

STUDY PROTOCOL

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Efficacy and safety of tangweian recipe in the treatment of diabetic gastroparesis: a protocol for a non-inferiority, double-blind, active drug, randomized controlled clinical trial

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Abstract

Background Diabetic Gastroparesis (DGP) is a syndrome characterized by delayed gastric emptying and upper gastrointestinal symptoms. As the incidence of diabetes mellitus continues to increase, so does the incidence of DGP, which severely affects the fasting plasma glucose (FPG) control and quality of life of diabetic patients. Tangweian recipe (TWA) is an effective recipe for treating DGP with spleen and stomach disharmony evidence. Previous clinical trials have provided preliminary verification of the effectiveness of TWA in treating DGP. However, high-quality clinical evidence supporting this treatment is lacking. Therefore, the purpose of this study is to conduct a clinical randomized controlled trial to obtain conclusive evidence regarding the effectiveness of TWA.

Methods and analysis This study is a randomized, positive, parallel controlled clinical trial in patients with DGP. A total of 72 patients were recruited and randomized using a random number method to receive either TWA combined with mosapride or mosapride alone for a treatment period of 4 weeks.

Primary outcome The American neurogastroenterology and motility society gastroparesis cardinal symptom index-daily diary (ANMS GCSI-DD).

Secondary outcomes Changes in FPG, weight, body mass index (BMI), gastric emptying rate testing, Wexner constipation scores, traditional chinese medicine (TCM) evidence scores and quality of life (QOL) assessment before and after treatment. In addition, we will also perform a safety analysis.

Trial registration The study was registered at ClinicalTrials.gov (NCT05720442) on February 9, 2023 (<https://clinicaltrials.gov/study/NCT05720442>), and the registration center is Guang'anmen Hospital, Chinese Academy of Traditional Chinese Medicine.

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Keywords Tangweian recipe, Diabetic gastroparesis, Clinical trial protocol, Traditional chinese medicine, Randomized controlled trial

Introduction

Gastroparesis is a common symptom in patients with a long history of diabetes. In China alone, the number of adults with diabetes has surpassed 140 million [1], with 50% of these individuals are experiencing delayed gastric emptying [2]. Diabetic Gastroparesis (DGP) is often caused by coordinated dysfunction of the autonomic nervous system, specific pacemaker cells of the gastrointestinal tract, and smooth muscle cells of the gastrointestinal tract [3], and the main clinical manifestations are early satiety, postprandial fullness, nausea, vomiting, abdominal distension, epigastric pain and weight loss [4]. Ye et al. found that patients with diabetic gastroparesis had a significantly higher mortality rate after diagnosis than patients with idiopathic gastroparesis (adjusted HR 1.9, 95% CI 1.2–3.0) [5]. DGP threatens the physical health of patients and significantly affects their mental state. Patients with severe abdominal pain are more likely to have symptoms of anxiety and depression [6]. Treatment of DGP can start with treating delayed gastric emptying and correcting fluid and electrolyte disturbances [7]. The principles of treatment for patients with type 2 diabetes mellitus combined with gastroparesis include eating smaller meals and avoiding a high-fat diet and pharmacological treatment focusing on gastropromotors and insulin [8]. Mosapride, metoclopramide (Reglan) and erythromycin have been reported as effective drugs for DGP [9]. Metoclopramide has been approved by the U.S. Food and Drug Administration (FDA) for the short-term treatment of diabetic gastropathy to alleviate symptoms of gastroparesis. However, with prolonged use, its efficacy diminishes, and it can lead to adverse events such as irreversible akathisia, Parkinsonism, and tardive dyskinesia [10]. The search for simpler and long-acting alternative therapies has been repeatedly emphasized in clinical practice.

Traditional Chinese medicine (TCM) approaches reportedly relieve patients from abdominal distension and nausea [11]. Tangweian recipe (TWA) is an effective traditional Chinese herbal recipe summarized based on years of clinical experience in the treatment of DGP, which consists of eight Chinese herbs: Seville Orange [*Citrus aurantium* L. *Citrus sinensis* Osbeck], Atractylodes Rhizome [*Atractylodes macrocephala* Koidz], Betel Nut [*Areca catechu* L.], Wine-processed Rhubarb Root and Rhizome [*Rheum palmatum* L. or *Rheum tanguticum* Maxim. ex Balf.], Pinellia Tuber [*Pinellia ternate* (Thunb.) Breit.], Ginger [*Zingiber officinale* Roscoe], Peach Kernel [*Prunus persica* (L.) Batsch or *Prunus davidiana* (Carr.) Franch.], Codonopsis

Root [*Codonopsis pilosula* (Franch.) Nannf. or *Codonopsis pilosula* Nannf. var. *modesta* (Nannf.) L.T. Shen]. In TCM theory, TWA can harmonize the spleen and stomach [12]. TWA may exert its effects by increasing the number of interstitial cells of Cajal in the gastric muscularis layer of rats and enhancing the expression of substance P protein in the hypothalamus [13], and the biomechanical remodeling of jejunum in diabetic rats was improved by upregulation of DNF, TrkA and TrkB [14]. Based on prior experimental evidence, the therapeutic efficacy of TWA in treating diabetic gastrointestinal dysfunction is demonstrated through multidimensional evidence: High-dose TWA significantly reduced glycated serum protein (GSP) levels ($315.03 \pm 29.51 \mu\text{mol/L} \rightarrow 246.96 \pm 31.04 \mu\text{mol/L}$, $P < 0.05$), indicating improved long-term glucose metabolism. TWA treatment reversed diabetic-induced intestinal remodeling, evidenced by decreased wall thickness ($1.87 \pm 0.07 \text{ mm} \rightarrow 1.38 \pm 0.03 \text{ mm}$), cross-sectional area ($19.66 \pm 0.66 \text{ mm}^2 \rightarrow 17.54 \pm 0.81 \text{ mm}^2$), and villus/crypt ratio (all $P < 0.05$) in a dose-dependent manner. High-dose TWA ameliorated intestinal viscoelasticity by reducing wall stiffness (rightward shift of stress-strain curve), opening angle ($91.85 \pm 2.70^\circ \rightarrow 75.18 \pm 3.98^\circ$), and residual strain magnitude. Immunohistochemistry revealed TWG inhibited advanced glycation end products (AGEs) deposition in intestinal villi, crypt epithelium, and muscular layers ($P < 0.05$), while downregulating RAGE receptor expression (crypt layer: $15.88 \pm 1.67 \rightarrow 9.43 \pm 1.29 \mu\text{m}$, $P < 0.01$). AGEs/RAGE levels showed strong positive correlations with morphological/biomechanical parameters ($r = 0.73\text{--}0.85$). These findings indicate that TWA exerts comprehensive therapeutic effects through multi-target interventions (metabolic regulation, tissue remodeling, and signaling pathway inhibition), with efficacy positively correlated to dosage [13–16]. Retrospective study data support that TWA plays a significant role in the three dimensions of symptom control, pathological regulation, and metabolic optimization. It can quickly relieve nausea and vomiting symptoms, improve gastrointestinal motility and nerve function, and optimize blood glucose [17]. The primary aim of this study is to conduct a parallel-controlled clinical trial that compares the therapeutic efficacy of simultaneous administration of TWA and mosapride with the use of mosapride alone. This comparison will serve to further validate the clinical effectiveness of TWA and provide high-quality evidence-based medical evidence supporting the use of TWA for the treatment of DGP.

METHOD

Research methods

This study was a non-inferiority trial in DGP patients, using a clinical study design approach of randomized, positive drug parallel control. A total of 60 patients diagnosed with diabetic gastroparesis were recruited in this study during the 4-week treatment period, the patients would be randomly assigned to either receive a combination of TWA and mosapride, or mosapride alone. This study protocol follows the Standard Protocol Items: Recommendations for Interventional Trials. The specific test procedure was shown in Fig. 1. All information related to the treatment schedule is presented in Table 1.

Sample size calculation

Based on the preliminary case summary research of the team, the expected efficacy rate of the Tangweian formula for diabetic gastrointestinal diseases is 70%, while the control group is projected to have an improvement rate of 30%. The two groups are calculated in a 1:1 ratio. Using a hypothesis test power of 90% and a confidence level of 95%, with Z for $1-\alpha/2=1.960$ and $\alpha=5\%$ for a two-tailed hypothesis, and accounting for a 20% dropout rate during follow-up, the total sample size is calculated to be 72 cases, with 36 cases in each group. Sample size

calculations were performed using PASS software (version 11.0; NCSS, LLC, Kaysville, UT, USA).

Patient recruitment

Sixty patients with diabetic gastroparesis would be recruited by Guang'anmen Hospital, China Academy of Chinese Medical Sciences (Beijing, China), and the hospital's webpage and bulletin board would post a recruitment advertisement to explain the purpose of the study, the drugs and physical examinations involved, eligibility criteria, and how to participate in the study. The investigator would explain the purpose of the study, requirements and interventions to potential patients and ensure that they understand the parameters of the study prior to obtaining their consent to participate. Patient eligibility would be checked by two physicians to confirm the patient's suitability for this study. In addition, demographic characteristics of ineligible patients and reasons for non-participation would be recorded. Recruitment would begin on March 10, 2023 and will continue until March 10, 2026. No patients would be involved in the design of this study, the recruitment process, the execution of study procedures, the reporting of results, or the dissemination of study findings. Physical examinations, laboratory tests, and interventions are free of charge.

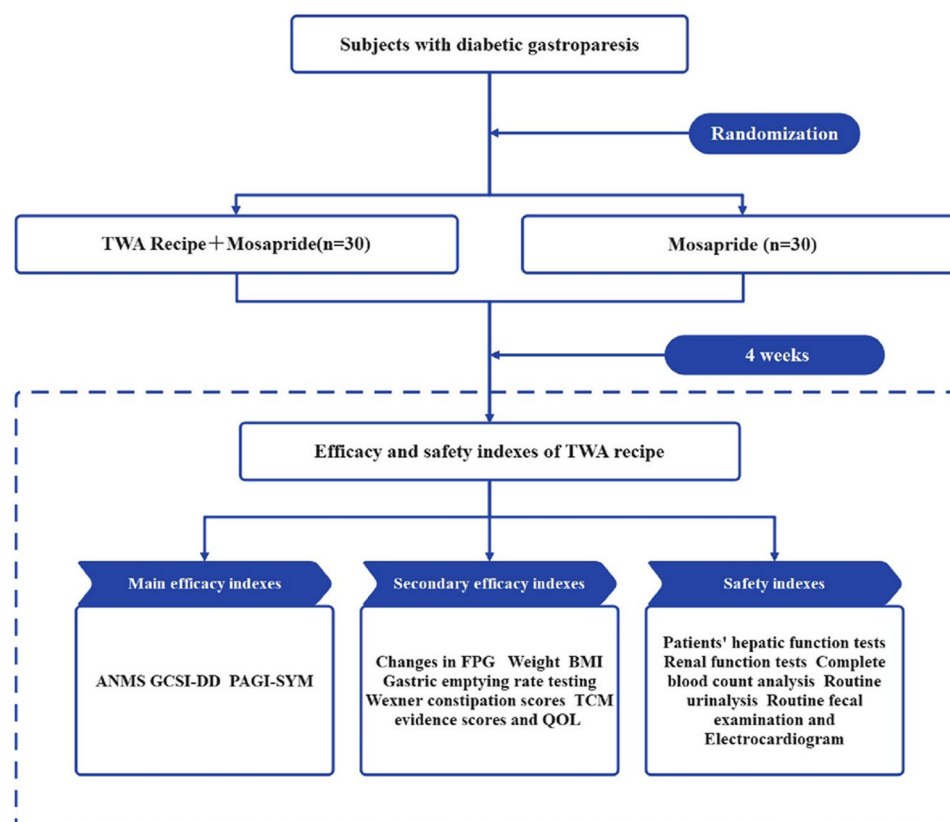


Fig. 1 Flow diagram of the study design

Table 1 Schedule of enrolment, assessments, and data collection

Period	Enrolment/Baseline	Treatment period		Follow-up period
Time points	Introduction period	0weeks	4weeks	12weeks
Eligibility screening	√	-	-	-
Informed consent	√	-	-	-
Physical Examination	√	√	-	-
Characteristic Random allocation	√	√	-	-
Interventions	-	-	√	-
Clinical Assessments	-	-	√	-
Medical history	-	√	√	-
ANMS GCSI-DD	√	√	√	√
PAGI-SYM	√	√	√	√
FPG	-	√	√	-
Weight	-	√	√	-
BMI	-	√	√	-
Gastric emptying rate testing	-	√	√	-
Wexner constipation scores	-	√	√	-
TCM evidence scores	-	√	√	-
QOL assessment	-	√	√	-
Hepatic function tests	-	√	√	-
Renal function tests	-	√	√	-
Complete blood count analysis	-	√	√	-
Routine urinalysis	-	√	√	-
Routine fecal examination	-	√	√	-
Electrocardiogram	-	√	√	-
Adverse event	-	√	√	-

Diabetes diagnosis criteria

The diagnostic criteria for Type 2 diabetes are based on the *Guideline for the prevention and treatment of type 2 diabetes mellitus in China* (2020 edition): a. Symptoms of diabetes (typical symptoms include polyhydramnios, polyuria and unexplained weight loss) plus any of the following: (1) random blood plasma glucose (meaning blood plasma glucose at any time of the day without regard to the time of the last meal) ≥ 11.1 mmol/L (200 mg/dl); (2) fasting plasma glucose (FPG) (fasting state means no calories eaten for at least 8 h) ≥ 7.0 mmol/L (126 mg/dl); (3) 2-hour plasma glucose (2hPG) ≥ 11.1 mmol/L (200 mg/dl); (4) glycosylated hemoglobin $\geq 6.5\%$. b. Those without diabetic symptoms need to be confirmed by re-examination on another day.

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Diagnostic criteria for diabetic gastroparesis

The diagnostic criteria of DGP are based on the *Diagnostic Criteria for Internal Diseases*: (1) History of diabetes mellitus > 5 years and the appearance of gastrointestinal symptoms later than the diagnosis of diabetes mellitus; (2) Stuffiness, fullness or distension and discomfort in the stomach and yard: recurrent episodes, early satiety, belching, nausea, vomiting, epigastric burning, poor appetite, malnutrition, weight loss and impaired glycemic control in severe cases; (3) Episodic diarrhea, more than 3 times a day, loose stools or watery stools, intermittent normal bowel movements, or alternating with constipation, symptoms lasting more than 1 day. Normal stool routine examination, negative culture of pathogenic bacteria; (4) Ultrasound, gastroscopy or barium meal examination of the digestive tract to exclude peptic ulcers, tumors, obstruction and organic lesions of the liver, bile and pancreas.

Diagnostic criteria of TCM syndrome

The diagnostic criteria for spleen insufficiency and stomach stagnation syndrome are based on the *International Traditional Chinese Medicine Guideline for Diagnostic and Treatment Principles of Diabetes*.

The patient has at least two or more main diseases, or one main disease and more than two secondary diseases, and the tongue and pulse are indispensable.

- 1) Main signs and symptoms: nausea, vomiting, premature satiety, abdominal distension.
- 2) Secondary symptoms: fatigue, pale complexion, lethargy, poor appetite, constipation, loose stool.
- 3) Tongue and pulse performance: pale tongue and greasy white fur, thin and smooth pulse.

Inclusion criteria

Patients would be enrolled in this study if they meet the following criteria: (1) Age of 18–70 years at the time of enrolment; (2) Clearly diagnosed with diabetic gastroparesis by a second-tier hospital or above, with gastrointestinal symptoms such as nausea/vomiting, early satiety, bloating, and epigastric pain for more than 3 months or longer; (3) A history of diabetes mellitus for more than 5 years, with stable blood plasma glucose within 1 month; (4) A mean Gastroparesis Cardinal Symptom Index (GCSI) score ≥ 2 ; or a C-spirulina-based gastric emptying breath test (GEBT) to confirm delayed gastric emptying at screening; (5) TCM evidence of spleen deficiency and gastric stagnation; (6) Signed informed consent.

Exclusion criteria

Those with any of the following will be excluded: (1) Acute complications of diabetes, such as diabetic ketoacidosis, hyperosmolar hyperglycemic state, severe infection, surgery or other stress conditions; (2) Patients with gastrointestinal reactions caused by oral hypoglycemic agents and those treated with GLP-1 class drugs; (3) History of or current severe gastrointestinal diseases, such as peptic ulcer, gastrointestinal bleeding, pyloric stenosis, etc.; (4) Prior history of gastric surgery, such as gastrectomy, fundoplication, vagotomy, pyloroplasty, bariatric surgery or gastric stimulation device implanted surgically within the past year; (5) Combined severe cardiovascular and cerebrovascular disease, hepatic and renal insufficiency, psychiatric patients, drug abuse and dependence; (6) Allergy or intolerance to eggs, wheat, milk or algae; (7) Pregnant, preparing for pregnancy or breastfeeding women; (8) Patients who have participated in other clinical studies or are participating in other clinical studies within the last month of participation in this study; (9) Other conditions or diseases that are judged by the investigator to reduce the likelihood of enrollment or complicate enrollment, such as frequent changes in work environment or unstable living conditions that may cause loss to follow-up.

Removal, withdrawal and termination criteria

Participants who have been enrolled in the study may be removed from the study if they meet the following criteria during the study: (1) Two consecutive FPG measurements ≥ 13.9 mmol/L or a significant change in condition; (2) Certain comorbidities, complications or specific physiological changes; (3) Poor compliance of the subject; (4) The subject is using less than 80% of the prescribed amount or more than 120% of the prescribed amount of medication; (5) Subjects are taking prohibited drugs as specified in the protocol during the study period. In cases where it is not appropriate to continue the study, the investigator may decide to withdraw the case from his study. Participants have the right to withdraw from the study at any time according to the informed consent form, or if they do not take medication or participate in testing and are lost to follow-up. The reasons for their withdrawal should be investigated as much as possible and recorded in the case report form. The final results will be based on their last test results, and a full dataset analysis will be conducted for their efficacy and adverse reactions.

Randomisation and allocation

In accordance with the randomization method, the allocation of subjects into the treatment and control groups will occur in a 1:1 ratio. The SAS statistical software PROC PLAN process statement will be employed to

generate a random arrangement of 60 subjects (including the trial and control groups) based on the given number of seeds. This procedure will produce a corresponding treatment allocation for each subject, along with a unique serial number ranging from 01 to 72, resulting in a random coding table.

Test drug and double-blind

The TWA used in the trial were provided by Jiangyin Tianjiang Pharmaceutical Co., Ltd, Jiangsu, China, and mosapride were provided by Guang'anmen Hospital. All drugs met the requirements of good manufacturing practice. Although this study is open, the research assistant who grouped the patients would not know the treatment assignment until the group assignment is provided. Efficacy assessments and outcome analyses would be performed by evaluators and statisticians who are unaware of group assignments. All samples and data would be anonymized prior to analysis and evaluation.

Interventions

TWA group was given TWA prescription (30 g/sachet), 1 sachet each time, 2 times a day, warm water after meals, Moxapride 1 tablet each time, 3 times a day, and added after meals. Control group was given placebo granule (30 g/sachet), 1 sachet each time, 2 times a day, warm water after meals, Moxapride, 1 tablet each time. If TWA was administered prior to randomization, a 2-week drug-eluting period was implemented to avoid any potential complications of TWA. All participants will receive the usual basic treatment for hypoglycemia.

During the trial treatment, each patient should continue to receive the same type and dose of drugs in the usual basal treatment regimen as before enrollment. No further adjustments can be made throughout the treatment period. If the condition requires a drug adjustment, it should be recorded in the case report form, and the investigator should record the joint endpoints and adverse events that occurred in patients receiving increased or reduced drug doses or different drug types. Compliance will be evaluated by complete records of drug distribution and recall, and subjects will be judged to be in compliance with the regimen if the actual dose is within the range of 80%–120% of the dose used.

Concomitant medication

Permit

Concomitant treatment of diabetes (e.g., diabetes, diabetic nephropathy, diabetic neuropathy, diabetic retinopathy). The investigator should accurately record concomitant administration and keep the dose stable during the trial. Patients will adhere to a diet that maintains blood sugar control during the trial, such as a low-carb diet and moderate exercise, in addition to receiving

counseling on appropriate lifestyle improvements, such as weight monitoring, physical activity, and smoking and alcohol cessation.

Taboo

The use of other drugs that affect gastrointestinal motility is prohibited during clinical trials, especially GLP-1 drugs, such as Semaglutide, Liraglutide, Duraglutide and so on, which are commonly used in clinical trials.

Outcome measures

Personal and basic patient statistics, including gender, age, height, weight, past medical history, test results, etc.

Primary outcomes

Gastrointestinal symptoms were assessed as the primary outcome of the study by daily recording of the American neurogastroenterology and motility society gastroparesis cardinal symptom index-daily diary (ANMS GCSI-DD) forms, weeks 0 and 4 for the Upper Gastrointestinal Symptom Severity Scale (PAGI-SYM) score for gastrointestinal symptoms.

Secondary outcomes

Changes in FPG, weight, body mass index (BMI), gastric emptying rate testing, Wexner constipation scores, TCM evidence scores, and quality of life (QOL) assessment were secondary outcomes, and all parameters were measured at weeks 0 and 4 of treatment initiation, respectively. The scoring process will be conducted independently by two lead Chinese medicine doctors with more than 5 years of medical experience, and any differences will be resolved through negotiation. The criteria for comprehensive efficacy were as follows: (1) ineffective: no significant improvement or even aggravation of symptoms and signs, symptom score reduction $\leq 30\%$; (2) Effective: symptoms and signs improved, symptom score reduction $\geq 30\%$; (3) Significant: symptoms and signs were significantly improved, and symptom score was reduced by $\geq 70\%$. TCM symptom score = [(post-treatment score - pre-treatment score)/pre-treatment score] $\times 100\%$.

Follow-up observation indexes

ANMS GCSI-DD and PAGI-SYM were detected at 4, 8, 12 and 24 weeks after enrollment.

Safety testing

Patients' hepatic function tests (aspartate aminotransferase, alanine aminotransferase), renal function tests (creatinine, urea nitrogen), complete blood count analysis, routine urinalysis, routine fecal examination and electrocardiogram were tested at weeks 0 and 4. The details of AEs will be recorded, including the onset time, severity,

duration, treatment, and outcomes. AEs related to the study drug will be categorized into mild, moderate, and severe, and any severe AEs occurring within 24 h of onset will be reported to the principal investigator and the ethics committee for analysis and determination of causality. All adverse events will be recorded in the CRF and reported to the principal investigator. Any serious adverse events will be reported to the Guang'anmen Hospital Ethics Committee of the China Academy of Chinese Medical Sciences within 24 h. A committee of medical experts will determine whether the adverse events are related to TWA.

Data management and quality control

The investigator ensured the accuracy, completeness, legibility, and timeliness of data inclusion in the case report forms by relying on original observation records of the subjects. The investigator also supervised the adherence to the trial protocol, verified the correct and complete completion of all case report forms, and promptly addressed any errors and omissions by requesting the investigator's input. Once reviewed, the case report forms were promptly submitted to the clinical trial's data manager.

Prior to the delivery of the first case report form, the data manager established a database. The data manager conducted a preliminary review of each case report form, which was independently entered into the database by two operators. Software was utilized to compare the two entries, with any inconsistencies promptly identified and addressed. The data manager then developed data checks, such as range and logical checks, in accordance with the range and interrelationship of the index values in the case report form. All error contents and correction results were recorded in detail and stored securely. As necessary, all or a sample of indexes in the database underwent manual verification, which was then cross-referenced with the case report form.

Statistical analysis methods

Statistical analysis was conducted using SPSS 26.0 software. All statistical tests were performed using two-sided tests, and a P-value less than or equal to 0.05 was considered statistically significant. Descriptive statistics were reported as mean $\pm$ standard deviation for continuous variables. For normally distributed continuous variables, between-group comparisons were conducted using the independent samples t-test or the paired samples t-test when appropriate. In cases of equal variances, the t-test was used, while in cases of unequal variances, the corrected t-test was used. Non-normally distributed continuous variables were analyzed using the Wilcoxon rank-sum test. For categorical and ordinal variables, frequency (proportions) were reported as descriptive

statistics. The chi-square test or Fisher's exact test was used for categorical variables, while the Wilcoxon rank-sum test or the Cochran-Mantel-Haenszel (CMH) test was used for ordinal variables.

Ethics

The study protocol was approved by the Ethics Committee of Guang'anmen Hospital, China Academy of Chinese Medical Sciences will obtain written informed consent from all participants.

Discussion

With the increasing incidence of diabetes, the number of patients with diabetes complicated with gastrointestinal diseases also shows an increasing trend. According to the statistics of the International Diabetes Federation, the number of adults with diabetes in China has exceeded 140 million, 40% of type 1 diabetes patients and 30% of type 2 diabetes patients are accompanied by gastrointestinal motility disorders, which seriously affects the quality of life of patients. Diabetic gastroenteropathy significantly delays the body's digestion and absorption of food, causing gastrointestinal discomfort in patients and reducing the quality of life of patients. Up to 50% of diabetic gastroenteropathy patients have symptoms of anxiety or depression, which affect the mental state of patients. Recurrent episodes of early satiety, postprandial fullness, nausea, vomiting, bloating or abdominal pain in DGP have a significant impact on the quality of life of patients [18]. According to statistics, about 2–5% of DGP patients require multiple hospitalizations due to severe symptom [18]. Current management and treatment modalities for DGP involve dietary modification, glyce-mic control, medications, endoscopic therapy, nutritional support, gastric electrical stimulation (GES), botulinum toxin injections, surgical interventions, and TCM therapy [19]. Complementary alternative therapies have been widely used to treat functional gastrointestinal disorders such as gastroparesis, dyspepsia, diarrhea, constipation, and irritable bowel syndrome [20]. Retrospective studies have demonstrated the significant benefits of herbal medicine in the treatment of DGP, with patients showing significant improvements in nausea and vomiting and ANMS GCSI-DD [21]. However, the lack of high-quality evidence-based medical evidence is an urgent issue to be addressed in the clinical promotion of TWA prescriptions. This trial protocol will provide investigators with detailed information about this study in accordance with the SPIRIT herbal formulation statement. It is believed that by strictly adhering to the protocol, higher quality evidence will be provided for the efficacy and safety of TWA recipe in the treatment of DGP, thus providing a reliable and personalized treatment plan for DGP patients.

According to the current literature review, this is the first randomized double-blind controlled trial to evaluate the effect of TWA prescription on the symptoms of diabetic gastrointestinal disease. Despite its limitations, this study aims to investigate the efficacy and safety of TWA prescription in the treatment of diabetic gastrointestinal disease and provide high-quality, intuitive medical evidence for the design of larger randomized controlled trials in the future.

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12906-025-05104-5>.

Supplementary Material 1.

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Authors' contributions

JXT conceived and initiated the study design. JXT was a grant holder. YXZ and RYY contributed equally to the protocol, helped with implementation, and drafted the manuscript. ML provided statistical expertise in clinical trial design. YJZ and HYJ designed the statistical analysis method. JZM and CZ coordinated the study. LLZ and XAW participated in the establishment of the CRF. All authors contributed to the refinement of the study protocol and have approved the final manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

The study involving human subjects was approved and cleared by the Ethics Committee of Guang'anmen Hospital, China Academy of Chinese Medical Sciences, and patients/participants provided written informed consent to participate in this study. Our study is a clinical trial, and the registration number is NCT05720442. You can find the detailed registration information at the following link: <https://clinicaltrials.gov/ct2/show/NCT05720442>, the registration center is Guang'anmen Hospital, Chinese Academy of Traditional Chinese Medicine.

Consent for publication

All authors agreed to the publication of the article.

Competing interests

The authors declare no competing interests.

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