Effect of Intradermal Thumbtack Needle for Functional Constipation: Study Protocol for a Real-World Clinical Trial

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Research Article

Keywords: Intradermal thumbtack needle, FC, Mosapride, Real world clinical trial, Clinical efficacy, protocol

Posted Date: November 15th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-832408/v1

Abstract

Background: Many high-quality clinical trials have proved the efficacy of acupuncture in the improving frequency of spontaneous bowel movements, stool characteristics, and et cetera of Functional Constipation (FC) [1]. However, the high requirement of time make many patients unable to attend, this clinical trial will demonstrate the efficacy of intradermal thumbtack needle in ameliorate spontaneous bowel movement of FC.

Methods: This multi-center real world clinical trial is performed involving 482 FC patients. All patients are randomly allocated into 2 group, which are group A to receive intradermal thumbtack needle twice a week for 4 weeks (intervention group n=241) or group B to take oral administration of mosapride 3 times a day for 4 weeks (control group n=241). This trial includes a 4-week treatment period and a 4-week follow-up period. The primary outcome is the number of completely spontaneous defecation per week, we use Weekly CSBMs analyze the frequency of spontaneous defecation per week during treatment and follow-up period to compared with the baseline. The secondary outcomes include FC patients' stool consistence, gastrointestinal or anorectal symptoms, quality of life, anxiety and depression levels during treatment and follow-up period and efficacy expectations. The relevant assessment tools include: Bristol tool Form Scale (BSFS), Cleveland Constipation Score (CCS), Patient Assessment of Constipation Quality of Life Questionnaire(PAC□QOL), Self-rating Anxiety Scale (SAS) , Self-rating Depression Scale (SDS) and Efficacy Expectancy Scale. At the end, the scales filled by patients and researchers will be entered by data administrator, all the outcome assessments will be performed by independent outcome assessors and will be analyzed by professional statisticians with SPSS 25.0 software.

Discussion: We hypothesize that intradermal needle is better than or equal to positive drugs in the improving frequency of spontaneous bowel movements, stool characteristics□and et cetera of FC patients . The results of this trial will provide us with a clinical basis for the application of intradermal needles in the treatment of FC.

Trial registration: Chinese Clinical Trial Registry, ChinCTR2100043684.Registered on 26 February 2021.

Background

Refer to Rome IV Standard : Functional constipation(FC)refers to a common functional intestinal disease which is caused by factors such as organic diseases, drugs, and does not meet the diagnosis of IBS, and the patient has defecation frequency, abnormal stool quality or even inability to defecate independently [2]. According to epidemiological studies, the incidence rate in the range of 14%-29% in the United States and some European countries [3–4]. Studies show that FC patients tend to be younger and are accompanied by Symptoms such as abdominal distension, fecal incontinence, urinary incontinence, anxiety, and depression [5–6] which seriously affect people's quality of life and mental health [7]. Medical expenses are a heavy burden on patients and Health department [8]. At present, the general measures to manage FC contain general therapy and drug therapy: general therapy Such as lifestyle adjustments, has

a long treatment period and inaccurate efficacy [9]; Drug therapy includes laxatives, stimulant drugs, and micro ecological agents, but most of these drugs are accompanied with many adverse reactions and side effects such as: abdominal pain, electrolyte disturbance, colonic disease and increasing the risk of cardiovascular disease. In addition, they have high dependence and recurrence rate [10]. Therefore, effective, safe, and non-toxic alternative treatments therapy of FC have become the main research direction. In recent years, many high-quality randomized controlled experiments have proved the efficacy of acupuncture in the treatment of FC [11]. It is a multi-channel, multi-target treatment that can improve the symptoms of FC through the central system, endocrine system, intestinal motility mechanism [12–16], etc. The efficacy of acupuncture is better than positive drugs especially in the post-treatment period [17]. However, the strong sense of needle and high requirement of time make many patients unable to attend, therefore, we hope to provide a therapy which with more comfort, simple operation, and long-lasting effect, so our research chose the intradermal needles therapy which is a thumbtack-like needle is shallowly punctured in dermis for 72 hours to continuously stimulate the acupoints to exert effects [18]. Based on previous studies of the clinical efficacy and mechanism of acupuncture in the treatment of FC, acupuncture could improve gastrointestinal motility, promote contractility of colonic tissue, and facilitate gut transit in constipated animals, meanwhile, high-frequency EA stimulation may regulate activity in the enteric nervous system and regenerate the lost enteric neurons [19]. This trial adopts a real-world research design, expands the clinical inclusion criteria, and allows the inclusion of patients with underlying diseases or complications to improve the extrapolation of experimental results, reflect the true clinical efficacy of intradermal acupuncture treatment of FC. So, we designed this real-world study as the main treatment method :(1) The experimental group takes Intradermal thumbtack needle which is characterized as " shallow needling, micro-needle feeling, and lasting effect " —as the main treatment method;(2) Use the real-world effective randomized controlled experimental model to obtain more suitable clinical results. (3) Test the efficacy of Intradermal thumbtack needle in the treatment of FC by using a control study of mosapride, a positive drug.

Methods And Design:

Design

This is a multi-center research includes Chengdu University of Traditional Chinese Medicine Hospital, Chengdu Chronic Disease Hospital and Sichuan Ba yi Rehabilitation Center. FC patients who meet the enrollment conditions are recruited into research, they get a number from the opaque envelope, then randomly divided into Intradermal thumbtack needle group (group A) or drug group (group B) in a 1:1 ratio by computer random number table. This trial includes a 4-week treatment period and a 4-week follow-up period. Patients receive intradermal thumbtack needle twice a week for 4 weeks in total 8 sessions or take Mosapride citrate dihydrate orally 3 times a day for 4 weeks. Patients in group B can adjust the frequency of oral medication according to the actual situation of defecation, they are asked to record the dosage frequency on the oral mosapride record form and feedback to the doctor. Result investigators and statistical analysts are blind to the procedure and intervention, participants group allocation.(See Fig.1: a detailed study schedule and Fig.2: Clinical flow chart).

This research follows the relevant provisions of the World Medical Congress "Helsinki Declaration" and has passed the review of the ethics committee of Chengdu University Hospital of Traditional Chinese Medicine. Participants are provided with an informed consent form when they are enrolled, which detailed introducing the experimental purpose, procedures, and risks of this study.

This trial is reported in accordance with the Standard Protocol Items: Recommendations for Intervention Trials (SPIRIT) guidelines [20] (Fig. 2, Additional file 1) and follows the principles of the CONSORT and STRICTA [21].

Participants

In this trial, all potential FC participants who match the diagnostic criteria need to undergo a physical examination including Vital signs (body temperature, pulse, respiration, blood pressure), routine blood test, routing urine test, stool test, hepatorenal and kidney function blood test, and blood coagulation.Medical physicians from Chengdu University of Traditional Chinese Medicine Hospital diagnosis all potential FC participants and decide who can be recruit into the research.

Diagnostic criteria

The diagnostic criteria refer to the "FC [12] Rome IV diagnostic criteria developed by the Rome Committee in 2016":(1) Including the following 2 or more symptoms. A: Difficulty defecation (at least 1 in every 4 bowel movements);B: The defecation is dry or hard (at least 1 in every 4 defecations);C: Feeling of incomplete defecation (at least 1 in every 4 defecations);D:A sense of anorectal obstruction and/or obstruction (at least 1 in every 4 bowel movements);E: Need manual assistance (such as fingers to assist defecation, pelvic floor support defecation) to promote defecation (at least 1 in every 4 defecations);F: Spontaneous defecation is less than 3 times a week. (2) loose stools rarely occurs when not in use laxatives. (3) Does not meet the diagnostic criteria for irritable bowel syndrome (IBS). (4) Symptoms appeared for at least 6 months before diagnosis, and the symptoms met the above criteria in the last 3 months.

Inclusion criteria

Participants who meet the following 3 criteria will be included in the trial: (1) Meet the FC diagnostic criteria of Rome IV; (2) Between the ages of 18-80 (male and female); (3) Accept and sign the informed consent form.

Exclusion criteria

Participants who meet the following 6 criteria will be excluded from the trial: (1) Those who do not meet the above diagnostic criteria and inclusion criteria; (2) Constipation caused by gastrointestinal dysfunction and intestinal stenosis due to organic diseases of the gastrointestinal tract, such as tumor, Hirschsprung's disease, inflammatory bowel disease, peptic ulcer, cancer, and perianal disease; (3) Patients with severe hemorrhagic disease or hypersensitivity, allergic to press needles or adhesives; (4)

Patients with damaged or infected skin at the acupuncture site; (5) Severe cognitive impairment, severe malnutrition, suffering from malignant tumors and other poor general conditions, unable to cooperate with examination and treatment; (6) Patients have participated in other clinical experimenter in the 8 weeks before the start of the study.

Weed out, Suspend and Shedding standard

(1) All cases that don't meet the inclusion criteria and are mistakenly entered should be eliminated. (2) Those who fail to treat as prescribed or who die or become worse due to accidents, and who terminate the trial due to incomplete observational data should be excluded. (3) In the course of clinical observation of this subject, if there are severe allergies to drugs or needle injections, severe adverse reactions, and other important system diseases, the trial should be terminated. (4) Those with adverse reactions should be included in the statistics of adverse reactions; those with more than 1/2 course of treatment and withdrew due to ineffectiveness should be included in the efficacy analysis.

Participant's recruitment

Participants of the study are recruited from 3 research centers through the outpatient clinic or inpatient, hospital-based advertising, and posters in community. Any participants who meet the diagnostic criteria but not exclusion criteria are recruited into the study. After being informed of the details of this study, participants are asked to sign the informed consent form, and delivered into intradermal thumbtack needle group or drug group. In this study, participants' drug combinations are recorded but not be intervened.

Intervention

The interventions in the 2 groups are as follows:

Intervention group (group A)

Patients in this group receive manual acupuncture with single-use disposable intradermal thumbtack needles (0.22×1.3mm, Wu jiang yun long Medical Instrument Co, Ltd). Patients receive a total of 8 sessions of acupuncture in 4 weeks with 2 sessions per week (leave needles for three days, follow by a one-day interval).

Process of the treatment in intervention group

(1) After routine disinfection with alcohol swab, clamp the end of the intradermal needle with tweezers, needle applicator inserts the thumbtack-like needles into the dermis, and press the round end of needle with fingers until patients have no irritation; (2) Instruct patients to pressure 3 times a day for 5 minutes each time; (3) According to the national standard (Part 8: Intradermal Pushpin) and the actual situation, the needle retention time is 3 days; (4)After the needle embedding period expires, clamp the tape with tweezers and pull out the needle body in opposite direction; (5) All acupuncturists who take part in the

study are qualified from the clinical operation training to ensure the accuracy and consistency of the treatment. Meanwhile, adverse reactions must be recorded that may occur during the study.

Acupuncture point

The location of acupuncture point are described as per the Nomenclature and Location of Acupuncture Points [22] (National Standard of People's Republic of China, 2006[GB/T 12346-2006]).Patients in Intervention group receive stimulation at bilateral Tianshu (ST25), bilateral Shangjuxu (ST37),bilateral Zusanli (ST36),bilateral Dachangshu (BL25),bilateral Zhigou (SJ6).According to patients' symptoms, patients are divided into 4 syndrome type groups: cold constipation, heat constipation, qi stagnation constipation, and constipation of deficiency type. Cold constipation at Guanyuan (RN4), Qihai (RN6). Heat constipation at bilateral Quchi (LI11), bilateral Zhaohai (KI6). Qi stagnation constipation at Zhongwan (RN12), bilateral Taichong (LR3). Constipation of deficiency type at Guanyuan (RN4), bilateral Pishu (BL20).

Control group (group B)

Patients in control group orally take Mosapride citrate dihydrate (Yabao Pharmaceutical Group Co. Ltd) 5 milligram 3 times a day for 4 weeks. Mosapride dosages and taken times can be adjusted according to the defecation situation, patients are asked to record the dosage frequency and feedback to the doctor. During the treatment, patients are allowed to use other laxatives if not be able to open bowel for more than 3 consistent days, however, the type and dosage of laxatives used must be recorded in the case report form (CRF). After complete the 4 weeks treatment period, patients are required to return all untaken drugs to monitor the adherence.

Outcomes

Primary outcome

The Primary outcome is the number of completely spontaneous defecation per week, CSBMs is used to record the time and frequency of spontaneous defecation each day by patient, return filled forms to researchers at the end of each week.

Secondary outcomes

The secondary outcomes include FC patients' stool consistency, gastrointestinal or anorectal symptoms, quality of life, anxiety and depression levels during treatment and follow-up period and efficacy expectations, the scales assessment tools are as follows:

Bristol tool Form Scale (BSFS)

The stool feature is measured by the BSFS [23], which is classifies the form of human feces into 7 types from separate hard lumps (type 1) to entirely liquid (type 7). Based on classification points, type 1

corresponds to 1 point, type 2 corresponds to 2 points, and so on, add up the fecal trait scores during spontaneous defecation in the previous week and divide by the CSBMs to get an average score. The lower the score, the more severe the patients' constipation.

Cleveland Constipation Score (CCS)

The CCS [24] is a designated scale to evaluate patients' gastrointestinal or anorectal symptoms. The CCS is composed of 8 items: defecation frequency; straining feeling; incomplete feeling; abdominal pain; defecating time; assisted measures to defecation; unsuccessful defecation frequency in 24 hours; and course of constipation. Each item is scored in the range of 0–4 or 0–2; the summation is in the range of 0–30. A higher score suggests more severe symptoms of constipation.

Patient Assessment of Constipation Quality of Life Questionnaire(PAC□QOL)

The PAC-QOL [25] is intended to reflect the QOL of FC patients in the last 2 weeks. It embodies 7 dimensions with a total of 28 questions involving physical discomfort, social discomfort, psychological discomfort, anxiety and concern, and satisfaction in daily life. There are 5 options for each question in the range of 1–5 ("1" indicates no discomfort or feeling very satisfied, "5" indicates extreme severity and always appears or feeling very dissatisfied). A higher score of the PAC-QOL suggests more severe symptoms, more discomfort, less satisfaction, and poorer QOL.

Self-rating Anxiety Scale (SAS) and Self-rating Depression Scale (SDS)

Anxiety and depression are emotional disorders commonly accompanied by FGIDs [26]. Hence, the SAS [27] and SDS [28] are used to assess the emotional health of FC patients. A higher score of the SAS and SDS suggests more obvious the anxiety tendency.

Efficacy Expectancy Scale

The efficacy expectancy scale [29] is used to assess the expected value of patients participating in treatment. A higher score of the Efficacy Expectancy Scale suggests more expectancy to the treatment.CSBMs, BSFS, CCS, and PAC-QOL were used to assess the changes in defecation and quality of life at the end of baseline, the 2nd,4th (end of treatment), and 8th (end of follow-up) weeks of treatment. SAS and SDS were used to assess the changes in the mental and psychological status of patients at the baseline, end of treatment, and the end of follow-up.

Safety measure

(1) Vital signs (body temperature, pulse, respiration, blood pressure), test of blood routine, urine routine, stool routine, hepatorenal and kidney function, blood coagulation.

(2) The hospitals have a high medical level and ability to handle crisis events, can guarantee the progress of this study.When a serious adverse event or other unexpected situation occurs,it must be dealt with immediately and reported to the project leader, unit inspector, main research unit and ethics

committee within 24 hours.Researchers should record the symptoms, treatment, results, and dates in detail on the Case Report Form(CRF).The follow-up must be carried out within 1 month. The methods can be selected according to the severity of adverse events, such as hospitalization, outpatient service, home visit, telephone, communication and other forms, so as to ensure the safety of patients.

Sample size calculation

Based on previous studies [30]: RCT study of acupuncture to treat FC, the control group used Mosapride citrate dihydrate. According to the average number of complete spontaneous defections per week, the sample size is estimated by referring to the 2 independent sample rate non-inferiority test calculation formulas $n_T = \frac{2(z_{\alpha/2} + z_\beta)^2 p(1-p)}{\delta^2}$. The standard deviation σ of the 2 methods is 1.8 times. The non-inferiority limit δ is 0.5 times. The test level is α=0.05. The test power is 1-β=0.80, and the ratio of the 2 group is 1:1. The number of FC samples in each group is 204 cases, and the loss rate is 15%. It is calculated that there are 482 cases in the 2 groups and 241 cases in each group.

Statistical analysis

Statistical analysis plan and statistical software

The statistical professional and the main researcher jointly formulate a statistical analysis plan according to the clinical trial plan, finalize the draft before the database is locked, and develop a table for statistical analysis. The data will be analyzed by professional statisticians with SPSS 25.0 software.

Statistical analysis content and methods

At the beginning of the research，according to the basic principle of Intention To Treat (ITT) analysis, all participants who are included in the group, receive at least one treatment, and have an efficacy index evaluation are included in the Full Analysis Set (FAS).The missing data is processed according to the Last Observation Carry Forward (LOCF) principle.All participants who do not violate the protocol in the full analysis set will be included in the Per Protocol Set (PPS) analysis.At the end of trail, the patients and researchers fill these scales during the statistical trial period, including: CSBMs, Efficacy Expectancy Scale, BSFS, CCS, PAC-QOL, SAS, SDS, and adverse reaction scale. Researchers collect these outcome index data at the time of patient enrollment and at 2, 4, and 8 weeks of the treatment period，then Perform Repetitive Measure Analysis Of Variance (ANOVA) to figure out results of Inter- and intra-group comparisons, and perform Mauchly's test of sphericity before data analysis to clarify whether there is a relevance between repeated measurement data, if P＞0.05, the measurement data meets the Huynh-Feldt condition, the one-way analysis of variance method to process is used; if the test result is P＜0.05 , Multivariate Analysis of Variance Method (MANOVA) is used or adjust the degree of freedom of the time-related F value in the repeated measures ANOVA test result.All the outcome assessments will be

performed by independent outcome assessors. These assessors are trained before participating in this trial and blinded to the randomization. The data will be analyzed by professional statisticians with SPSS 25.0 software.

Data management

The database is established by the administrator, including: CSBMs, Efficacy Expectancy Scale, BSFS,CCS,PAC-QOL, SAS, SDS and adverse reaction scale. The date, inclusion criteria, exclusion criteria, dropouts, missing values, and so on should be checked again before entry. The data should be kept properly and information of potential and enrolled participants only can be collected by researchers,all researchers have been trained and signed a guarantee to prevent leakage of patient privacy. The data entry staff perform remote data entry. Each case report form adopts the double entry method and completed by 2 persons independently. The computer database verification function is used for logical inspection and automatic comparison to ensure that the data is consistent with the results in the case report form. The Evidence-based Medicine Center of the CDUTCM will be responsible for monitoring the study and data every three months and will make the final decision to terminate the trial. Only the main researchers, statisticians, data administrators will have access to the final trial data set.

Discussion

A randomized controlled trial using real-world research and effectiveness

Our research adopts real-world research design which originated from practical clinical trials, it has the advantages of strong practicability, high external validity, and ease of development, this research model has a longer clinical observation period\follow-up period, and a larger sample. This new scientific research model is more in line with the advantages and characteristics of traditional Chinese medicine. Research results can be more easily transformed into clinical practice and provide guidance for personalized medicine [31–33]. In order to balance the known and unknown prognostic factors in research, improve inter-group comparability and reduce selective bias, we adopt an individual random approach to guide the subjects into the group; the intervention does not use placebo, but use the current internationally recognized treatment of functional constipation drugs: Mosapride citrate [34]. And during the experiment, the intervention has a certain degree of flexibility: professional doctors will make individualized adjustments to the patient's treatment plan.

Intradermal thumbtack needle:

Intradermal thumbtack needle is a therapy in which thumbtack-like needles are punctured into dermis for 48–72 hours to continuously stimulate the acupuncture point to exert effects. The clinical pathological state of the patient can be immediately improved by it in superficial tissues to achieve a long-term continuous "acupuncture ". According to the theory of Chinese medicine: meridians and collaterals connect internal organs, when gastrointestinal diseases occur, the corresponding acupuncture points are

used to stimulate the qi in the meridian to regulate internal organs' function. In modern medicine: It plays a therapeutic role through stimulate nerve endings and transmit impulses to the center, finally release the human body corresponding hormones and neuropeptides to act on target organs. The therapy has the characteristics of "minimally invasive, shallow thorn, micro-needle feeling, long-stay needle ,non-toxic side effects, low cost and simple operation",patients can complete it at home under the guidance of professional physicians. The implantation of it can last for 24 hours [35] which is more suitable for chronic intractable diseases or often painful diseases with long retention time include FC. Therefore, we would like to use it as an intervention. However, there are few clinical studies on the FC of Intradermal thumbtack needle treatment, so we hope to conduct a real-world study-effective randomized controlled experiment to provide objective clinical basis and methodology for Intradermal thumbtack needle treatment of FC.

Mosapride citrate as a positive control drug

Mosapride is a non-selective receptor agonist, which promotes the release of acetylcholine by stimulating the receptors of the myenteric nerve plexus and enhancing gastrointestinal peristalsis but does not affect gastric acid secretion [36]. Animal pharmacological studies have shown that mosapride can improve gastric emptying delay, promote antral and duodenal movement, and enhance the contraction caused by ileal electrical stimulation. Mosapride has obvious clinical effects and low side effects based on almost no impact on blood and biochemical indicators. It can avoid long-term intestinal injury. Only a few people accompanied by fatigue, thirst, abdominal pain, dizziness, and low immunity. Systematic reviews indicate that mosapride is effective and there is no evidence of cardiovascular damage. And it may be more cost-effective for chronic constipation [37].

Quality control: the guarantee of reliability and repeatability of research results

Although this study is based on real-world clinical practice with a lot of flexibility, but it is not random and unconstrained. Strict quality control is a guarantee to improve the reliability and repeatability of research results: (1) Random grouping and distribution hiding to minimize selection bias during research implementation; (2) Due to the use of intradermal thumbtack needle and mosapride as two comparative treatments, the failure to achieve double blindness will lead to a certain degree of bias. However, clinically, patients' understanding of the treatment itself and expectations of curative effect are also factors that affect the results of treatment in the real world, so they may not have a negative impact on the research. Moreover, during the treatment, patients in group A receive intradermal acupuncture treatment in the allocated treatment rooms of hospitals, and patients in group B take medication at home to avoid communication between patients from different group. And in order to overcome the reporting bias caused by randomization, the result investigator and statistical analysts will be blind to the procedure and result of randomization, group allocation, and intervention. (3) In this experiment, Standard Operating Procedures (SOP) were developed prior to the implementation of the study, and all participants have uniformly trained, and all medical operations are performed by professionally trained physicians. (4) In order to ensure the data quality of the study, the case report form is synchronized with the experimental

design to ensure that the data collection in the scheme is reasonable and feasible. In short, although intradermal thumbtack needle in the clinical treatment has been widely used, still lack of objective clinical studies to prove its effectiveness in the treatment of FC. This trial is the first real-world study on the treatment of FC with intradermal thumbtack needle, aims to explore the clinical efficacy of it in the treatment of FC.

Trial status

This trial registered on 26 February 2021 (Registration Number: ChinCTR2100043684, the protocol version number: F2.0). The trial is currently in the stage of recruiting patients. The first patient was included on 15 March 2021. To date, 82 patients have been included.

Abbreviations

FC: Functional Constipation; CSBMs: Complete spontaneous bowel movements; BSFS: Bristol tool Form Scale; CCS: Cleveland Constipation Score; PAC□QOL: Patient Assessment of Constipation Quality of Life Questionnaire; QOL: Quality of Life; SAS: Self-rating Anxiety Scale; SDS: Self-rating Depression Scale; IBS: Irritable Bowel Syndrome; EA: electroacupuncture; FGIDs: Functional gastrointestinal disorders; CRF: Case Reporting Form; RCT: Randomized Controlled Trial; TCM: Traditional Chinese Medicine; SPIRIT: Standard Protocol Items Recommendations for Intervention Trials; SOP: standard operating procedures; CONSORT: the Consolidated Standards of Reporting Trials; STRICTA: the Standards for Reporting Interventions in Clinical Trials of Acupuncture; ITT: Intention To Treat; FAS: Full Analysis Set; LOCF: Last Observation Carry Forward; PPS: Per Protocol Set; ANOVA: Analysis Of Variance; MANOVA: multivariate analysis of variance method

Declarations

Ethics

The study will be conducted under the Declaration of Helsinki principles, as well as following the norms of good clinical practice. The study protocol has been approved by the ethics committee of the Hospital of Chengdu University of TCM (Approved number 2020KL-073).

Consent for publication

Not applicable

Availability of data and materials

Not applicable.

Funding

The trial is financially supported by Science and Technology Department of Sichuan Province(No.2019YFS0197).

Authors' contributions

DL and JL are responsible for this study. WZ, YX, JC, and LW

conceived and designed the study. DL,YX and YT participated in drafting

the trial protocol and preparing the manuscript. WZ, YX, JC, and LW

and JG participated in data collection and were in charge of recruitment and

treatment of patients. All authors read and approved the final manuscript.

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Competing interests

The authors declare that they have no competing interests.

Acknowledgments

We thank Chengdu University of Traditional Chinese Medicine Hospital, Chengdu Chronic Disease Hospital and Sichuan Ba yi Rehabilitation Center, for the instruction of clinical trial.

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Figures

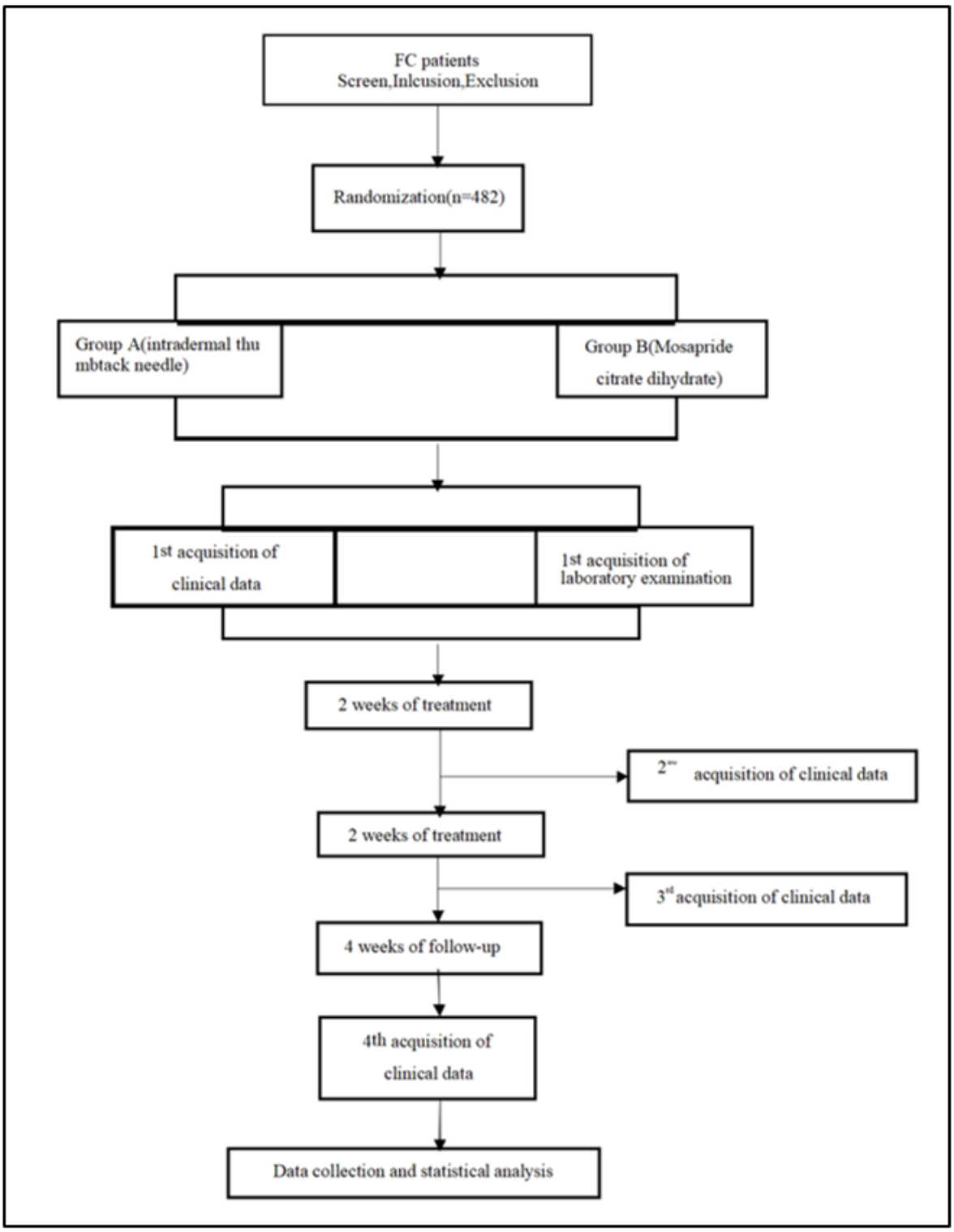

Figure 1

study schedule: 482 eligible patients will be randomly allocated into two groups with a 1:1 ratio.Clinical data will acquired at four time points:baseline,the 2nd,the 4th(end of treatment),and 8th(end of follow-up) weeks of treatment. FC functional constipation.

	STUDY PERIOD					
	Enrolment		Allocation		Post-allocation	
TIMEPOINT	-2 week	-1-week	0-week	2-week	4-week	8-week
ENROLMENT:						
Eligibility consent	×					
Informed consent	×					
Physical examination		×				
Allocation		×				
INTERVENTION:						
Group A(Intradermal thumbtack needle)				×	×	
Group B(Mosapride citrate dihydrate)				×	×	
ASSESSMENTS:						
CSBMs			×	×	×	×
BSFS			×	×	×	×
CCS			×	×	×	×
PAC-QOL			×	×	×	×
SAS and SDS			×		×	×
Efficacy Eepectancy Scale			×			
PARTICIPANTS SAFETY:						
Adverse events			×	×	×	×

Figure 2

Standard Protocol Items:Recommendations for Interventional Trials (SPIRIT) schedule of the trial.Our study includes a two-week baseline period,a four-week treatment period and a four-week follow-up period.In the baseline period,recruited patients are screened according to the inclusion criteria and exclusion criteria;then,eligible FC patients will give informed consent and receive a physical examination.After allocation,the patients receive 4-week intradermal thumbtack need,or mosapride during the treatment period.The outcome assessments:CSBMs, BSFS, CCS, PAC-QOL will be evaluated at baseline,the 2nd,4th(end of treatment),and 8th (end of follow-up)weeks of treatment.The SAS and SDS will also be evaluated at the baseline,end of treatment,and the end of follow-up.Physical examination(body temperature,pulse,respiration,blood pressure,test of blood routine,urine routine,stool routine, hepatorenal and kidney function,blood coagulation) are performed at the allocation period to evaluate risks correlated with acupuncture and mosapride.Adverse events are recorded in the CRFS at any time during the treatment.BSFS Bristol tool Form Scale,CCS Cleveland Constipation Score, PAC-QoL

Patient Assessment of Constipation Quality of Life Questionnaire, SAS Self-rating Anxiety Scale, SDS Self-rating Depression Scale.

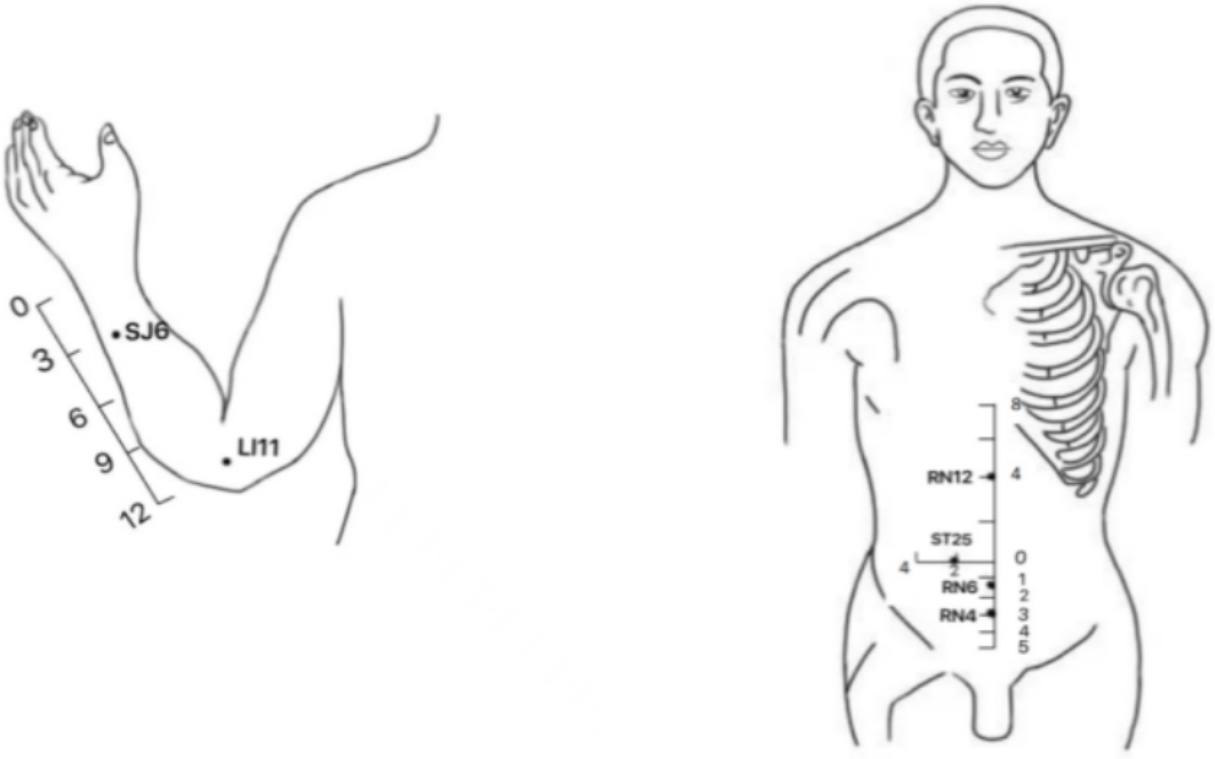

Figure 3

the location of Zhigou (SJ6),Qu chi (LI11),Zhong wan (RN12),Tianshu (ST25),Qihai (RN6),Guanyuan (RN4)

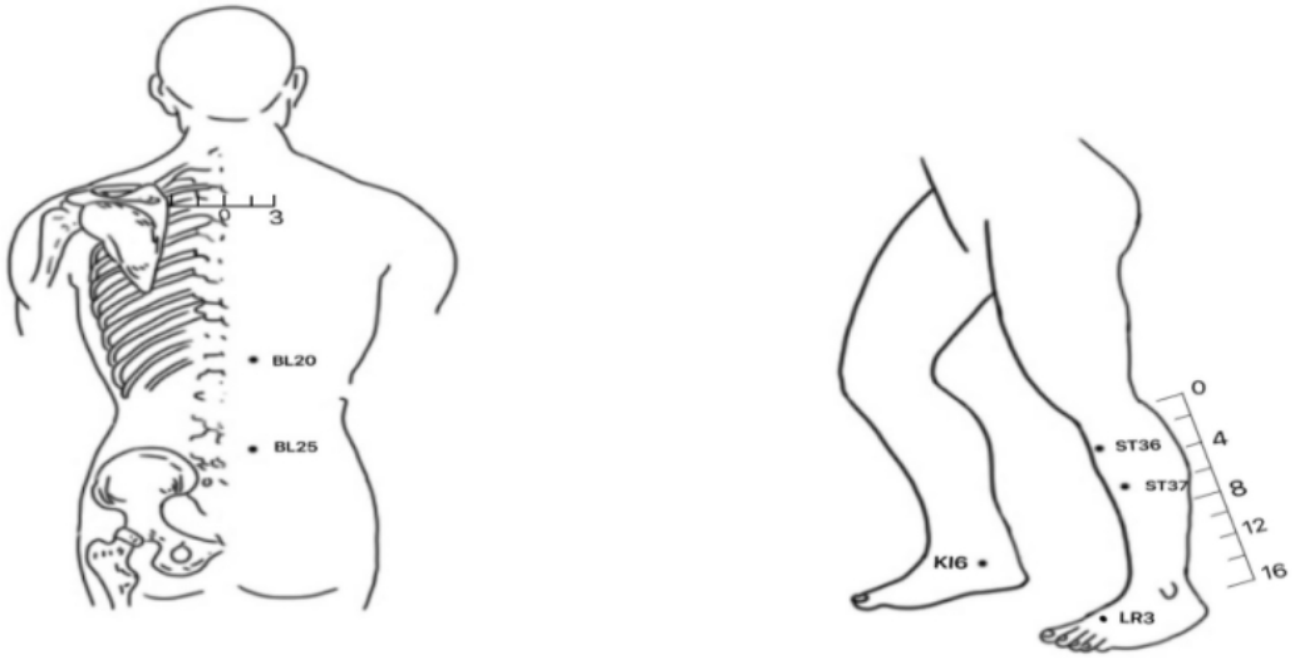

Figure 4

the location of Pishu (BL20),Dachangshu (BL25),Zusanli (ST36) ,Shangjuxu (ST37),Zhaohai (KI6),Taichong (LR3)

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SPIRITchecklist9.1.docx