



Meta-analysis of TCM in the Treatment of AIDS Diarrhea

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Abstract

Objective The aim of the study is to systematically evaluate the effect of Traditional Chinese medicine (TCM) in the treatment of AIDS diarrhea.

Methods The computer system was used to comprehensively search database of Wanfang (WF), VIP, and China National Knowledge Infrastructure (CNKI) for relevant literature on the application effect of Chinese medicine in the treatment of AIDS diarrhea. The retrieval time was set from January 1, 2010 to August 15, 2021. The documents that did not meet the inclusion criteria were eliminated, and the quality of the qualified literature was evaluated according to the improved Jadad scoring standard. The main outcome indicators were entered into the literature, and Review Manager 5.0 software was used for meta-analysis.

Results Eight eligible articles were included, a total of 536 cases of AIDS diarrhea patients were included. All eight eligible articles observed the clinical efficacy of TCM in the treatment of AIDS diarrhea, among which four observed the TCM syndrome changes in the treatment of AIDS diarrhea, and four observed adverse reactions of TCM in the treatment of AIDS diarrhea. All articles were extracted for valid data. After entering all the main observation index data, the results of meta-analysis showed that the effect of TCM in the treatment of AIDS diarrhea was better, the difference was statistically significant [$MD = 2.92$, 95% CI (1.81, 4.70), $p < 0.001$]; TCM in the treatment of AIDS diarrhea was more conducive to improving the TCM syndrome scores of patients, the difference was statistically significant [$MD = -2.55$, 95% CI (-3.37, -1.73), $p < 0.001$]; the adverse effects of TCM in the treatment of AIDS diarrhea were mild, and the difference was statistically significant [$MD = 1.70$, 95% CI (0.48, 5.97), $p = 0.41$].

Conclusion The effect of TCM in the treatment of AIDS diarrhea patients is remarkable, which can effectively improve the TCM symptom scores of patients without increasing the incidence of adverse reactions.

Keywords

- AIDS diarrhea
- TCM
- syndrome score
- adverse reaction
- Meta-analysis

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Introduction

Diarrhea is a common symptom of AIDS patients. It is reported that AIDS diarrhea occurs in 60% of AIDS patients in developed countries and 90% in developing countries.¹ Different degrees of malnutrition and malabsorption may occur in patients with AIDS diarrhea, which affects the quality of life of patients and is also one of the important reasons for the risk of death in AIDS patients.² At this stage, Western medicine mostly adopts etiological and symptomatic antidiarrheal drugs for AIDS diarrhea, such as imodium and octreotide, but the clinical treatment effect is not ideal, and long-term use has certain adverse reactions.³ Traditional Chinese medicine (TCM) believes that AIDS diarrhea belongs to the categories of “diarrhea” and “dysentery.” Due to the complex pathogenesis, AIDS diarrhea is caused mainly by spleen deficiency and dampness. Spleen disease lasts for a long time, and it affects the kidney and forms deficiency in both spleen and kidney. Due to long-term consumption and injury, the spleen Yang does not rise and the qi movement is disordered. Therefore, AIDS diarrhea occurs repeatedly for a long time.⁴ At present, several studies have observed TCM treatment of AIDS diarrhea patients. Common TCM remedies include Jianpi Zhixiefang granule, moxibustion, Shenling Fuzheng Capsule, Chinese herbal packet hot compress, and Huopu Xialing decoction, etc., but lacks systematic review. This study used meta-analysis to evaluate the effect of TCM on AIDS diarrhea patients.

Materials and Methods

Data Sources and Retrieval Methods

The articles of randomized controlled trials related to the treatment of AIDS diarrhea by TCM were systematically searched, including database of Wanfang (WF), VIP, and China National Knowledge Infrastructure (CNKI) as well as China Biomedical Literature Service System, etc. The search period was set to January 1, 2010 to August 15, 2021. The search keywords were AIDS, diarrhea, TCM, Chinese herbs, randomized controlled experiments, etc. When searching, it is searched by subject word + free word.

Literature Inclusion and Exclusion Criteria

(1) Inclusion criteria: The research method was randomized control; the subjects included in the experiment were patients with AIDS diarrhea; the observation indicators of the literature included clinical efficacy, TCM symptom scores, and adverse reactions; the patients in the included literature observation group/study group all received TCM treatment. (2) Exclusion criteria: duplicate publications or literature with no source data; non-randomized controlled research literature such as expert experience, reviews, etc., no control group, or two groups without specifying treatment times; lack of specific data for observation indicators.

Literature Screening and Quality Evaluation of Extractants

(1) Literature screening and extraction: two evaluators reviewed and assessed the collected literature and extracted relevant data. The evaluation method was to first read the relevant literature titles and abstracts, eliminate unqualified literature according to the inclusion and exclusion criteria. A database was established and the data such as the publication time of the literature, research grouping method, and author that met the requirements were the inputs. For literature with differences, the evaluators would reach a final conclusion after discussion. (2) Evaluation of literature quality: The literature quality was evaluated according to the modified Jadad scale,⁵ including the four procedures of randomization, blinding, withdrawals and dropouts, and randomized concealment.

The first three procedures were scored on a 0 to 2 scale, the last procedure uses a 0 to 1 scale, the score ranges from 0 to 7 points, and ≥ 3 points are considered high-quality articles. Among them, the first three items adopted the 0 to 2 scores, grade 3 scoring method, and the last item adopted the 0 to 1 score, grade 1 scoring method. The score range was 0 to 7 points, and ≥ 3 points were high-quality documents.

Statistical Methods

RevMan 5.0 software was used for analysis, the mean difference of 95% confidence interval [MD (95% CI of MD)] was used to represent the measurement data, and $p < 0.05$ was considered statistically significant. The heterogeneity between literature was tested by I^2 and p -value; $p < 0.1$ or $I^2 > 50\%$ indicated statistical heterogeneity between literature, and the random effect model was adopted. The inverted funnel chart was used to analyze the bias of each published literature. If $p \geq 0.1$ and $I^2 \leq 50\%$, there is no statistical heterogeneity between literature, and a fixed effect model was used for analysis.

Results

Literature Screening

A total of 262 articles were selected at the preliminary stage of screening, 254 were excluded, and eight articles were finally included, totaling 536 patients with AIDS diarrhea. The screening flowchart is shown in ►Fig. 1.

Basic Characteristics of Included Literature Studies

A total of 536 patients with AIDS diarrhea were included. Among them, there were 289 cases in the observation groups/research groups and 247 cases in control groups, all of which were domestic studies. The research characteristics of the eight included studies are shown in ►Table 1.

Quality Evaluation of the Included Literature

The Jadad score of 5 of the eight included articles was 2, indicating low quality. The Jadad score of the three articles was 3, indicating the literature was of higher quality. No

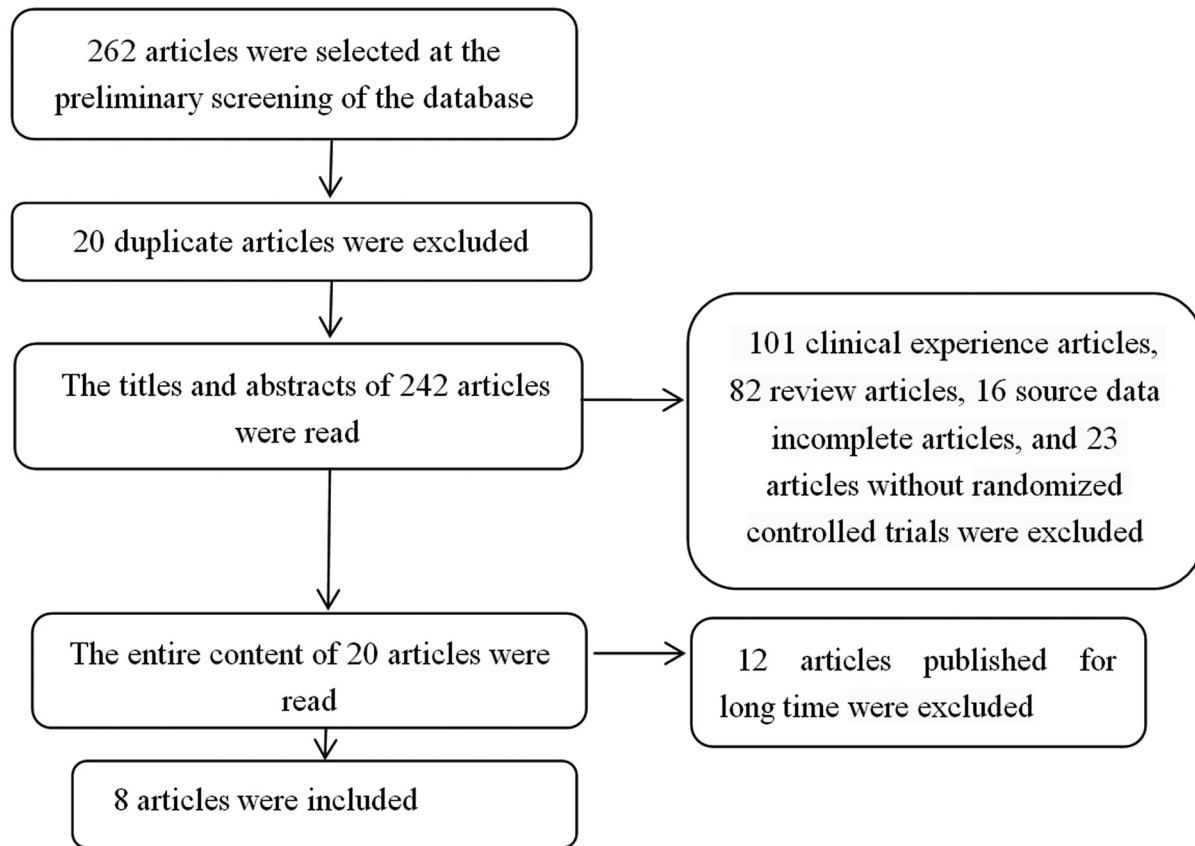


Fig. 1 Flowchart of literature screening.

Table 1 Basic characteristics of included literature studies

Number	Included research literature	Research time	Number of patients included (cases)		Treatment method		Course of treatment
			Observation group/ Experimental group/ Treatment group	Control group	Observation group/Study group	Control group	
1	Li et al ⁶	2016	19	18	Jianpi Zhixiefang Granule	Norfloxacin capsule, montmorillonite powder	2 wk
2	Li et al ⁷	2016	14	22	Moxibustion	Saline rehydration	2 wk
3	Yang and Sun ⁸	2018	30	30	Xielikang Capsule + basic western medicine treatment	Basic western medicine treatment	2 wk
4	Wen et al ⁹	2016	33	32	Highly active anti-retroviral therapy + Shenling Fuzheng Capsule	Highly active anti-retroviral therapy + loperamide	6 wk
5	Jiao et al ¹⁰	2021	44	44	Comprehensive western medicine + Chinese herbal packet hot compress	Comprehensive western medicine treatment	2 wk
6	Tian et al ¹¹	2012	94	46	Chinese herbal prescriptions of invigorating spleen to stop diarrhea	Imodium capsule	2 wk
7	Yang et al ¹²	2013	41	41	Huopu Xialing Decoction + acupoint injection with water needle	Flufenamic Capsule	2 wk
8	Ren ¹³	2013	14	14	Herbal prescriptions of invigorating spleen to stop diarrhea	Flufenamic Capsule + Smectite	2 wk

Table 2 Quality evaluation of the included literature

Included research literature	Sample size (cases)	Randomization method	Blinding	Randomized concealment	Withdrawal and dropout	Jadad score
Li et al 2016	37	Random number table	Not mentioned	Not mentioned	Not mentioned	3
Li et al 2016	36	According to the patient's wishes	Not mentioned	Not mentioned	Not mentioned	2
Yang and Sun 2018	60	Random number table	Not mentioned	Not mentioned	Not mentioned	2
Wen et al 2016	65	Random number table	Not mentioned	Not mentioned	Not mentioned	3
Jiao et al 2021	88	Single blinding	Adequate	Not mentioned	Not mentioned	2
Tian et al 2012	140	Random grouping (without indicating method)	Not mentioned	Not mentioned	Having dropout (without affecting results)	2
Yang et al 2013	82	Random number table	Not mentioned	Not mentioned	Not mentioned	2
Ren 2013	28	Double Blinding randomization	Adequate	Not mentioned	Not mentioned	3

literature mentioned blinding, withdrawal, and dropout (►Table 2).

Meta-analysis of Main Outcome Measures

Clinical Efficacy

The clinical effects of TCM on AIDS diarrhea were observed in eight articles; Because $p \geq 0.1$ and $I^2 \leq 50\%$, there was no statistical heterogeneity among the literature. The meta-analysis of the literature was performed by using the random effect model. The results showed that the effect of TCM on AIDS diarrhea was better, and the difference was statistically significant [$MD = 2.92$, 95% $CI (1.81, 4.70)$, $p < 0.001$] (►Fig. 2).

TCM Syndrome Scores

Four of the eight articles observed the effect of TCM on TCM syndrome scores of AIDS patients with diarrhea, and effective data can be obtained. The included literature was statistically consistent ($I^2 = 59\%$, $p = 0.06$). The literature

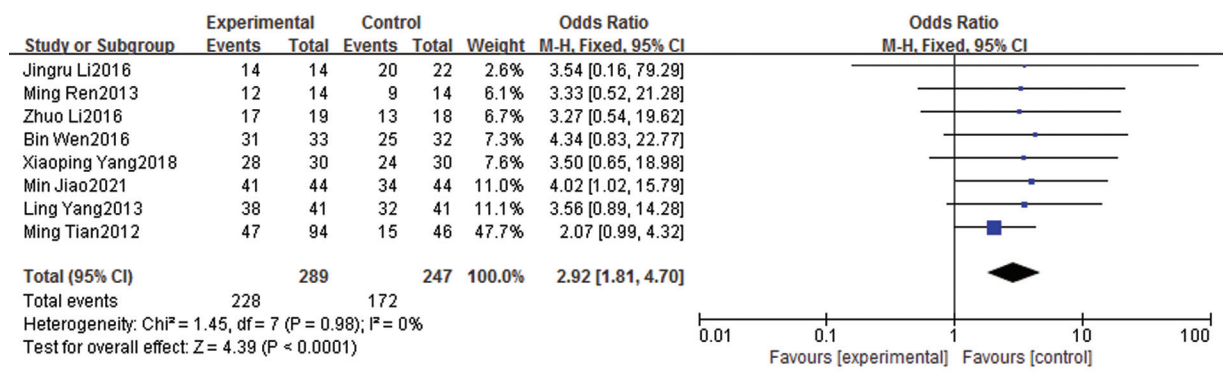
was meta analyzed by random effect model. The results showed that TCM treatment of AIDS diarrhea was more conducive to improve the TCM syndrome scores of patients [$MD = -2.55$, 95% $CI (-3.37, -1.73)$, $p < 0.001$] (►Fig. 3).

Adverse Reactions

Four of the eight articles observed the adverse reactions of AIDS diarrhea patients treated with TCM, and effective data can be obtained. The included articles were statistically tested ($I^2 \leq 50\%$, and $p \geq 0.1$) and meta-analysis was performed by using random effect model. The results showed that the adverse reactions of TCM in the treatment of AIDS diarrhea were slight, and the difference was statistically significant [$MD = 1.70$, 95% $CI (0.48, 5.97)$, $p = 0.41$] (►Fig. 4).

Publication Bias of Main Outcome Measures

The TCM syndrome scores of the four articles were compared and the inverted funnel chart was compiled. SE (MD) at the vertical axis and MD at the horizontal axis. The results show

**Fig. 2** Meta-analysis forest plot of efficacy in two groups.

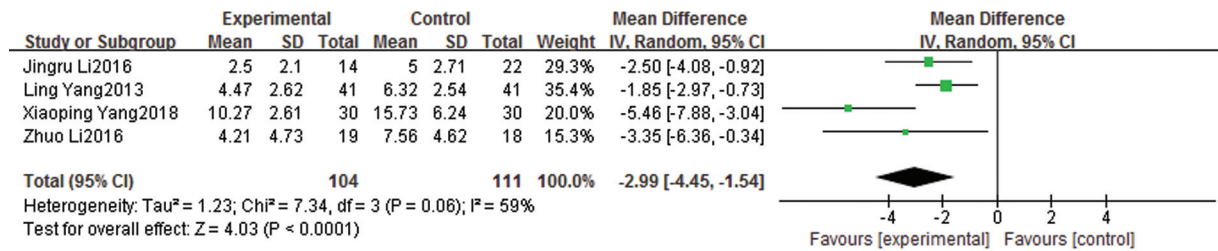


Fig. 3 Meta-analysis Forest plot of efficacy in two groups.

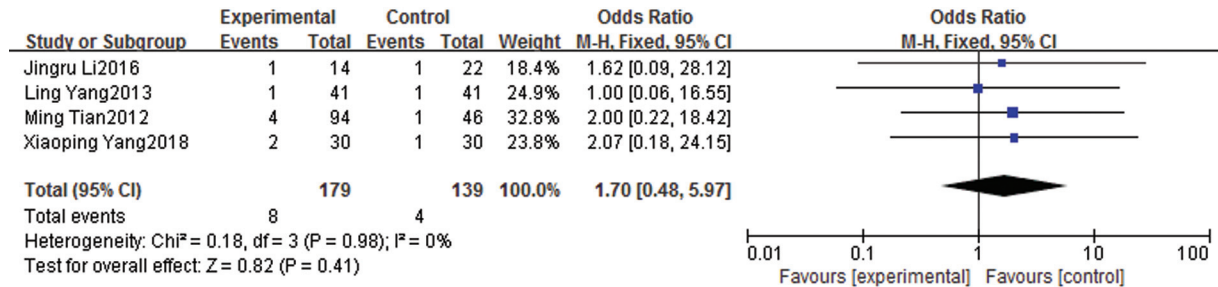


Fig. 4 Meta-analysis forest plot of adverse reactions in two groups.

that the distribution of the number and position of each point on both sides are not symmetrical (\rightarrow Fig. 5).

Discussion

Diarrhea is a common complication in AIDS patients. Long-term diarrhea will lead to significant weight loss and seriously affect the survival treatment of patients. Therefore, it is of great significance to make a clear effective treatment plan for AIDS diarrhea. At present, Western medicine treatment of AIDS diarrhea varies according to the different sources of infection; corresponding treatment drugs include antibacterial drugs, antiprotozoal, sulfonamides, etc. They all have a certain clinical effect, but their long-term use can develop drug resistance, which may cause intestinal flora disorder and high recurrence rate after drug withdrawal. So, we see there are certain limitations in clinical application.¹⁴

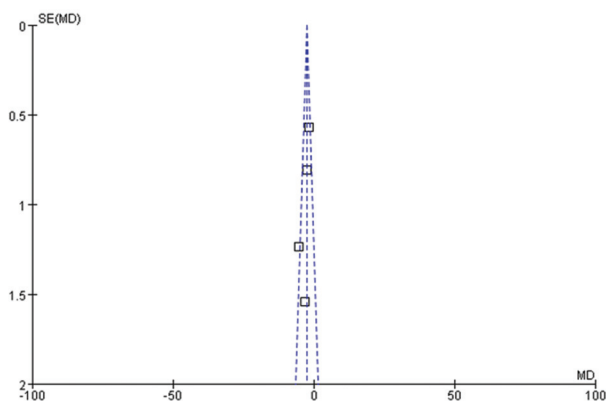


Fig. 5 Meta-analysis funnel chart of TCM syndrome scores in two groups.
 TCM, traditional Chinese medicine.

TCM believes that AIDS diarrhea belongs to “diarrhea dysentery” and other categories, and among them, spleen qi deficiency syndrome is the most common. The main pathogenesis is spleen deficiency and serious dampness in the body, which is usually caused by damage to the spleen and stomach caused by exogenous pathogens and endogenous dampness inside the body.¹⁵ There are many treatment schemes for AIDS and diarrhea mentioned in the existing TCM research studies, including Jianpi Zhixiefang Granule, moxibustion, Shenling Fuzheng Capsule, Chinese herbal packet hot compress, Xielikang Capsule, and Huopu Xialing Decoction. Among them, Xielikang Capsule has the effect of killing bacteria, improving dysentery, invigorating the spleen and tonifying the kidney, soothing intestines, and stopping diarrhea. Jianpi Zhixie Fang is astragalus-based and is used together in the treatment with various Chinese herbs according to different symptoms of patients, reflecting the principle of strengthening the body resistance to eliminate pathogenic factors, simultaneously treating both principal and subordinate symptoms.¹⁶ Huopu Xialing Decoction was originated from *Yiyuan*, and it was designed for treating bodies with serious dampness and heat, which has the effect of invigorating the spleen, removing the dampness, and stopping diarrhea.¹⁷ The method of Chinese herbal packet hot compress originated from Shiji Wu, a doctor in the Qing Dynasty. Applying Chinese herbal packet hot compress to Shenque (CV 8) acupoint, Zhongwan (CV 12) acupoint, and Tianshu (ST 25) acupoint from outside to the inside can promote the transmission of the medicine to the focus of infection through the channel, so as to achieve the effects of regulating spleen and stomach, strengthening the kidney and nourishing blood, stopping diarrhea and so on.¹⁸ Moxibustion is one of the external treatment methods of TCM. Moxibustion is used in the treatment of AIDS diarrhea patients with the

method of syndrome differentiation and acupoint, which can effectively relieve the symptoms of diarrhea, loss of appetite, and fatigue.¹⁹ Shenling Fuzheng Capsule is based on the Sijunzi Decoction, which has the effects of calming the heart and soothing the mind, strengthening the spleen, and nourishing the kidney. At the same time, when taken during Sanfutian (the hottest and the most humid day of the year), the medicine can directly treat the sickness, which not only strengthens the body but also eliminates the “cold” caused by Yang deficiency, fundamentally improving the patient’s immune system and balancing the body’s Yin and Yang. This would cause the diarrhea situation to self-recover.²⁰

At present, many studies have used the above methods to treat AIDS diarrhea, but there is a lack of systematic evaluation of relevant treatment methods. Meta-analysis is a kind of literature quality evaluation method, which can confirm some specific research results and evaluate the value of clinical studies by searching through relevant literature that meets the requirements and integrates the search results.²¹ This study conducted a meta-analysis on the effect of TCM on AIDS diarrhea; the results showed that TCM was effective in the treatment of AIDS and diarrhea, and could improve the TCM syndrome scores of patients without increasing the risk of adverse reactions. Analysis of possible reasons: TCM treatment of AIDS and diarrhea is conducted based on the theory of TCM syndrome differentiation, overall adjustment, focusing on the person’s body, and the combination of TCM internal and external treatment, which can all achieve good results. It can effectively improve TCM syndrome scores, and the adverse reactions are slight.²² This study further analyzed the publication bias of the included literature, and the results showed that there was a certain bias in the comparison of TCM syndrome scores between the two groups. In view of these results, it is suggested that using different test methods to observe the bias of the unified index in the future will improve the credibility of the literature. In addition, only a few articles included in this study observed the CD4⁺ level of patients’ defecation times. Therefore, it was not taken as a key analysis index, and future studies should focus on observing the influence of TCM on the CD4⁺ level of defecation times in AIDS diarrhea patients.

In conclusion, TCM in the treatment of AIDS diarrhea shows a more ideal result. It can effectively improve the TCM syndrome scores of patients, and will not increase the occurrence of adverse reactions.

Credit Authorship Contribution Statement

Shaotian Wu: Conceptualization, data curation, formal analysis, and writing—original draft. **Liran Xu:** Conceptualization, methodology, funding acquisition, and writing—review & editing. **Feng Sang:** data curation, formal analysis, writing—review & editing. **Liangping Li:** data curation, software, writing—review & editing. **Yaya Guo:** data curation, writing—review & editing.

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Conflict of Interest

The authors declare no conflict of interest.

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