

Fire needle acupuncture or moxibustion for chronic plaque psoriasis: study protocol for a randomized controlled trial

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Study protocol

Keywords: Fire needle therapy, Moxibustion, Plaque Psoriasis, Clinical effectiveness, Relapse rate

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Abstract

Background: Psoriasis is a chronic, immune-mediated disorder with chronic plaque psoriasis during remission stage. Patients often have a slow course and long history of the disease. The refractory type of psoriasis is a stubborn rash that does not subside easily. We designed this randomized controlled trial to compare the effectiveness and relapse rates of plaque psoriasis in patients treated with either acupuncture, moxibustion or calcipotriol ointment. The ultimate aim of the study is to select an effective traditional Chinese medicine (TCM) clinical program for patients with plaque psoriasis. **Methods:** The study will be a multi-center, prospective randomized controlled trial (RCT), which compares the effectiveness of fire needle therapy, moxibustion and calcipotriol ointment. A total of 160 plaque psoriasis patients will be recruited and randomly assigned to receive either fire needle therapy (group A1), moxibustion (group A2) or calcipotriol ointment (group B). All participants will receive a 8-week treatment and then be followed up for another 24 weeks. The primary outcomes measured are relapse rates and Psoriasis area and severity index (PASI) score of the target lesions. The secondary outcomes are target lesion onset time, area and severity score. In addition, the overall clinical cure and improvement rate, dermatology life quality index (DLQI), TCM syndrome score, target recurrence rate and interval of the target lesion will be measured. **Discussion:** This study is to determine whether fire needle therapy or moxibustion could improve the clinical effectiveness of psoriasis lesions and reduce the relapse rate. Once completed, it will provide information regarding therapeutic evaluation on fire needle therapy or moxibustion for plaque psoriasis, which will assist clinicians select the most effective treatment options for patients. Trial registration: ChiCTR1800019588; Pre-results; Registered on 19 November 2018; International Clinical Trials Registry Platform (ICTRP). URL: <http://apps.who.int/trialsearch/Trial2.aspx?TrialID=ChiCTR1800019588> Keywords: Fire needle therapy, Moxibustion, Plaque Psoriasis, Clinical effectiveness, Relapse rate

Background

Epidemiology and current management

Psoriasis is a chronic, immune-mediated disorder with cutaneous and systemic manifestations. It has a severe impact on the patients' quality of life [1], with an estimated global prevalence of 2–3% [2,3]. Psoriasis is a polygenic disease and is concurrently observed with rheumatoid arthritis and cardiovascular diseases, especially psoriatic arthritis [4,5]. The pathophysiology is characterized by abnormal keratinocyte proliferation and immune cell infiltration in the dermis and epidermis involving both the innate and adaptive immune system [6,7]. The degree of skin damage is variable with most patients having disease progression for a few weeks and then relief for a certain period or even remission [8,9].

Plaque psoriasis is the primary manifestation of psoriasis during remission and is termed refractory type. Current treatments for moderate to severe plaque psoriasis include; topical agents, photo-based therapies, traditional systemic drugs and biologic agents [10]. Biologic therapies that target specific disease

mediators have become popular treatment strategies for moderate to severe disease. They are usually bimodal targeting T-cells and inflammatory cytokines, i.e., tumor necrosis factor-alpha and interleukin 12/23. At present, there are five biological treatment options approved by the FDA [11-13], whereas there are limited treatment options for mild-to-moderate disease.

Although pharmaceutical agents have been effective in rash relief, there are safety concerns with regards to its long-term use due to rash relapse. Apart from the high treatment costs, the adverse events of these treatments include headaches, muscle joint aches, increased risk of cancer [14], infection [15] and lupus [16]. Although as a first-line treatment strategy for moderate plaque psoriasis, calcipotriol ointment is prone to induce itching, skin irritation, dry skin, erythema, rash and other adverse reactions, and may even induce abnormal blood lipid profiles after prolonged use of large administered doses [17,18].

Unfortunately, disease relapse is common after drug cessation [19-21]. It has been demonstrated that the recurrence rate of psoriasis was 42.9% post narrow band ultra violet B irradiation after 3 months of significant remission, while patients treated with methotrexate had a 73.7% recurrence rate 3 months' post-treatment [20]. Finding new therapies to prolong remission and prevent disease recurrence are essential to improve the quality of life in patients with psoriasis.

Rational for use of intervention

More studies are currently focusing on alternative treatment strategies for psoriasis. These include acupuncture and moxibustion, which have been used in clinical practice as a treatment strategy for psoriasis. Based on the syndrome differentiation of blood stasis due to clod accumulation, for the plaque psoriasis, the fire needling therapy and moxibustion can warm channels and expel the cold, tonify Yang-qi and dredge meridians. This will help to remove slough, and promote tissue regeneration [22]. Several pilot studies reported that fire needling acupuncture and moxibustion is effective in delaying recurrence compared to conventional therapies [17-19]. These preliminary studies concluded its beneficial effect as an adjunct therapy. However, randomized clinical studies using larger sample size are essential to validate these preliminary findings.

Rational for the trial design

In current, there is lack of comparative effectiveness studies using acupuncture related techniques for plaque psoriasis. Systematic reviews have reported the benefit of needling, but with relatively low methodological quality [23] and lacking of comparison of effect to different interventions [24]. Besides, merely few studies focused on the relapse rate after the skin lesion subside [25]. So we designed this prospective RCT to determine the clinical effectiveness of fire needling and moxibustion in reducing psoriasis relapse and compared them to calcipotriol ointment, the conventionally and most frequently used treatment strategies.

Although the double-blind and placebo controlled trial is the golden standard to assess the therapeutic effect, for the non-drug and manipulation technique, sham needling and moxibustion is difficult to be performed. Containing the warm stimulation, the process of manipulation for fire needle and moxibustion

is easy to be distinguished [26]. So blinding and placebo will not be involved in this study. In addition to the outcome measurement choice, this study will also evaluate additional patient reported outcomes, including target lesion onset time, target lesion area and severity score, the overall clinical efficacy and improvement rate, DLQI, as well as the TCM syndrome score.

Methods/design

Aim, design and setting of the study

The key objectives for this study are as follows:

To compare the effectiveness and relapse rates of plaque psoriasis in patients treated with either acupuncture, moxibustion or calcipotriol ointment, mainly focus on the relapse rates and PASI score of the target lesions. The ultimate aim of the study is to select an effective TCM clinical program for patients with plaque psoriasis.

The proposed study is a multi-center, prospective RCT that will compare the three currently available treatment options for patients with plaque psoriasis. It will be consisted of a 8-week treatment phase followed by a 24-week follow-up phase. Figure 1 shows the trial procedure and table 1 details the trial schedule.

Figure 1 Flowchart of the trial procedure.

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Table 1. Schedule of enrolment, interventions and assessments

Patients will be recruited from the Dermatology Clinic of Beijing Hospital of Traditional Chinese Medicine, Capital Medical University, Dongzhimen Hospital of Beijing University of Chinese Medicine and Gulou Hospital of Traditional Chinese Medicine of Beijing. All patients will be required to provide written informed consent to participate in the study.

Eligibility criteria

Patients diagnosed with psoriasis based on the American Dermatology Expert Association criteria will be selected to participate in this study [27].

The inclusion criteria for patient selection are as follows:

- TCM syndrome types with blood stasis.
- No new skin lesions appearing within the last two weeks, and lesions are mainly of the plaque-type.
- Mild and moderate disease, and the lesion area is no more than 10% of the body surface area.
- Stage of the psoriasis in rest or regression.
- Patients between 18 and 65 years old.

Exclusion criteria are as follows:

- Use of glucocorticoids, immunosuppressive drugs, retinoic acid drugs, calcineurin inhibitors, retinoids and/or vitamin D3 derivative preparations in the past month.
- Blood-stasis syndrome together with blood-heat symptoms.
- Pregnant or lactating women.
- Diagnosed with severe primary disease and mental illness such as cardiovascular, cerebrovascular or hematopoietic.
- Allergy to the investigational therapies.
- Patients with severe episodes of fainting and halo.
- Patients participating in other clinical trials.

Interventions

For the Group A1, patients will be treated with fire needling. The acupoints used for all participants in the intervention group are shown in Figure 2.

Filiform needles will be used prior to fire needles. This is based on the treatment principles of WeiTong as well as "promoting blood circulation" and "removing blood stasis" using the He's SanTong method from the Beijing Hospital of Traditional Chinese Medicine. The needles will be purchased from the Beijing Zhongyan Taihe medical equipment co., LTD. The dimensions of the filiform needles are 0.25mm×40mm, while the fire needles are 0.5mm×40mm.

Filiform needle treatment procedure:

The LI11 (Quchi), SP10 (Xuehai) and SP6 (Sanyinjiao) acupuncture points on both sides of the body will be punctured one inch perpendicular. Positioning of the body acupoints will be based on the Chinese-English bilingual innovation textbook of the National College of Advanced Chinese Medicine in the new

century- "Meridians and Acupoints (Chinese-English)" [28]. The following acupoints (with their locations [29]) will be used:

- LI11: On the lateral aspect of the elbow, at the midpoint of the line connecting LU5 (Chize, on the anterior aspect of the elbow, at the cubital crease, in the depression lateral to the biceps brachii tendon) with the lateral epicondyle of the humerus. When the elbow is fully flexed, LI11 is located in the depression on the lateral end of the cubital crease.
- SP10: On the anteromedial aspect of the thigh, on the bulge of the vastus medialis muscle, 2 B-cun superior to the medial end of the base of the patella.
- SP6: On the tibial aspect of the leg, posterior to the medial border of the tibia, 3 B-cun superior to the prominence of the medial malleolus. 1 B-cun superior to KI8 (Jiaoxin, on the medial aspect of the leg, in the depression posterior to the medial border of the tibial bone, 2 B-cun superior to the prominence of the medial malleolus).

After acquiring Qi, the needles will be positioned for 20 minutes. The target lesions will be mostly evaluated from the back and lower limbs. The area of a single lesion should be less than 1% of the body surface area (1 palm size). After treatment with filiform needles, fire needles will be inserted perpendicularly at the edge and center of the target lesion. The lesion will be punctured once per 1 cm², at a depth of the 4 mm. The lesion area should not be exposed to water for 24 hours, and no skin care products should be used. Treatment frequency and course will be three times a week for eight consecutive weeks.

For the Group A2, patient treatment with moxibustion. The acupoints used for all participants in the intervention group are shown in Figure 1. Baixiao moxibustion device will be used for patient treatment (Chongqing Baixiao Medical Equipment Co., Ltd.).

Based on the treatment principles of WenTong and using the He's SanTong method from the Beijing Hospital of Traditional Chinese Medicine, acupoints will be selected. The main acupoints will be the target lesion. The selection principles will be similar as to the Group A1. The similar acupoints will be ST36 (Zusanli), SP10 and BL24 (Qihai). In addition, the acupoints will be positioned similar to the previous reference [21] and with Group A1. Acupoints (with their locations [29]) will be positioned as follows:

- ST36: On the anterior aspect of the leg, on the line connecting ST35 (Dubi, on the anterior aspect of the knee, in the depression lateral to the patellar ligament) with ST41 (Jiexi, on the anterior aspect of the ankle, in the depression at the center of the front surface of the ankle joint, between the tendons of extensor hallucis longus and extensor digitorum longus), 3 B-cun inferior to ST35. ST36 is located on the tibialis anterior muscle.
- SP10: On the anteromedial aspect of the thigh, on the bulge of the vastus medialis muscle, 2 B-cun superior to the medial end of the base of the patella.

· BL24: In the lumbar region, at the same level as the inferior border of the spinous process of the third lumbar vertebra, 1.5 B-cun lateral to the posterior median line.

Moxibustion on the target lesion will be performed for 30 minutes/time, with the matching acupoints treated for 15 minutes/time. The target lesion and all matching acupoints will be treated with moxibustion simultaneously. After moxibustion, artemisia oil will be used to massage the area for absorption. Treatment frequency and course will be three times a week for eight consecutive weeks.

Figure 2 Schematic sites of acupuncture points in intervention group A1 and group A2.

*These images are from *WHO STANDARD ACUPUNCTURE POINT LOCATIONS IN THE WESTERN PACIFIC REGION* [29]

Control

Patients in the group B will be treated with calcipotriol ointment. Calcipotriol ointment will be purchased from Leo pharmaceutical co., LTD., Ireland (15g/ bottle). Patients will be required to return the used tube for recycling and verification after every visit.

Treatment of the target lesion will be similar as the intervention groups. For each skin lesion (area the size of the palm), a 1/2 fingertip unit [30] of calcipotriol ointment will be administered. A fingertip unit refers to the dosage of a topical drug that is squeezed from a standard packaging hose with a diameter of 5 mm to an adult fingertip. Calcipotriol ointment will be applied based on the actual lesion area. Treatment frequency and course of intervention and control group both will be once every morning and evening for eight consecutive weeks.

Criteria for discontinuing or modifying allocated interventions

The physician will manage the intervention and related harms of all enrolled patients. Any suspected adverse events related to the treatment will be discussed with the Principal Investigator of the project team. Both the Principal Investigator and physician will be notified of all adverse events and the research team will conduct a quarterly review of all adverse events that may occur during the trial.

Adverse events may occur during the study. Patients who receive fire needling treatment may suffer from fainting, bleeding, body heat, dizziness and so on. Correspondingly moxibustion treatment may cause scalding injury, allergy, dyspnea, asthma, etc. Topical drugs may cause local redness, irritation, burning, etc. We will establish detailed medical records of the above possible adverse reactions or suspected adverse events and have the necessary treatment measures in place to deal with these adverse events.

If the patient has any discomfort, changes in condition, or any unexpected adverse effects, whether related to treatment or not, the patient will be instructed to inform the physician. The physician will provide the necessary medical treatment to alleviate any adverse conditions. The physician will determine whether the study treatment is ineffective due to poor effect or may be due to other medical reasons.

Patients will be informed of the risks of intervention and possible reasons of adverse effects. The patient may make an appointment with the physician on discontinuing or modifying interventions.

Sample size estimation

The sample size that will be required was estimated based on the 3-month disease recurrence rate, which was recorded our previous observations. The ratio of the three groups was 2:1:1. The relapse rate after fire needle therapy was 38%, while it was 67% for the calcipotriol ointment group [16], correspondingly the moxibustion group was also set as 67%, $\alpha=0.025$ and $\beta=0.2$. Sixty-six patients were assigned to test group A1 using PASS11.0 software, while 33 patients were assigned to test group A2 and group B. The sample size used in our study was increased by an additional 20%. Hence, the final sample size was 80 in group A1, and 40 each in group A2 and group B. A total of 160 patients were included in the study.

Patient recruitment

Advertisements will be posted in the clinic to recruit patients. The rationale of the study, risks and patient randomization will be explained to all patients who meet the inclusion criteria. Patients will receive a written informed consent document with ample time to understand the associated risks and benefits before being asked to sign it. It will be the responsibility of the investigator to ensure that patients have enough time to properly understand and decide whether to participate in the study. Patients who have signed the informed consent to participate in the study will be randomized and assigned a unique ID number (sub-center code and sequence number).

Randomization and allocation concealment

Sequence generation will be performed using the PROC PLAN process in SAS 9.4 software (Beijing Hospital of TCM Version. Order Number: 9C1XJD). The numbers for each center will be randomly assigned. Proportion of randomization will be set at 2:1:1 for the group A1 (fire needle combined with acupuncture): group A2 (moxibustion): group B (calcipotriol). A statistician will then encode the grouping results and seal it in an envelope, which will then be handed to patients based on their enrollment order. Outcome assessment and statistical analysis will be performed by independent statisticians from the Beijing Institute of Traditional Chinese Medicine who are blinded to the group assignments.

Blinding

In view of to be easily identified of the fire needle procedure and moxibustion, the blinding method could not be used on researchers, patients and outcome evaluators involved in the treatment, hence only the statisticians were blinded.

Strategies to improve adherence

The practitioners of the intervention will be the physician which have senior title and more than 3 years of clinical experience. This is to ensure that the treatments will be administered consistently. The patient

may have the prior to get the subsequent visit to physician in the follow-up time of the study, which is to enhance compliance.

Relevant concomitant care

Patients in this study will be discouraged from any additional specific complementary treatments related to psoriasis throughout the trial, including herbal medicine, psychotherapy, phototherapy and so on. If patients need medications such as glucocorticoid drugs and immunosuppression, the relevant information will be recorded in the Case Report Form.

Study outcomes

Primary outcomes

The primary outcomes will include recurrence rates and clinical efficacy of the target lesions [31]. The recurrence rates will be defined as recurrence of skin lesions after recovery that reaches 50% of the original PASI score, based on the American Academy of Dermatology Expert Association.

Secondary outcomes

These will include target lesion onset time, target lesion area and severity score [32], comprehensive efficacy rate, overall clinical cure rate, overall clinical improvement rate, DLQI, TCM syndrome score, the relapse interval and the recurrence rate of the target lesion.

Data collection

Data will be collected using case report form (CRF). The research medical records and case reports will be completed by the researcher for all enrolled patients. Completed case reports will be reviewed by the clinical monitor, and then handed over to the data administrator for data entry and management.

Patient information will be collected as follows: General information (including name, gender, birth date, marriage, time for disease diagnosis and onset) complaint and symptoms, family history, use about pharmaceutical drugs, physical examination, skin lesions, additional symptoms evaluated using the TCM scale, target lesion imaging and scoring, and the DLQI questionnaire. Information regarding adverse events will be recorded during the procedure and on follow-up. Images of skin lesions, PASI scores, TCM syndrome assessment, DLQI, etc. will be performed at patient enrollment and after 2, 4, 6 and 8 weeks during treatment and followed-up period (12 and 24 weeks after intervention withdrawal).

Patient dropouts

Investigators will have the authority to terminate patient participation at any time if the investigator deems it is in the best interest of the patient. Furthermore, the patient will have the right to withdraw consent to participate in the study at any time for any reason without any consequences for further medical treatment. Patient study discontinuation will be documented.

Termination criteria is as following:

(1) Patients with serious adverse event based on the investigator's judgment, will terminate the patient study participation; (2) The patient's condition is aggravated during the course of the disease, and serious complications or rapid deterioration of the condition will result in patient treatment discontinuation;(3) Other adverse symptoms affecting the study observation or patient wellbeing; (4) Unrelated medical reasons;(5) Deviations in the clinical trial protocol, such as poor compliance or difficulty in evaluating drug effects; (6) Patients thinks there is a lack of effec and voluntarily withdraws; (7) The patient is unwilling to continue clinical treatment during the clinical trial protocol; (8) Patients are administered glucocorticoids and/or immunosuppressive drugs, calcineurin inhibitors, retinoids, and vitamin D3 derivative preparations during the study.

Study retention

Follow-up observation study protocol is as following

(1) After 8 weeks of treatment, the patients will enter the follow-up period. Patients who benefited from the treatment will be maintained on the treatment but at a reduced treatment frequency, with treatment not exceeding two months.

(2) During the follow-up period, patients will be monitored using a mobile application software, telephone, text or other methods to communicate on a regular basis. Additionally, patient health management, regular health education and life guidance will be provided. Record of the patient's medications will be monitored. Patients who benefited from treatment and were still in relapse at the 6-month follow-up period will be further evaluated for long-term efficacy. The patient's recovery will be monitored using application software or telephone feedback information every 4 weeks. Changes in target lesions area will be monitored via application every 2 weeks. Patients will be required to visit the clinic every three months to monitor symptoms and signs, conditions, PASI score, skin disease quality of life index and TCM syndrome efficacy score.

(3) If the patient relapses, the follow-up will terminate. Patients will then be required to seek medical advice and treatment promptly.

Data management

Database will be established using EpiData 3.1 software (EpiData Association, Denmark). For the entry and management, medical statisticians will appoint data administrators. In order to ensure the accuracy of the data, two data entry technicians will independently enter and verify the data twice. Proper training will be provided to the technicians before data entry.

After completion of the data entry, reports on the consistency of the database will be generated. Any inconsistencies found in the database will be verified and corrected.

SAS (Version 9.4) software will be used for data verification. Verification will include logical errors, missing data and extreme data. Afterwards, a data verification report will be generated to be sent to the clinical monitor for verification. Any inaccuracies will be checked by the data administrator, who will perform data modification, confirmation, and entry based on the researcher's response. After both parties are satisfied with the final data version, it will be locked for statistical analysis.

Statistical analysis

Statistical analysis will be performed using the SAS (Version 9.4) software by a statistician who is blinded to the patient grouping. Continuous variables will be presented as mean \pm standard deviation (normally distributed data) or medians and ranges (non-normally distributed data). Frequencies and percentages will be used for count data.

Additional statistical tests will be performed using a bilateral differential test, with p value ≤ 0.05 considered as statistically significant. For the primary outcome of relapse incidence, survival analysis will be used. Measurement data will be analyzed using t test and rank sum test. Count data will be analyzed using chi-square test and Fisher's exact test, while grade data will be analyzed using Ridit and CMH. Overall evaluation index and the main efficacy indexes will simultaneously be analyzed using per-protocol and intention-to-treat analysis, while multi-center count data will be analyzed using the CMH method. Variance analysis will be performed for measurement data. For confounding factors that are difficult to predict or uncontrolled before treatment, i.e., imbalance between the groups before treatment, the least squares mean (LSMEAN) of covariance analysis (ANCOVA) and its 95% confidence limit or logistic will be used as covariates. Regression will be used to determine differences in efficacy between the groups and to eliminate the effects of these confounding factors on efficacy.

Confidentiality of data

Researchers are responsible for maintaining the anonymity of the subjects. Participants information can be identified in the CRF or other documents only by capital letters, numbers and/or code, rather than using the name of the subject. For the data storage, research records will be kept safely by researchers of the clinical trial according to the relevant provisions of the Chinese Good Clinical Practice after trial termination for 10 years. After expiration, the researchers will keep data based on the specific circumstances.

Data monitoring and auditing

In consideration of the intervention are not belong to pharmaceutical and post-marketing drug, for-profit bias would not be involved in this process, the research study team will not engage a data monitoring committee in this study. The research study team will assign a dedicated qualified individual to conduct inspection, and entrust a third party professional institution (Beijing Clinical Research Quality Promotion Center) not affiliated with the study to conduct regular inspections. This center will prove the data source and ensure the data reliability. External inspection will be organized by the Beijing Municipal Health

Commission every year. The Beijing Clinical Research Quality Promotion Center will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators.

Dissemination policy

We will disseminate the results of the study widely through workshops, conference presentation and publication. Once this manuscript is published, a brief summary of results using plain language will be sent to all participants. Authors of the publication should be the directly related researchers of this study.

Post-trial care

This study will not provide any post-trial care.

Protocol amendments

During the implementation of the study, if this protocol changes, researchers will communicate the important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to the relevant parties, including the funds regulator (Beijing Municipal Health Commission), trial participants, trial registries and journals.

Roles and responsibility

This study was not sponsored by pharmaceutical company. It is funded and regulated by Beijing Municipal Health Commission. All the authors participated in the trial design, and will collect data and write reports. Being entrusted by Beijing Municipal Health Commission, Beijing Clinical Research Quality Promotion Center will play the role of coordinating and steering and auditing of the study. The Center for Evidence-based Chinese Medicine in Beijing Institute of Chinese Medicine will analyze the collected data and publish the statistical analysis report.

Discussion

Psoriasis is a chronic, inflammatory, immune-mediated skin disease [33,34]. The pathogenesis of the disease is complex with many pathogenic factors. These factors may include infection, genetic, environmental, psychological and immune-related. Stress, trauma, alcoholism, etc., may be triggering factors [35], and may increase or decrease with age [36]. The disease is characterized by frequent relapses [37], and lingering. Psoriasis may not be confined to the skin only, the joints may also be involved, such as both the axial and peripheral joints [38], and may also be associated with psychological distress [39]. It seriously affects the quality of life and is an economic burden to the patient, their family and society.

At present, western medicine is used to treat local or systematic disease and can alleviate rash, but is unable to prevent recurrence. The recurrence rate of psoriasis is still relatively high [20,21]. In addition, the use of western medicine has several adverse effects. Previous studies have shown that patients treated

with Brodalumab (IL17 targeted biological), the 3-month recurrence rate was 78% [40], while the 48-week recurrence rate in patients treated with ixekizumab was as high as 87% [41], in addition, the 4-month recurrence rate in patients treated with narrow-spectrum UVB was 54.55% [42]. Hence, physicians have developed interest in using simple and low-cost acupuncture and moxibustion methods to treat psoriasis in order to reduce the recurrence rate. From the perspective of Traditional Chinese Medicine, plaque psoriasis at rest stage is mostly a “blood stasis” syndrome. Acupuncture and moxibustion can promote blood circulation and remove blood stasis, regulate qi and blood circulation, warm meridians and disperse cold. Previous studies have demonstrated that acupuncture and moxibustion have good application prospects for the treatment of plaque psoriasis [43-46]. In addition, studies have shown that acupuncture had an obvious advantage over western medicine in reducing the recurrence rate of psoriasis [47]. However, many studies have focused on the combination of multiple treatments simultaneously, such as acupuncture and moxibustion combined with traditional Chinese medicine, western medicine, lasers, etc. They have not evaluated the efficacy of acupuncture or moxibustion alone. Hence, this study evaluated the efficacy of acupuncture or moxibustion for the treatment of plaque psoriasis at the rest stage without the compounding interference of combination treatment strategies. We found that the combination of fire and filiform acupuncture and the simple use of moxibustion had a beneficial effect in the regression of plaque psoriasis in preliminary clinical studies using small patient cohorts.

We hypothesized that acupuncture and moxibustion could improve the effective treatment rate for plaque psoriasis and reduce the recurrence rate and related adverse events. Because of the high incidence and recurrence of psoriasis, current treatment strategies are not ideal. We believe that the results of this study will have important clinical significance, even if our study demonstrates that acupuncture and moxibustion has no clinical efficacy. This will demonstrate that more clinical studies are needed to find a safe and effective treatment strategy for plaque psoriasis. Finding an effective treatment for short and long-term efficacy is key for psoriasis treatment. This will promote and popularize TCM for psoriasis treatment and other dermatological ailments. This is one of the main benefits of performing the current study.

Several limitations to our research design and study should be noted. First, because of the particularity of fire needle procedure, the method was difficult to blind. The moxibustion method has the risk of scalding and other adverse events. Second, patients visiting traditional Chinese medicine hospitals may be inclined to choose TCM methods over western medicine treatment, i.e. the reluctance to use calcipotriol ointment. This may lead to a lower enrollment rate and longer time to recruit patients for the control group. Third, because of fear of the fire needle procedure, patients may be reluctant to comply to the procedure or volunteer to be enrolled in the experimental group. Finally, the sample cohort was not large, with only patients in Beijing being selected for the study.

In summary, this project will utilize He's SanTong method from the Beijing Hospital of Chinese Medicine to perform this study. Using this method, we hope to form a comprehensive treatment plan for plaque psoriasis (blood stasis syndrome) to improve clinical efficacy. The recurrence rate and time of long-term

efficacy will be observed to determine whether fire acupuncture could further reduce the recurrence rate of psoriasis compared to western medicine, and in addition, provide evidence for acupuncture treatment of psoriasis. At the same time, we advise that future clinical studies adhere to strict quality controls to fully understand the characteristics of psoriasis, as well as extend follow-up time, focus on the occurrence of adverse reactions, and standardize the use of a subjective PASI scoring standard with a combination of modern skin imaging techniques. Determining these indicators will improve the accuracy and clinical value of the data generated. It will be important to design rigorous, high-quality multi-center large-cohort randomized controlled clinical trials and conduct basic research to determine the mechanism of how acupuncture and moxibustion alleviates psoriasis. Our study should help with standardizing acupuncture and moxibustion treatment strategies for psoriasis.

Trial status

The trial protocol version and date are No. 2.0 on 13th, November, 2018. This RCT began recruiting patients in 1st, April, 2019. The approximate date when recruitment will be completed is estimated to be December in 2020. Active enrollment is open until the required number of patients are enrolled for statistical analysis. A report on the results of our study will be submitted for publication approximately 10 months after data collection and analysis.

List Of Abbreviation

TCM: traditional Chinese medicine; RCT: randomized controlled trial; PASI: Psoriasis area and severity index; DLQI: dermatology life quality index; CRF: case report form.

Declaration

Ethics approval and consent to participate

This study was conducted in accordance with the principles of the Declaration of Helsinki and Good Clinical Practice guidelines. It has gained ethical approval at both central and local levels. Central ethical approval has been confirmed from the Ethics Committee of Beijing Hospital of Traditional Chinese Medicine (ref approval no. 2018BL-064-02, on 15th November, 2018) and we will not begin recruiting at other centers in the trial until local ethical approval has been obtained. The trial has been registered on the platform of Chinese Clinical Trial Registry (<http://www.chictr.org.cn/>; registration No. ChiCTR1800019588).

Before randomization, written informed consent will be obtained from all participants. Patient who participated in the study voluntarily were not remunerated and were able to withdraw from the study at any time.

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated or analyzed are available from the corresponding author upon reasonable request.

Competing interests

None declared.

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Authors contribution

PL was responsible for developing the study protocol, conducting and supervising the clinical study and drafting the manuscript as a primary investigator. ZXC participated in the research design, revised the manuscript and performed project and quality control. DMZ, YW, HBL, XWD, BHL and JXZ conceived the study, enrolled patients and assigned treatment interventions. WL, ZRL, TTD, XWG and JCZ participated in data collection, analysis and interpretation. BL generated the computerized randomized schedule for patient allocation and analyzed the data. SF contributed to the design of the study, supervised the study protocol and revised the manuscript. All authors read and approved the final manuscript.

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Table

The table could not be inserted due to technical limitations. It can be found as an image file in the supplementary files section.

Figures

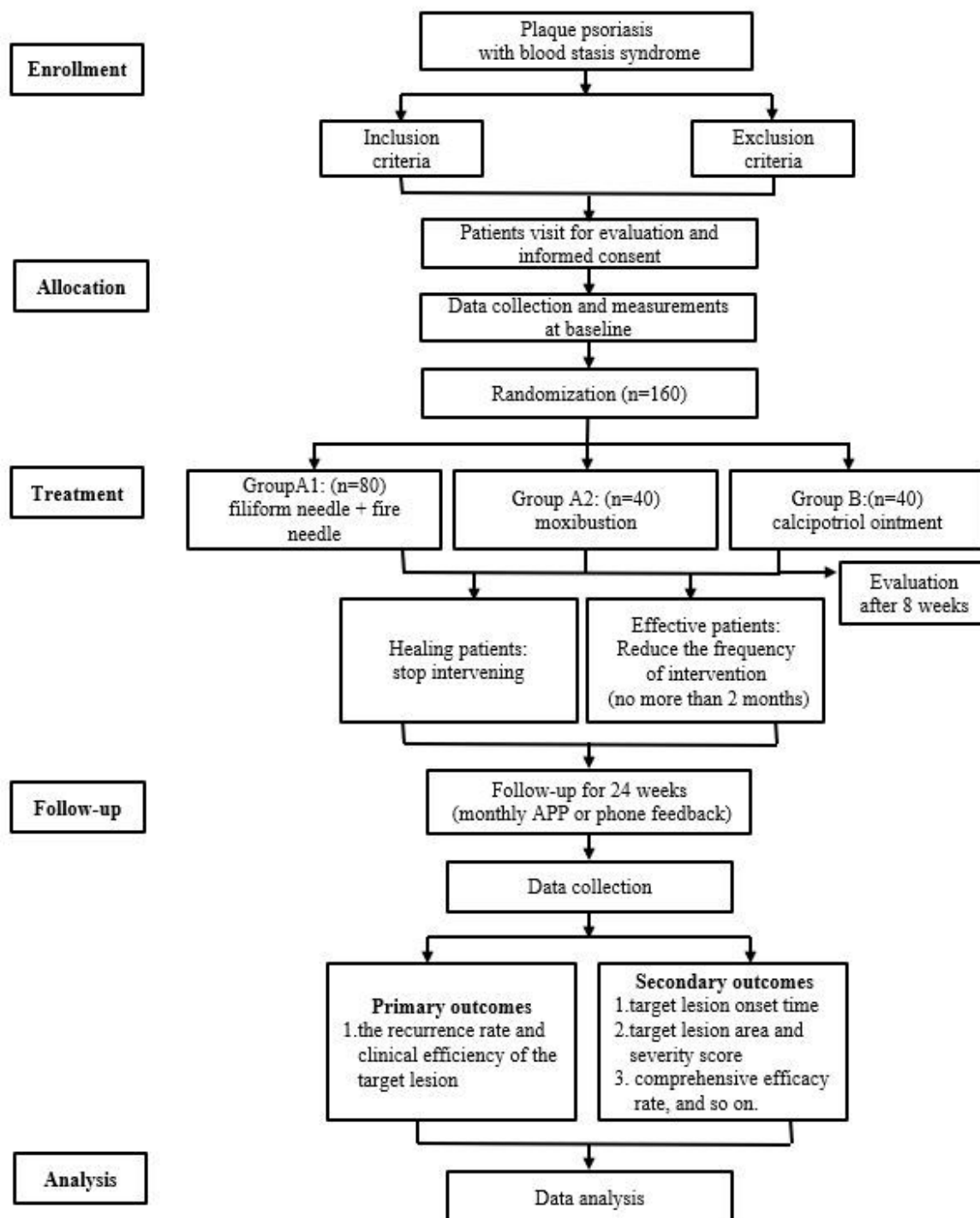
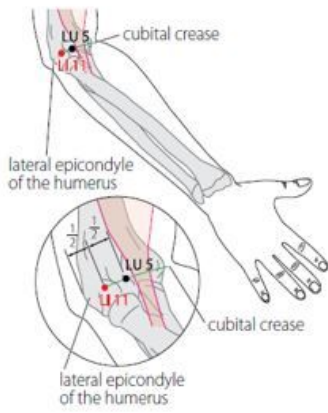
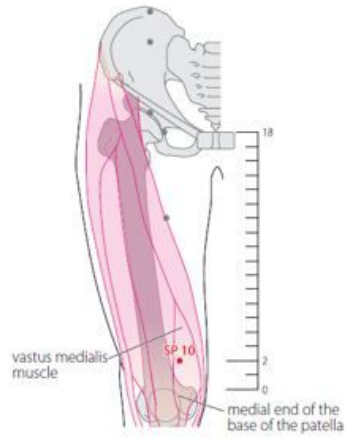


Figure 1

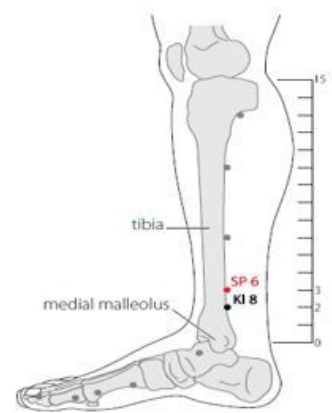
Flowchart of the trial procedure.



LI11: Quchi

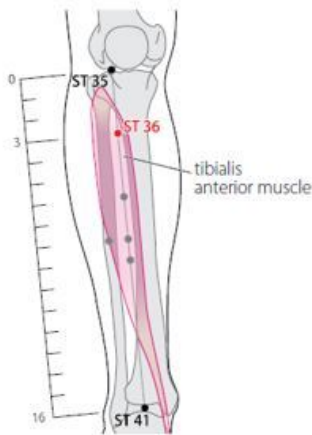


SP10: Xuehai

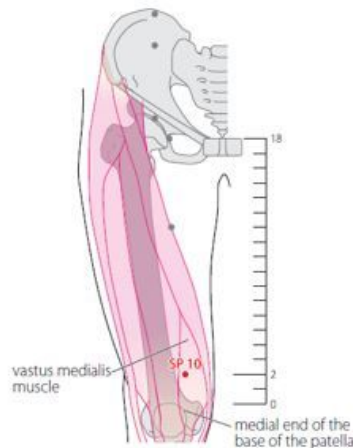


SP6: Sanyinjiao

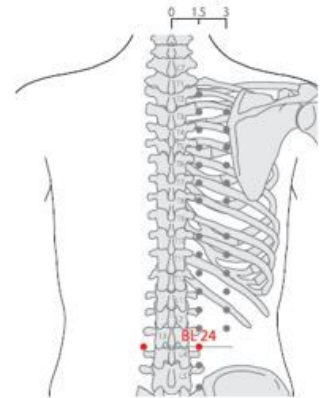
Location of points in intervention groupA1



ST36: Zusanli



SP10: Xuehai



BL24: Qihai

Location of points in intervention groupA2

Figure 2

Schematic sites of acupuncture points in intervention group A1 and group A2. *These images are from WHO STANDARD ACUPUNCTURE POINT LOCATIONS IN THE WESTERN PACIFIC REGION [29]

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