Effect of Thunder-Fire Moxibustion for Lumbar Disc Herniation: Study Protocol for a Randomized Controlled Trial

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Abstract

Background

Lumbar disc herniation (LDH) is one of the common diseases in orthopedics and traumatology, which is caused by nucleus pulposus herniation stimulating cauda equina nerve, nerve root and intervertebral disc degeneration. Its clinical manifestations are low back pain, radiation pain of lower limbs and cauda equina symptoms, which seriously affect the quality of life of patients. At present, oral analgesics are commonly used in clinical non drug therapy for LDH, but oral analgesics will produce gastrointestinal reactions and other side effects. Thunder-fire moxibustion is one kind of moxibustion method, which has been applied widely for treating pain syndromes in China. The aim of our research is to design a randomized controlled trial of thunder-fire moxibustion in the treatment of lumbar disc herniation to explore whether it is safer and more effective than oral analgesic drugs.

Methods

90 patients will be randomly divided into thunder-fire moxibustion group and acetaminophen group. The intervention included 10 days as a course of treatment, lasting for 20 days. The acetaminophen group took two acetaminophen sustained-release tablets every other day, while the thunder fire moxibustion group will be treated with thunder fire moxibustion once every other time for 30 minutes. Japanese Orthopaedic Association (JOA) score, visual analogue scale (VAS) and oswestry disability index (ODI) will be used as the main the observation indexes. Meanwhile, the occurrence of adverse events (AES) will also be recorded. The assessment will be conducted at baseline and at the end of the first and second course of treatment.

Discussion

The aim of this study is to determine whether thunder-fire moxibustion is more effective than acetaminophen in the treatment of patients with LDH.

Trial registration

Chinese Clinical Trial Registry (http://www.chictr.org.cn), ChiCTR2000036079. Registered on 21 August 2020.

Background

Lumbar disc herniation (LDH) is one of the most common causes of low back pain[1]. It is a syndrome caused by degeneration of lumbar intervertebral disc, rupture of annulus fibrosus, protrusion of nucleus pulposus tissue and stimulation of lumbosacral nerve root and cauda equina nerve[2]. From 1999 to 2013, 188 countries in the world investigated the prevalence of 301 kinds of acute and chronic diseases, and found that the top ten causes of disability in every country was low back pain and depressive disorder[3]. At present, the treatment strategies for LDH include surgical and non-surgical treatment, and

non-surgical treatment includes acupuncture and moxibustion, traction, drugs, functional exercise and physical therapy[4][5].

In the treatment of LDH, oral nonsteroidal anti-inflammatory drugs (NSAIDs) can be used as the first-line drugs for acute and chronic pain. Acetaminophen and NSAIDs are recommended as the first-line medication options for most patients with low back pain (grade 1A evidence) in 2007 by the Diagnosis and treatment of low back pain: a joint clinical practice guideline from the American College of Physicians and the American Pain Society[6]. The efficacy of acetaminophen in the treatment of LDH has also been reported[7], but it can only relieve pain and has no effect on other symptoms of LDH. However, acupuncture, massage and other complementary therapies have been widely used in the treatment of lumbar disc herniation[8]. Among them, thunder-fire moxibustion, as an important alternative therapy, plays a good role in promoting peripheral blood circulation, accelerating the absorption of inflammatory exudates. Thunder-fire moxibustion is composed of moxa fleece, activating blood circulation and removing blood stasis, and analgesic Chinese medicine[9]. In the past clinical trials, thunder fire moxibustion for lumbar disc herniation in the experimental group was mostly thunder-fire moxibustion combined with other treatment methods[10][11][12]. Previous clinical studies have not evaluated the clinical effect of thunder-fire moxibustion alone in the treatment of lumbar disc herniation. Thus, in this study, our aim is to investigate and compare the efficacy of thunder-fire moxibustion and acetaminophen in the treatment of LDH pain and dysfunction.

Methods

Trial design

A single center randomized controlled trial (RCT) was designed to compare the efficacy of thunder-fire moxibustion and acetaminophen in the treatment of LDH. Participants will receive ten treatments within 20 days. The acetaminophen group took two acetaminophen sustained-release tablets every other day, while the thunder-fire moxibustion group will be treated with thunder-fire moxibustion once every other time for 30 minutes.

In this study, 90 LDH patients were randomly divided into thunder-fire moxibustion group or acetaminophen group according to the ratio of 1:1 (Fig. 1). Our study follows the general clinical trial rules (Helsinki Declaration). The SPIRIT checklist is given in Additional file 1.

Inclusion criteria

Participants will be enrolled with the following criteria in this study: (1) The age of the patients ranged from 25 to 80 years old. (2) It met the diagnostic criteria of LDH in criteria of diagnosis and therapeutic effect of diseases and syndromes in traditional Chinese medicine[13] and evidence-based clinical guideline for the diagnosis and treatment of LDH with radiculopathy[14]. (3) The clinical manifestations

and imaging findings of the patients were consistent with lumbar disc herniation. (4) the subjects informed consent and signed the informed consent.

Exclusion criteria

(1) Those under 25 years old or over 80 years old.

(2) Severe heart, brain, liver and hematopoietic system diseases, or other serious diseases that affect their survival.

(3) Patients with known hepatic and renal insufficiency or cirrhosis.

(4) Patients with high fever and infectious diseases.

(5) Pregnant or lactating women.

(6) Mental patients or other actions can not cooperate with the treatment.

(7) All patients with treatment allergy or suspected allergy involved in this trial.

(8) The patients with severe illness need surgical treatment.

(9) Patients who have been participating in another clinical study more than 3 months before admission.

Recruitment

We will recruit participants by advertising on bulletin boards, located at the department of acupuncture and massage, nanling Hospital of traditional Chinese medicine. Recruitment staff working in these departments will recruit subjects who meet the inclusion criteria. Subject details will be kept by the data monitoring committee (DMC) and will not be disclosed to any other individuals or organizations unrelated to this study.

Random assignment

Patients with LDH will be randomly assigned to the group of thunder-fire moxibustion or acetaminophen in a 1:1 ratio. The random numbers list generated will be concealed using opaque and sealed envelopes with an independent custodian.

Blinding

The participants will be blinded to group allocation throughout the study. They will get an explanation that they will receive LDH treatment using with or without moxibustion. The assessor, data recorder, acupuncturist and statistician will all operate independently; the randomization staff and acupuncturist will know the allocation information, while the assessor and statistician will stay blinded to this information throughout the study. Each participant will be treated separately to prevent any exchange of

study information. In the case that withdrawal occurs, the study research assistant would provide the relevant information for the participant, which includes the participant's treatment assignment and outcome data.

Interventions

The operators(acupuncturists) of this experiment have more than 2 years work experience, and they have been trained again before the test. Moxa stick is produced by Nanyang Xiancao Industry Co., Ltd. Each moxa stick was 40mm in diameter, 109g in weight and 15cm in length. The treatment site was at the lower waist. The BL25 (Dachangshu), GV3 (Yaoyangguan), BL23 (Shenshu) and GV4 (Mingmen) were taken (Fig 2). The subjects will be in a prone position. One moxa stick is held by the operator and ignites the top of the stick. Then put the moxa stick on the treatment site, and the fire head is 3cm away from the skin. After 15 minutes of local whirling moxibustion, the contralateral acupoints were treated with moxibustion for 15 minutes. Five times in ten days, lasting for 20 days, a total of 10 times. Acetaminophen (0.65g per tablet) administered by Shanghai Johnson & Johnson Pharmaceutical Co. Ltd. will also last for 20 days, taking two tablets orally every other day.

Outcome Measures

All outcome measurements will be recorded at the baseline (before treatment) and the 10 days after treatment and 20 days after treatment (Fig. 3).

Primary outcome measurement

Japanese Orthopaedic Association (JOA) scores [15]

JOA included subjective symptoms, clinical examination and activities of daily living, with a total score of 29. The lower the score, the more obvious the dysfunction.

Visual analogue scale (VAS)[16]

Visual analogue scale (VAS) is mainly used to evaluate pain. It is widely used in China. The basic method is to use a 10 cm long swimming scale with 10 scales on one side. The two ends are "0" and "10" points respectively. 0 point means no pain, and 10 points represents the most severe pain that is unbearable.

Oswestry disability index (ODI)[17]

The Oswestry Disability Index questionnaire (ODI) is composed of 10 questions, including pain intensity, self-care ability, carrying heavy objects, walking, standing and so on. There are 6 options for each question, and the highest score of each question is 5. The higher the score, the more severe the dysfunction.

Sample size and statistical analysis

Sample-size

This study aims to estimate the exact effect of thunder-fire moxibustion compared to acetaminophen. The sample size has been estimated based on the results of a previous study that had shown an extract of thunder-fire moxibustion combined with massage eases LDH[18].

The Visual analogue scale (VAS), Oswestry disability index (ODI) and Japanese Orthopaedic Association (JOA) scores will be used as the primary outcome measure to assess the effect of thunder-fire moxibustion in this trial. Results from a previous study showed that the mean changes in the Visual analogue scale (VAS) were 0.89 ± 0.37 (massage and thunder-fire moxibustion group) and 1.94 ± 0.51 (control group) [18]. SPSS 21.0 software was used to calculate the sample size. The confidence of the trial sample size was 90% and the significance level was 0.05. Results showed that clinically significant differences would be detected using a sample size of 40 individuals in each group. With the consideration of a 10% drop-out rate, at least 45 patients are required in each group. In view of the equality of distribution of all cases in the 2 group, there will be a total of 90 cases with 45 patients in each group.

Statistical analysis

To eliminate artificial error, two statisticians will be involved to independently run statistical analysis via SPSS software (version 24.0) and R statistical package (version 3.5.0).

If the continuous variables can meet a normal distribution or T distribution, the data between the two groups will be compared by Student's t test. Otherwise, we will use the Mann–Whitney test or Wilcoxon test. For categorical data, the Fisher's exact or the Chi-square test will be adopted. It is statistically significant when the p value is under 0.05. We will select the intention-to-treat principle to perform this statistical analysis. Thus, multiple imputations will be used to address the missing data. We will use two different methods: intention-to-treat and per-protocol, for sensitivity analysis. Moreover, we will establish a multiple regression model to control the covariates.

Safety and adverse events

The group of thunder-fire moxibustion may encounter adverse events including xerostomia, dizziness, and fainting. If the above situation occurs, we should immediately stop the treatment of thunder fire moxibustion and have a rest. Adverse events caused by acetaminophen mainly include acute liver failure, tinnitus, dizziness, drowsiness, abdominal distension, itching, dyspepsia, and blurred vision. Once these adverse reactions occur, participants must stop the acetaminophen and select symptomatic treatment. These AEs will be subcategorized by severity: mild, moderate, and severe adverse events (mild adverse events = adverse events are transient and tolerable; moderate adverse events = adverse events will cause discomfort and interfere with the subject's normal life; severe adverse events = serious impact on the participants' physical health and even lead to the risk of life). The record form will be filled in if adverse

events occur during the treatment period including the time, duration, performance, measures to be taken, and the outcome.

Data management and monitoring

A case report form (CRF) will be used in data collection. Data information on demographics and assessment after each treatment of every participant will be recorded completely by the data monitoring committee. The cause of patient drop-out should be clarified in the CRF for all shedding cases. At the end of the study, the investigator will submit the case report form to the data management committee for all patients enrolled in the trial. Continuity of the trial will be assessed if more than 25% of the patients discontinue intervention due to moderate or severe adverse events.

The data will be double entered. Double entry of CRF data will be performed by two experienced independent data entry staff within 2 weeks of data collection. The data stored in the final clinical trial database will ensure that it accurately reflects its source and meets specific quality standards.

The research and monitoring will follow the principle of good clinical practice and will be carried out by Nanling Hospital of traditional Chinese medicine. The clinical research assistant (CRA) will attend every two weeks to monitor and ensure the quality of the recorded data. The CRA will examine medical records, informed consent, original documents and CRF.

Discussion

Lumbar disc herniation (LDH) is a kind of syndrome with low back and leg pain caused by partial or complete rupture of annulus fibrosus and protrusion of nucleus pulposus alone or with annulus fibrosus and cartilage endplate after degenerative disease of lumbar intervertebral disc, stimulating or compressing sinus vertebral nerve and nerve root. The main manifestations were low back pain and sciatica, accompanied by the limitation of lumbar activity and the changes of sensation, movement, and reflex in the affected nerve root[]. At present, non-surgical treatment (including drug therapy and physical therapy) and surgical treatment are commonly used in clinic. However, through moxibustion and other traditional Chinese medicine treatment for lumbar disc herniation has achieved significant curative effect.

At present, moxibustion is widely used in the prevention and treatment of digestive[], bone and joint[], cardiovascular[], urinary system[] and other system diseases. In clinical practice, moxibustion for LDH has also achieved a certain effect. However, this kind of clinical research is usually the application of moxibustion combined with other therapies, such as acupuncture, massage, cupping, etc. We need to independently evaluate the clinical effect of moxibustion on LDH. Therefore, we choose thunder-fire moxibustion as intervention means, its penetration of soft tissue pair is stronger than ordinary moxibustion.

During the process of moxibustion, infrared radiation will be generated[]. Far infrared ray is easy to penetrate the skin of human body, and heat is transmitted and diffused, while the near infrared ray

generated can penetrate deep tissues through capillary network. On the one hand, the local heat stimulation plays a role through sensory afferent, on the other hand, it accelerates the blood circulation and promotes the rapid diffusion of local pain causing substances (such as histamine, bradykinin, prostaglandin, etc.). But related studies have also reported the adverse reactions of thunder-fire moxibustion[], so we should prevent excessive smoke and potential scald risk.

In the previous clinical studies[][], the schemes of the experimental group were all thunder-fire moxibustion combined with other treatment methods, and there was no single use of thunder-fire moxibustion as the scheme for the treatment of lumbar disc herniation. Therefore, there may be bias, and the efficacy of thunder-fire moxibustion cannot be confirmed clearly. In this study, thunder-fire moxibustion was separated from oral medicine to evaluate the actual effect of thunder-fire moxibustion. The trials were randomly referred to the acupoint selection methods recorded in the textbook of acupuncture and moxibustion[12]. For example, local selection of lumbar acupoints BL23 (Shenshu), BL25 (Dachangshu) and distal selection of BL40 (Weizhong), BL57 (Chengshan), KI3 (Taixi). In fact, the penetration of thunder-fire moxibustion is stronger than that of general moxibustion[], especially in diameter, which is longer than ordinary moxa stick, with wide coverage and strong permeability. Therefore, thunder-fire moxibustion is more suitable for local acupoint selection. According to the characteristics of thunder-fire moxibustion, BL25 (Dachangshu), GV3 (Yaoyangguan), BL23 (Shenshu) and GV4 (Mingmen) were selected in this study. These acupoints are based on our previous clinical experience[], using parallel arrangement of surgical methods, trying to clinical effect on lumbar disc herniation.

This study has limitations. One limitation is blindness. This trial can not be double-blind for patients and acupuncturists, so open label study is used, which may lead to bias. However, in this study, we tried to adjust the bias by using blind method to measure the results and statisticians. The trial time is short (20 days treatment), because we only focus on the short-term analgesic effect of thunder-fire moxibustion. In addition, acetaminophen is not suitable for long-term use[]. In China, thunder-fire moxibustion is a special traditional Chinese medicine therapy. However, as far as we know, there is no clinical study on the treatment of LDH in the experimental group with simple thunder-fire moxibustion. Therefore, the results of randomized controlled trials on the efficacy and safety of thunder-fire moxibustion in the treatment of LDH are expected to provide high-level evidence.

Trial Status

This protocol is version 4.0. 2019-03-17. The participants will be recruited from March 1, 2019 to June 1, 2020. But no one will be enrolled until this paper is submitted.

Abbreviations

LDH: Lumbar disc herniation

JOA: Japanese Orthopaedic Association

VAS: Visual analogue scale

ODI: Oswestry disability index

AEs: Adverse events

NSAIDs: Nonsteroidal anti-inflammatory drugs

RCT: Randomized controlled trial

DMC: Data monitoring committee

CRA: Clinical research assistant

CRF: Case report form

Declarations

Availability of data and materials

The datasets analyzed during the current study are available from the corresponding author on reasonable request.

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Authors' contributions

LW and HT conceived the idea for this study. JZ organized the outline, drafted the manuscript. XZ provided a few studies, ideas and some revised opinion. XW participated in the study design and helped to draft the manuscript. TX and LS contributed to the final version of the manuscript. All authors read and approved the final manuscript.

Corresponding authors

Correspondence to Liuqing Wang or Hongxuan Tong.

Ethics declarations

Ethics approval and consent to participate

This study has been approved by the ethics review committee of nanling hospital of traditional Chinese medicine (LJP No.007). All participants must provide informed consent when they are aware of the potential risks and benefits. We will send a special person to keep secret for the subjects. There was no anticipated damage or compensation for participating in this trial.

If participants choose to withdraw from the trial, we will ask them in the consent form whether they agree to use their data. This trial does not involve the collection of biological samples for storage.

In some cases, the protocol may be modified for the sake of clinical trial science and subject protection. We will first inform the sponsor and then add a copy of the revised protocol to the Investigator Site File. We will also update the protocol in the Chinese Clinical Trial Registry (http://www.chictr.org.cn), and any deviation from the protocol will be fully recorded using the breach report form.

Consent for publication

All participants have agreed to publish the report individually.

Competing interests

The authors declare that they have no competing interests.

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Figures

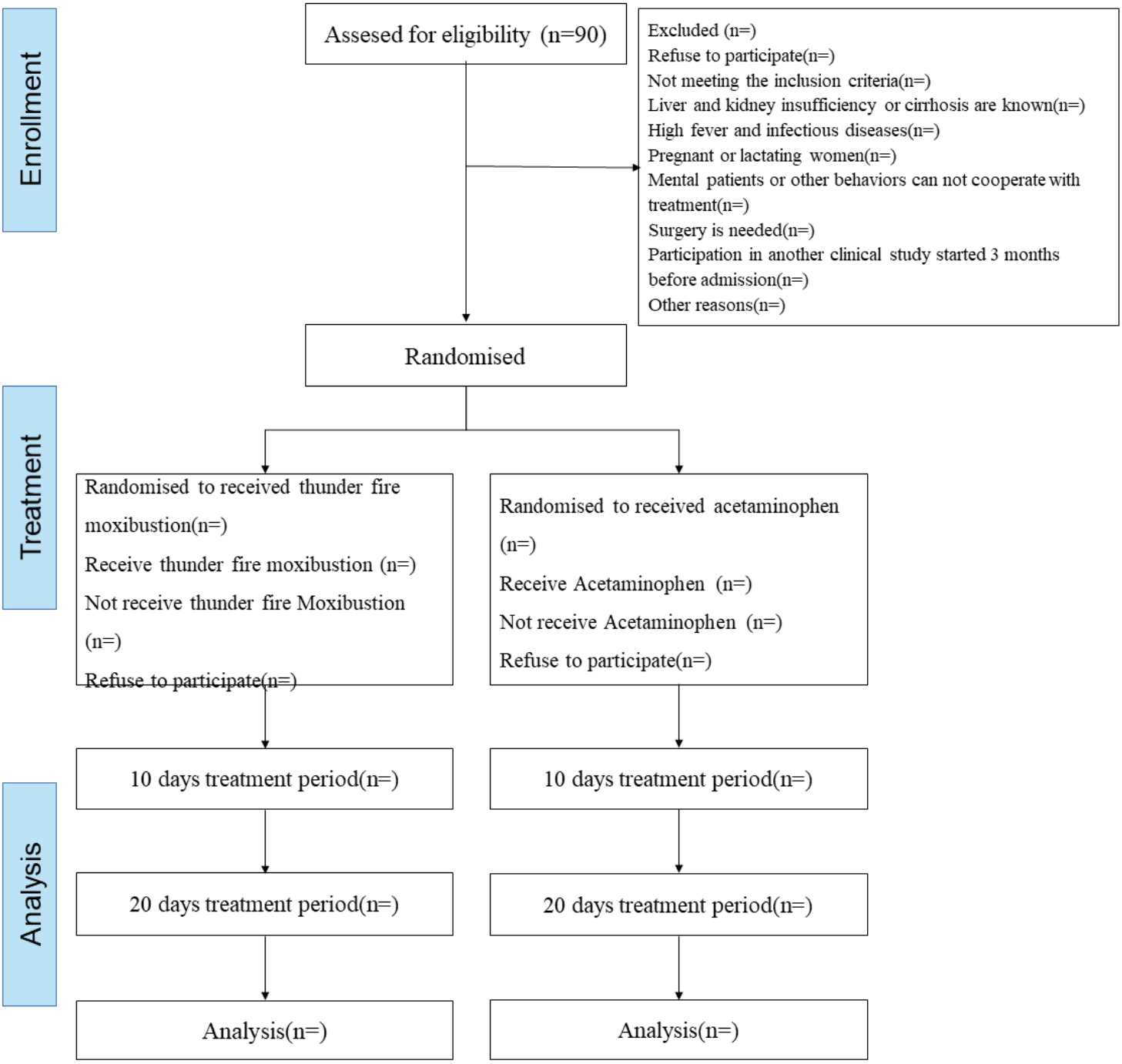

Figure 1

Trial flow chart

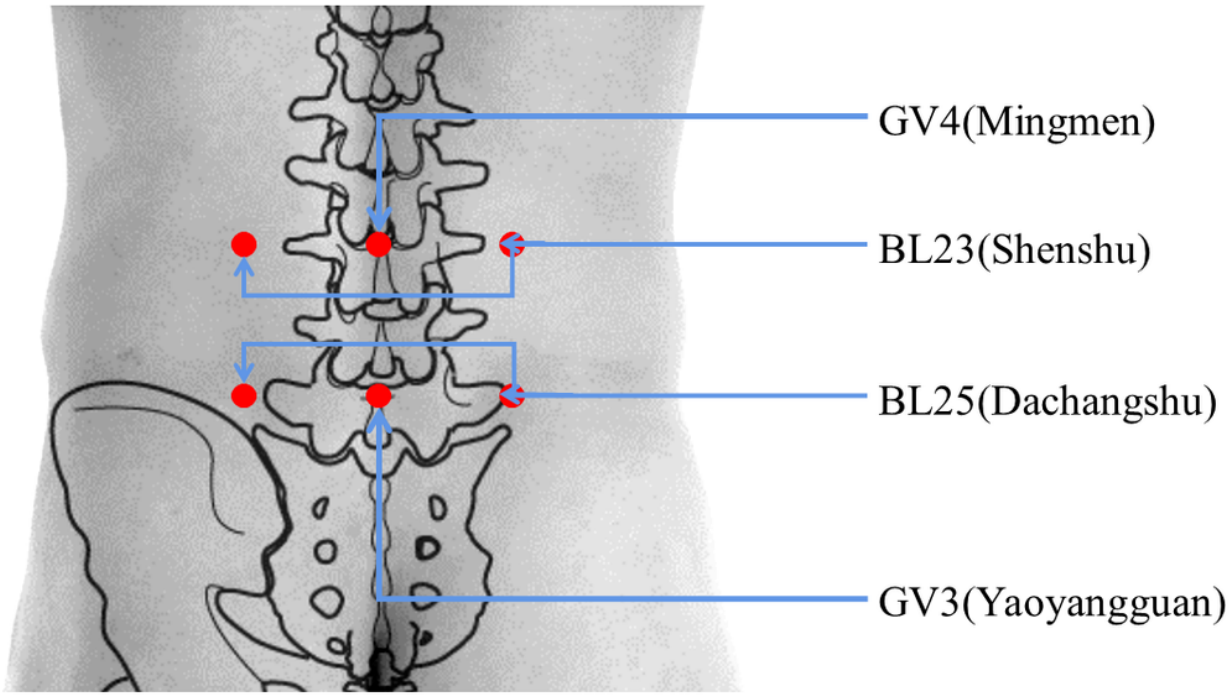

Fig.2 Location of acupoints

Figure 2

Location of acupoints

	STUDY SCHEDULE			
	Screening	Baseline	Intervention	
TIMEPOINT	Week -1	Week 0	10 days	20 days
ENROLMENT				
Eligibility screen	×			
Informed consent	×			
Allocation		×		
INTERVENTION				
Thunder fire moxibustion group			×	×
Acetaminophen group			×	×
OUTCOMES				
Japanese Orthopaedic Association Scores (JOA)		×	×	×
Visual analogue scale (VAS)		×	×	×
Oswestry disability index (ODI)		×	×	×
MONITOR				
Adverse events			×	×
Patient' compliance			×	×
Trial continuity			×	×

Figure 3

Study Schedule

Supplementary Files

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

- Additionalfile1SPIRITchecklist.docx