y	N	Y	Y	Y	N	Extremely low
Su *et al.* 2009 (18)	Y	N	Y	PY	Y	Y	N	N	N	N	Y	N	Y	Y	Y	N	Extremely low
Wang *et al.* 2017 (19)	Y	N	Y	PY	Y	Y	N	PY	PY	N	Y	N	Y	Y	Y	N	Extremely low
Shi *et al.* 2007 (20)	Y	N	Y	PY	Y	Y	N	PY	PY	N	Y	N	Y	Y	Y	N	Extremely low

Items 2, 4, 7, 9, 11, 13, and 15 are key items. Item 1, whether the research questions and inclusion criteria in the literature are consistent with the PICO principle; Item 2, whether the research methods in the literature have been determined before implementation, and whether the inconsistency with the plan is explained; Item 3, whether the literature explains the types and reasons of research design included; Item 4, whether the retrieval strategy described in the literature is comprehensive; Item 5, whether the literature screening is completed independently by two people; Item 6, whether the extraction of literature data is completed by 2 people; Item 7, whether the literature provides a list of excluded literature and explains the reasons; Item 8, whether the basic characteristics included in the study are described in detail in the literature; Item 9, whether the literature uses reasonable tools to evaluate the bias risk included in the study; Item 10, whether the sources of funding for inclusion in research are reported in the literature; Item 11, whether appropriate statistical methods were used for meta-analysis of literature; Item 12, whether the potential influence of the bias risk included in the study on the results or other evidence integration is considered in the meta-analysis of the literature; Item 13, whether the RoB included in the literature is considered when explaining or discussing the systematic evaluation of each result in the literature; Item 14, whether the literature gives a reasonable explanation or discussion on the heterogeneity in the system evaluation results; Item 15, whether publication bias is fully considered in quantitative synthesis of literature, and its possible influence on research results is discussed; Item 16, are all potential conflicts of interest reported in the literature, including any funding received to complete the system evaluation? AMSTAR-2, A MeaSurement Tool to Assess systematic Reviews-2; Y, yes; PY, partially; N, no. PICO, population, intervention, control, and outcomes; RoB, risk of bias.

the spleen meridian and an assistant. The combination of the 4 drugs can tonify the spleen and overcome dampness to stop diarrhea, soften the liver and regulate qi to relieve pain, make the spleen nourish the liver, and stop pain and diarrhea. Compared with western medicine, TXYF is more suitable for the treatment of irritable bowel syndrome with complex pathogenesis (25). All 10 of the literatures included in this study showed that TXYF is effective in treating D-IBS with low recurrence rate and few adverse reactions. Clinical and animal experiments also show that Tongxie yaofang can regulate the intestinal movement of IBS (26-27), regulate brain gut interaction (28), reduce inflammatory reaction (29), regulate intestinal flora (30), regulate metabolism (31), and protect intestinal mucosal barrier function (32). However, Tongxie Yaofang also has some limitations, such as bad taste and inconvenient decoction.

This study evaluated the methodological and evidence quality of each systematic evaluation, summarized the efficacy and safety of TXYF in treating IBS-D, and provided an evidence-based medicine reference for its clinical application. However, from the results of AMSTAR-2 scale evaluation, there were some methodological deficiencies remained in the 10 systematic evaluations included in this study. As only 1 study was registered on the relevant platform, its transparency and credibility are not high; the literature search and screening was not satisfactorily comprehensive, which was limited to published literature, so there was serious publication bias, and the influence of individual research bias risk on meta-analysis results was not evaluated. The general information included in the literature was unknown, such as the research subject, research location, usage and dosage of control drugs, and so on. All studies did not provide a list of excluded literatures and none of the published literatures in China detailed their

Table 3 GRADE grading

References	Outcome indicator	Limitations	Inconformity	Not directly	Inaccuracy	Publication bias	Classification of evidence quality
Bian *et al.* 2006 (11)	Total effective rate	−1I	0	0	−1III	−1IV	Extremely low
Zhou *et al.* 2019 (12)	Total effective rate	−1I	0	0	0	−1IV	Low
	Abdominal pain	−1I	−1II	0	−1III	−1IV	Extremely low
	Stool frequency integral	−1I	−1II	0	−1III	−1IV	Extremely low
	Fecal trait score	−1I	−1II	0	−1III	−1IV	Extremely low
	Total symptom score	−1I	−1II	0	−1III	−1IV	Extremely low
	Incidence of adverse reactions	−1I	0	0	−1III	−1IV	Extremely low
	Recurrent rate	−1I	0	0	−1III	−1IV	Extremely low
Dai *et al.* 2018 (13)	Total effective rate	−1I	0	0	0	−1IV	Extremely low
	Abdominal pain	−1I	−1II	0	−1III	−1IV	Extremely low
	Abdominal discomfort	−1I	−1II	0	−1III	−1IV	Extremely low
	Diarrhea	−1I	−1II	0	−1III	−1IV	Extremely low
	Fecal frequency	−1I	−1II	0	−1III	−1IV	Extremely low
Xu *et al.* 2017 (14)	Total effective rate	−1I	0	0	−1III	−1IV	Extremely low
	Effective efficiency	−1I	0	0	−1III	0	Low
	Effective rate	−1I	0	0	−1III	0	Low
	Effective rate	−1I	0	0	−1III	0	Low
Guo *et al.* 2015 (15)	Total effective rate	−1I	0	0	−1III	−1IV	Extremely low
Yao 2016 (16)	Total effective rate	−1I	−1II	0	−1III	−1IV	Extremely low
Zhao *et al.* 2017 (17)	Total effective rate	−1I	0	0	−1III	0	Low
Su *et al.* 2009 (18)	Total effective rate	−1I	0	0	−1III	−1IV	Extremely low
Wang *et al.* 2017 (19)	Total effective rate	−1I	0	0	0	−1IV	Low
	Cure rate	−1I	0	0	−1III	−1IV	Extremely low
	Recurrent rate	−1I	0	0	−1III	−1IV	Extremely low
Shi *et al.* 2007 (20)	Total effective rate	−1I	−1II	0	0	−1IV	Extremely low

0, do not downgrade; −1, drop 1 level; CT, basic treatment; (I) the included research methodology is of low quality, and it is biased in randomization, distribution concealment, and blind method; (II) the heterogeneity included in the study is large, and I is large after examination, and the confidence interval overlap between the studies is not high; (III) the sample size included in the study is small and the confidence interval is wide; (IV) the funnel graph is asymmetric, and the published bias is found by Egger test, or the results are all positive and there is no published bias evaluation. GRADE, Grading of Recommendations, Assessment, Development and Evaluations.

conflicts of interest. There were also many problems in the evaluation of GRADE's evidence quality: for example, there was a great bias in randomization, distribution concealment, and blind method of clinical trials; less research was included; asymmetry of funnel diagram; literature without negative results, and so on. Therefore, the evidence quality of outcome indicators of TXYF in treating IBS-D is low, and its credibility is doubtful.

Table 4 Efficacy results included in the systematic reviews

References	Outcome indicator [number of studies]	Effect quantity	95% CI	P value
Bian *et al.* 2006 (11)	Total effective rate [12]	RR =1.35	1.21, 1.50	<0.05
Zhou *et al.* 2019 (12)	Total effective rate [37]	OR =4.61	3.67, 5.78	<0.00001
	Abdominal pain [11]	MD =−0.41	−0.56, −0.27	<0.00001
	Stool frequency integral [6]	MD =−0.47	−0.58, −0.35	0.0005
	Fecal trait score [11]	MD =−0.38	−0.48, −0.27	<0.00001
	Total symptom score [8]	MD =−2.75	−3.66, −1.84	<0.00001
	Incidence of adverse reactions [10]	OR =0.26	−0.08, 0.86	0.03
	Recurrence rate [3]	OR =0.7	0.25, 1.96	0.06
Dai *et al.* 2018 (13)	Total effective rate [23]	OR =4.04	3.09, 5.27	<0.00001
	Abdominal pain [14]	MD =−1.27	−1.99, −0.56	<0.00001
	Abdominal discomfort [8]	MD =−0.37	−0.73, −0.01	0.04
	Diarrhea [8]	MD =−1.10	−1.95, −0.25	0.01
	Fecal frequency [7]	MD =−1.42	−2.19, −0.65	0.0003
Xu *et al.* 2017 (14)	Total effective rate [9]	OR =5.62	3.78, 8.36	<0.00001
	Effective efficiency [9]	OR =3.02	2.30, 3.95	<0.01
	Effective rate [9]	OR =0.71	0.53, 0.94	0.02
	Effective rate [9]	OR =0.18	0.12, 0.26	<0.01
Guo *et al.* 2015 (15)	Total effective rate [9]	OR =3.75	2.43, 5.78	<0.00001
Yao 2016 (16)	Total effective rate [12]	RR =1.30	1.14, 1.48	<0.00001
Zhao *et al.* 2017 (17)	Total effective rate [7]	OR =4.17	2.62, 6.65	<0.00001
Su *et al.* 2009 (18)	Total effective rate [22]	OR =5.61	4.33, 7.25	<0.00001
Wang *et al.* 2017 (19)	Total effective rate [26]	OR =5.16	4.05, 6.58	<0.00001
	The cure rate [21]	OR =2.75	2.24, 3.36	<0.00001
	Recurrence rate [3]	OR =0.29	0.14, 0.61	0.01
Shi *et al.* 2007 (20)	Total effective rate [23]	RR =1.33	1.21, 1.45	<0.01

CI, confidence interval; OR, odds ratio; RR, relative risk; MD, mean difference.

Conclusions

From the 10 studies included in this research, TXYF can improve the total clinical effective rate, improve abdominal pain, diarrhea and other symptoms, and does not increase adverse reactions. However, due to the low quality of research methodology and evidence, the reliability of research results is not strong. Therefore, it is necessary for clinicians to design more rigorous and high-quality RCT, and concurrently, it is necessary to improve the systematic evaluation methodology and the quality evaluation level of outcome evidence, so as to provide more reliable evidence-based medicine substantiation.

Acknowledgments

Funding: This project was supported by the Key Projects of Jiangsu Province Science and Technology Development Plan of Traditional Chinese Medicine, China (ZD201911).

Footnote

Reporting Checklist: The authors have completed the

PRISMA reporting checklist. Available at https://dx.doi.org/10.21037/apm-21-1612

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://dx.doi.org/10.21037/apm-21-1612). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References

1. Xu XJ, Liu L, Yao SK. Nerve growth factor and diarrhea-predominant irritable bowel syndrome (IBS-D): a potential therapeutic target? J Zhejiang Univ Sci B 2016;17:1-9.
2. Kibune Nagasako C, Garcia Montes C, Silva Lorena SL, et al. Irritable bowel syndrome subtypes: Clinical and psychological features, body mass index and comorbidities. Rev Esp Enferm Dig 2016;108:59-64.
3. Wu H, Zhang Z. Consensus on treatment of irritable bowel syndrome (2018, USA). Chinese Journal of Microecology 2019;31:944-6.
4. Spleen and Stomach Disease Branch of Chinese Traditional Medicine Association,Consensus opinion of TCM diagnosis and treatment experts of irritable bowel syndrome (2017). Journal of Traditional Chinese Medicine 2017;58:1614-20.
5. Liu Y, Yuan J, Yang K, et al. Brief introduction of making method of system evaluation and re-evaluation and analysis of related data. Chinese Journal of Evidence-based Pediatrics 2011;6:58.
6. Ge L, Pan B, Pan J, et al. Unscramble amstar-2-a quality evaluation tool based on random and/or non-random controlled trial system evaluation. Chinese Drug Evaluation 2017;34:334.
7. Zhang F, Shen A, Zeng X, et al. Explanation of quality evaluation tool AMSTAR2 in systematic evaluation methodology. Chinese Journal of Evidence-based Cardiovascular Medicine 2018;10:14.
8. Shea BJ, Reeves BC, Wells G, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. BMJ 2017;358:j4008.
9. Chen Y, Yao L, Susan N, et al. The necessity and precautions of applying GRADE in system evaluation. Chinese Journal of Evidence-based Medicine 2013;13:1401.
10. Yang N, Deng W, Chen Y, et al. The principles, methods and challenges of applying GRADE in the systematic evaluation of prognosis research. Chinese Journal of Evidence-based Medicine 2015;15:1112.
11. Bian Z, Wu T, Liu L, et al. Effectiveness of the Chinese herbal formula TongXieYaoFang for irritable bowel syndrome: a systematic review. J Altern Complement Med 2006;12:401-7.
12. Zhou Y, Han S, He Y. Clinical Effects and Safety of Tongxieyaofang on Diarrhea Predominant Irritable Bowel Syndrome: A Meta-Analysis of Randomized Trails. Evid Based Complement Alternat Med 2019;2019:4893876.
13. Dai YK, Li DY, Zhang YZ, et al. Efficacy and safety of Modified Tongxie Yaofang in diarrhea-predominant irritable bowel syndrome management: A meta-analysis of randomized, positive medicine-controlled trials. PLoS One 2018;13:e0192319.
14. Xu L, Chen K, Gao X. Meta-analysis of the treatment of irritable bowel syndrome with Shenling Baizhu Powder and Tongxie Yaofang. Chinese Journal of Clinical Gastroenterology 2017;29:159-63.
15. Guo Z, Su Z, Wang Z, et al. Meta-analysis on the treatment of diarrhea-predominant irritable bowel syndrome with Sijunzi Decoction and Tongxie Yaofang. Chinese Journal of Experimental Traditional Medical Formulae 2015;21:209-13.
16. Yao P. Systematic evaluation of the curative effect of Sinisan combined with Tongxie Yaofang and western medicine on irritable bowel syndrome. Tianjin Traditional Chinese Medicine 2016;33:279-84.
17. Zhao H, Hu N, Huang S, et al. Meta-analysis of clinical research on diarrhea-predominant irritable bowel syndrome. Journal of Traditional Chinese Medicine 2017;23:78-81.
18. Su G, Liu W, Chen H, et al. Systematic Review of Randomized Controlled Trials on Irritable Bowel

Syndrome Based on Tongxie Yaofang. Journal of Guangzhou University of Traditional Chinese Medicine 2009;26:113-9.
19. Wang Y, Shi Y, Wang W. Systematic evaluation of clinical efficacy of treating irritable bowel syndrome with liver depression and spleen deficiency based on Tongxie Yaofang. World Traditional Chinese Medicine 2017;12:2223-2227+2231.
20. Shi J, Wang C W, Fan K. Meta-analysis of the curative effect of Tongxie Yaofang on irritable bowel syndrome. World Chinese Journal of Digestology 2007;1934-9.
21. Bellini M, Gambaccini D, Stasi C, et al. Irritable bowel syndrome: a disease still searching for pathogenesis, diagnosis and therapy. World J Gastroenterol 2014;20:8807-20.
22. Teruel C, Garrido E, Mesonero F. Diagnosis and management of functional symptoms in inflammatory bowel disease in remission. World J Gastrointest Pharmacol Ther 2016;7:78-90.
23. Yu Y, Wu S, Li J, et al. The effect of curcumin on the brain-gut axis in rat model of irritable bowel syndrome: involvement of 5-HT-dependent signaling. Metab Brain Dis 2015;30:47-55.
24. Saulnier DM, Ringel Y, Heyman MB, et al. The intestinal microbiome, probiotics and prebiotics in neurogastroenterology. Gut Microbes 2013;4:17-27.
25. Li B,Miao L,Rui J, et al. Multi-target network construction and mechanism analysis of main effective components of Tongxie Yaofang. Chinese Journal of Experimental Traditional Medical Formulae 2018;24:206-13.
26. Yin Y, Zhong L, Wang JW, et al. Tong Xie Yao Fang relieves irritable bowel syndrome in rats via mechanisms involving regulation of 5-hydroxytryptamine and substance P. World J Gastroenterol 2015;21:4536-46.
27. Zhang Y, Bo P, Li X. Increased incidence of bowel and psychological symptoms in Chinese female D-IBS patients with premenstrual syndrome. Gastroenterol Nurs 2014;37:351-9.
28. Zhuo B, Zhang Y, Ning X. Effect of Tongxieyaofang combined with Sijunzi Decoction on brain gut peptide in patients with diarrhea predominant irritable bowel syndrome. Journal of Nanjing University of Traditional Chinese Medicine 2019;35:25-8.
29. Zhang B, Wang W, Wang F, et al. Tang Xudong. Effect evaluation of Tongxie Yaofang on diarrhea predominant irritable bowel syndrome model rats with liver depression and spleen deficiency syndrome. Chinese Journal of Traditional Chinese Medicine 2018;33:4341-6.
30. Li J, Cui H, Cai Y, et al. Tong-Xie-Yao-Fang Regulates 5-HT Level in Diarrhea Predominant Irritable Bowel Syndrome Through Gut Microbiota Modulation. Front Pharmacol 2018;9:1110.
31. Zhao XY, Wang JW, Yin Y, et al. Effect of Tong Xie Yao Fang on endogenous metabolites in urine of irritable bowel syndrome model rats. World J Gastroenterol 2019;25:5134-51.
32. Hou Q, Huang Y, Zhu Z, et al. Tong-Xie-Yao-Fang improves intestinal permeability in diarrhoea-predominant irritable bowel syndrome rats by inhibiting the NF-κB and notch signalling pathways. BMC Complement Altern Med 2019;19:337.

(English Language Editor: J. Jones)

Cite this article as: Chen X, Yu X, Shi Y, Shen H. Overview of systematic evaluation of efficacy of Tongxie Yaofang in treating diarrhea-predominant irritable bowel syndrome. Ann Palliat Med 2021;10(8):9223-9232. doi: 10.21037/apm-21-1612

