Therapeutic effect of combined acupuncture and moxibustion for patients with benign prostatic hyperplasia: study protocol of a randomized controlled trial

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Study protocol

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Abstract

Background

Combined acupuncture and moxibustion have shown benefits for a variety of illnesses. However, few studies have reported the therapeutic effect of this combined therapy for benign prostatic hyperplasia. Here, we report the study protocol of a randomized controlled clinical trial investigating the therapeutic effect of this combined therapy by comparing with the effect of conventional medical treatments.

Methods

A single-center, two-arm designed, randomized controlled clinical trial will commence in Shanghai Fourth People's Hospital, China. Two hundred participants with moderate to severe benign prostatic hyperplasia will be recruited and assigned to the combined therapy group and the conventional western medicine group in a ratio of 1:1. They will be treated for 18 weeks and assessed after 8- and 18-weeks treatment. The primary outcome is the International prostate symptom score (IPSS), the Aging Male Symptoms score (AMS); secondary outcomes include constitution in Chinese Medicine Questionnaire (CCMQ), post-voiding residual urine volume, maximum flow rate (Qmax) and average flow rate (Qave), voided volume (VV), voiding time and time to maximum flow, the change of urgency/24 h, the change of voiding frequency/24 h, the change of nocturnal frequency/24 h, the change of urge urinary incontinence frequency/24 h.

Discussion

The result of this trial will confirm whether combined acupuncture and moxibustion is effective in managing benign prostatic hyperplasia as well as the superiority of inferiority of this therapy to conventional medical treatments.

Trial registration:

chictr.org.cn, ID: ChiCTR2000030504/ChiMCTR2000003082.

Administrative Information

Note

the numbers in curly brackets in this protocol refer to SPIRIT checklist item numbers. The order of the items has been modified to group similar items (see http://www.equator-network.org/reporting-guidelines/spirit-2013-statement-defining-standard-protocol-items-for-clinical-trials/).

Title {1}	Therapeutic effect of combined acupuncture and moxibustion for patients with benign prostatic hyperplasia: study protocol of a randomized controlled trial
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Name and contact information for the trial sponsor {5b}	Health and Family Planning Commission of Hongkou District + 86 21 2311 1111
Role of sponsor {5c}	Provide financial support for conducting this trial but not involved in study design and performing the listed procedures in the study protocol.

Introduction

Background and rationale {6a}

Benign prostatic hyperplasia (BPH) is a medical condition that is defined by the enlargement of the prostate gland predominantly due to stromal and glandular epithelial hyperplasia in the transition zone of the prostate [1]. It generally leads to lower urinary tract symptoms including obstructive ones such as hesitancy, weak urination stream, incomplete bladder emptying and irritative ones like urgency, frequency, and nocturia [2]. It affects over 50% of men over 50 years old [3, 4] and nearly all men by the age of 90 [3]. The incidence of this condition and the number of patients are steadily increasing around the world due to the increased life expectancy [5].

BPH is well known to be linked with aging and the hormone levels of testosterone (T) and dihydrotestosterone (DHT), but its etiology remains largely unknown. It was proposed that reawakening of the prostatic stroma to proliferate might be an important mechanism, resulting in newly formed ductal structures in the transition zone of the prostate gland [6, 7]. Whereas, others proposed that this condition might be related to inflammation and metabolic abnormalities, which is evidenced by the close link

between the lower urinary tract symptoms and inflammation in the prostate as well as the metabolic syndrome [8–13].

Treatment for this condition has been evolving in the past a few decades. Both medications and surgical methods have been developed and their efficacy as well as side effects have been evaluated.

Alpha blockers such as doxazosin and tamsulosin decrease the tone of smooth muscle cells of the prostate and bladder neck [14], resulting in relaxation of the prostate and bladder and subsequent improvement in symptoms and the urinary flow rate. However, alpha blockers present with common side effects like orthostatic hypotension and consequent dizziness, fatigue as well as retrograde ejaculation.

5α-reductase inhibitors such as finasteride and dutasteride decrease the activity of the enzyme converting testosterone to dihydrotestosterone, and as a result inhibit the proliferation of the prostate gland, improve the symptoms, and increase the urinary flow rate [15]. Its side effects mainly include sexual dysfunction due to reduced levels of testosterone. Evidence shows that the combination of these two types of medications might be better in relieving the symptoms than either of the medications given alone [10, 16]. Phosphodiesterase type 5 inhibitors (PDE5-I) have been shown to improve symptoms in large clinical trials by relaxing the smooth muscle cells of the genitourinary tract through increasing nitric oxide signaling [17–21]. Combined use of alpha blocker and PDE5-I has been studied on patients with both prostatic hyperplasia and erectile dysfunction and the results show better outcome than single use of alpha-blockers [22–25].

However, drug therapies always have side effects more or less. In searching of potential therapies, acupuncture receives popularity in Asian countries as well as some western countries. Based on the Traditional Chinese Medicine meridian theory, “Qi” of the Kidney is responsible for excreting the urine. In aging men, “Qi” of the kidney is degenerating and the power of expelling the urine is weak. As a result, urinating takes longer time than younger adults. Based on the TCM theory, “Qi” is also leading the blood flow. Weakened “Qi” results in blood stasis, which aggravates the difficulty in urinating (see review of [26]). Therefore, replenishing “Qi” of the kidney is a key step in restoring prostate health. A large number of empirical studies conducted in China have been published using herbs or acupuncture or moxibustion (see review of [27]). However, few of them met the criteria of randomized clinical trials including both herbal treatment and acupuncture studies. Among acupuncture studies, the majority of them use different combinations of acupoints or together with herbs, and few of them use acupuncture along with moxibustion together.

Objectives {7}

It is known that acupuncture and moxibustion are both well accepted without known side effects, but their efficacy in managing benign prostatic hyperplasia has not been tested when used in combination. The present study aims to test the efficacy of acupuncture along with moxibustion by selecting a few acupoints which are effective in increasing “Qi” of the kidney as well as facilitating urination. In addition,

whether the combined therapy is superior or inferior to conventional medical therapies will be investigated.

Trial Design {8}

The present study is an investigator-initiated, single-center, randomized clinical

trial investigating the efficacy of acupuncture combined with moxibustion in managing benign prostatic hyperplasia. The therapeutic effect will be compared before and after the combined management. Participants conservatively managed with conventional medicines serve as controls. Two hundred participants will be recruited from both the Urology and Traditional Chinese Medicine clinics of Shanghai Fourth People's Hospital. They will be randomly assigned to two groups using a random number table after giving consent to participate in the present study. Whether the combined therapy is superior or inferior to conventional medical therapies will be investigated as well.

Methods: Participants, Interventions And Outcomes

Study setting {9}

Two hundred participants will be recruited from both the Urology and Traditional Chinese Medicine clinics of Shanghai Fourth People's Hospital in Shanghai, China.

Eligibility criteria {10}

Inclusion criteria

Participants will be included if they meet the following criteria:

1. Males aged 45 years or older.
2. Subjects with benign prostatic hyperplasia diagnosed by digital rectal examination.
3. Volume of the prostate equals to or over 30 ml.
4. Maximum urinary flow rate <15 ml/s.
5. Subjects with lower urinary tract symptoms suggestive of benign prostatic hyperplasia, who voluntarily agree to join and sign to the consent form.
6. Have been treated with conventional first-line western medicine for more than three months.
7. Patients with moderate to severe benign prostatic hyperplasia (IPSS score 8-19 points).

Exclusion criteria

Patients with any of following will be excluded:

1. Subjects who have a history of the lower urinary tract cancer, including prostate cancer and bladder cancer within the past 5 years.
2. Subjects who have acute urinary retention within 4 weeks before screening.
3. Subjects who have clinically significant severe cardiovascular disease (unstable angina, myocardial infarction or arrhythmia) within 6 months before screening.
4. Subjects who have concerns about acupuncture.
5. Subjects who are suspected or confirmed calculus of lower urinary tract, calculus of bladder (except for complete recovery).
6. Subjects who are judged by the investigators to be unsuitable to participate in the clinical trial.
7. Concurrent use of other Chinese herbal medicines or alternative medicine (including drugs and acupuncture) for more than one month.
8. Syphilis, gonorrhea, and other sexually transmitted diseases or urinary tract infections.
9. Congenital abnormalities such as bladder neck fibrosis, interstitial cystitis, or urethral stricture.
10. A history of genital trauma or surgery affecting the muscle or nervous system.
11. Patients with upper urinary tract obstruction, renal edema, etc. affecting renal function.
12. Unable to sign a consent form or unable to communicate with researchers.

Who will take informed consent? {26a}

Qianqian Yu will obtain informed consent or assent from potential trial participants by briefing the study details to the potential participants

Additional consent provisions for collection and use of participant data and biological specimens {26b}

Not applicable.

Interventions

Explanation for the choice of comparators {6b}

Conventional medical therapies including α-blockers, 5α-reductase inhibitors, and phosphodiesterase type 5 inhibitors are commonly used for mild to moderate BPH patients. We hypothesize that combined acupuncture and moxibustion is as effective as these medical therapies if not superior to them and with few side effects. If confirmed, the combined therapy can be used for managing these BPH patients with better outcomes.

Intervention description {11a}

Participants in the combined treatment group will receive acupuncture and burning moxa which is attached to the blunt end of the acupuncture needle. The acupoints include: Qihai, Zhongji (RN3), Shuidao (ST28, bilateral), Shenshu (BL23, bilateral), pangguangshu (bilateral). Qihai is 1.5 *cun* inferior to the umbilicus along the anterior midline. The acupuncture needle is inserted into the body with the tip reaching 1-1.5 *cun*. One *cun* is defined as the width of the patient's thumb at the level of the 1st interphalangeal joint. Zhongji-RN3 is 4 *cun* inferior to the umbilicus along the anterior midline. The acupuncture needle is inserted into the body with the tip reaching 0.5-1*cun*. Shuidao is 3 *cun* inferior to the umbilicus and 2 *cun* lateral to the anterior midline. The acupuncture needle is inserted into the body with the tip reaching 1-1.5 *cun*. Shenshu (BL23) is 1.5 *cun* lateral to the spine of the 2nd lumbar vertebra on the back. The acupuncture needle is inserted into the body with the tip reaching 1 *cun*. Pangguangshu is 1.5 *cun* lateral and inferior to the spine of the 2nd sacral vertebra on the back. The acupuncture needle is inserted into the body with the tip reaching 1 *cun*. When participants have a feeling of "Teh Chi", such as heaviness, numbness, and swelling, the needles will be kept in situ and burning moxa attached to the blunt end of the needle. The moxa will be changed after burning out until it reaches 60 minutes. These participants will be treated with acupuncture and moxibustion once a week for 18 consecutive weeks. Participants in the control group will receive conventional medicines prescribed by specialists.

Criteria for discontinuing or modifying allocated interventions {11b}

Discontinuing or modifying the combined therapy will take place when a severe adverse event occurs or upon participants' request to stop participating the study.

Strategies to improve adherence to interventions {11c}

Participants in the combined acupuncture and moxibustion group will be managed by Dr Huajun Bo who is an experienced TCM doctor. Apart from acupuncture and moxibustion in the treatment room, participants are not required to take any actions. Therefore, their adherence will be good.

Participants in the control group will be taking conventional medicines that are known to take effect after taking the medications for some time. Therefore, we will explain how the medications work to the participants and ask them to take the pills at the designated time. In the beginning we have told the participants that we are conducting a study investigating whether acupuncture and moxibustion are as effective as the medications or superior to the medications, we can tell them which is better before the study completes. Therefore, we tell them to persist till the end of the study and then they can make a choice whether to take medications or do acupuncture and moxibustion. This will increase the participants' adherence to the allocated treatment.

Relevant concomitant care permitted or prohibited during the trial {11d}

No specific care will be stopped because of the participation in this study.

Provisions for post-trial care {30}

Not applicable.

Outcomes {12}

Primary outcomes are:

1. International prostate symptom score (IPSS) (Time Frame: baseline, eight weeks, ten weeks, eighteen weeks)

To measure the severity of lower urinary tract symptoms. Each item is scored 0-5, yielding a total between 0-35.

2. Aging Male Symptoms score (AMS) (Time Frame: Baseline, eight weeks, ten weeks, eighteen weeks)

To evaluate health-related quality of life in aging men. Each item is scored 1-5, yielding a total between 17-85.

Secondary outcomes include:

1. Constitution in Chinese Medicine Questionnaire (CCMQ) (Time Frame: Baseline, eight weeks, ten weeks, eighteen weeks)

It has 60 items measuring the 9 body constitution types: gentleness, Qi-deficiency, Yang-deficiency, Yin-deficiency, phlegm-wetness, wetness-heat, blood-stasis, Qi-depression, and special diathesis.

2. Post-voiding residual urine (Time Frame: Baseline, eight weeks, eighteen weeks)

To measure and compare the amount of urine left in the bladder after urination before and after treatment.

3. Maximum flow rate (Qmax) and Average flow rate (Qave (Time Frame: Baseline, eight weeks, eighteen weeks)

To determine peak urine flow rate and average urine flow rate.

4. Voided volume (VV) (Time Frame: Baseline, eight weeks, eighteen weeks)

To calculate the amount of urine (ml) excreted.

5. Voiding time and time to maximum flow (Time Frame: Baseline, eight weeks, eighteen weeks)

To calculate the length of time it takes to empty bladder completely and the time to peak urine flow time (sec)

6. The change of urgency/24 h (Time Frame: Baseline, eight weeks, eighteen weeks)
7. The change of voiding frequency/24 h (Time Frame: Baseline, eight weeks, eighteen weeks)
8. The change of nocturnal frequency/24 h (Time Frame: Baseline, eight weeks, eighteen weeks)
9. The change of urge urinary incontinence frequency/24 h (Time Frame: Baseline, eight weeks, eighteen weeks)

Participant timeline {13}

Please see **Fig. 1**.

Sample size {14}

To calculate sample size, we used available data from the pilot study in our hospital on the efficacy of acupuncture in combination with moxibustion (unpublished). In the study, the efficacy of combined therapy is estimated to be 80%, and the efficacy of conventional medicinal therapy is estimated to be 60%, α is 0.05, 1-β is 0.8, the loss of follow-up is estimated to be 20%. The number of subjects in each group is calculated to be 80 using Two Independent Proportions (Null Case) Power Analysis (Pass 11 software). Considering the 20% loss of follow-up during the treatment period, 96 subjects are needed for each group.

Recruitment {15}

Shanghai Fourth People's Hospital is a teaching hospital affiliated to Tongji University School of Medicine. It has over 100 patients in the outpatient of Urology and over 60 patients presenting with urological symptoms in the outpatient of Traditional Chinese Medicine. The triage nurse will help to explain our study objectives and procedures to the patients and recruit those who are eligible for our study.

Assignment of Interventions: Allocation

Sequence generation {16a}

All participants will be assigned to the combined group or the control group in a ratio of 1:1 by Ms Qianqian Yu who is not involved in management using a random number table due to the small sample size.

Concealment mechanism {16b}

Patients who agree to participate in the study in the outpatient will be asked to do screening tests. If they are eligible for the study, they will be pooled together and assigned to the combined acupuncture and

moxibustion group or the conventional medical group using a random number table. Their sequences will be written on cards and sealed in envelops and kept by Ms Qianqian Yu (who will not be involved in the study database). The steering committee will be keeping aware of these results and the codes will not be broken until the last participant has completed the 18-weeks follow-up.

Implementation {16c}

Ms Qianqian Yu along with the statistician Wenchao Qiu will generate the allocation sequence, enroll participants, and assign participants to interventions.

Assignment of Interventions: Blinding

Who will be blinded {17a}

The investigator who manages participants is unaware of the participation of the participants as they will be mixed with other patients in the clinic. The investigator who assesses these participants during the follow-up is also blinded. So is the statistician.

Procedure for unblinding if needed {17b}

Unblinding will be performed when a severe adverse event occurs or upon the request of participants who like to withdraw from the study.

Data Collection And Management

Plans for assessment and collection of outcomes {18a}

Primary outcome measures and a secondary outcome measures are questionnaires which will be completed by Dr Minzhi Zhuang who has been trained by urologists to fill the primary outcome questionnaires and he is able to complete the CCMQ because he is also a TCM doctor. The other outcome measures are objective measurements from urodynamic examination which will be conducted by specialist staff in the Urology Department. They have substantial experience in performing this test. Our data collection form is the same as Fig. 1. Each result from the abovementioned tests will be recorded in the space designated for each time point.

Plans to promote participant retention and complete follow-up {18b}

We will emphasize the importance of completing this study by helping to provide follow-up results so that other patients with BPH may have a better choice of selecting their preferred treatment. For the same reason, we do not know which treatment is better than the other. We need their follow-up results to inform our health care providers. If some participants determine to withdraw this study, they will be asked to help

complete the primary and secondary outcome questionnaires and the urodynamic examination on the day they withdraw from the study. These results might be useful for future analysis. From his will increase the participants' adherence to the allocated treatment.

Data management {19}

An independent Data and Safety Monitoring Committee oversees the entire process and reviews the information collected from these participants. The Committee includes an intensive care unit (ICU) physician and a registered nurse who are not involved in the present study. Data will be entered by Dr Minzhi Zhuang and coded with A and B. The results will be stored in the data entry computer and a copy will be sent to the Data and Safety Monitoring Committee for backup and to double check the authenticity of the statistical results if any doubt exists. Dr Wenchao Qiu will perform statistical analysis after checking the data quality including double data entry, range checks for data values, etc.

Confidentiality {27}

Participants' names will be concealed after they agree to participate in the study, instead their medical record numbers will be used to represent their IDs. This way, all investigators including the statistician will be blind to the personal information of the participants.

Plans for collection, laboratory evaluation and storage of biological specimens for genetic or molecular analysis in this trial/future use {33}

Not applicable.

Statistical Methods

Statistical methods for primary and secondary outcomes {20a}

All data will be audited by two investigators before performing statistical analyses by a statistician who is blinded from the allocation of groups. SPSS 22.0 software will be used to compare the difference in nominated parameters before and after treatment within each group and the difference between groups. Data from all participants who are assigned to the combined treatment group and the control group will be compared to those from participants who complete the follow-up assessments in order to check the consistency of our results. Either Student's *t* test or the Mann-Whitney U test will be used for continuous variables depending on their characteristics, and χ^2 test for categorical variables. Both primary and secondary outcome parameters will be compared along with the incidence of adverse events.

Interim analyses {21b}

After completing 8 weeks treatment and follow-up assessment, the statistician will be able to analyze the collected results. If significant difference is observed from the available data, the chief investigator will be informed and a decision will be made regarding whether to continue or terminate the trial.

Methods for additional analyses (e.g. subgroup analyses) {20b}

The present study aims to answer the question whether combined acupuncture and moxibustion are as effective as conventional medical therapies first. If there is no significant difference between these two types of treatments, subgroup analysis will be performed based on the results of IPSS and AMS at screening. The scores of IPSS and AMS will be categorized into two levels, and the corresponding follow-up results of IPSS and AMS will be analyzed using the multiple logistic regression analysis modeling with the “Enter” method.

Methods in analysis to handle protocol non-adherence and any statistical methods to handle missing data {20c}

A representative from the Data Monitoring Committee will review all the CRFs frequently. Once the missing data are found, they will be recorded immediately. If not available, we will discuss with statistical experts about how to deal with and compensate for the missing data.

Plans to give access to the full protocol, participant level-data and statistical code {31c}

After completing the trial, all data will be uploaded to the Chinese Clinical Trial Registry website so that the public will have access to the protocol as well as the data and statistical analysis results.

Oversight and Monitoring

Composition of the coordinating centre and trial steering committee {5d}

Dr Huajun Bo, Huazheng Liang, and Quanbao Yao are steering the trial by forming the coordinating centre, Dr Minzhi Zhuang and Jisheng Peng are managing data along with the statistician Dr Wenchao Qiu. A neurologist Shaoshi Wang and a scientific administrative staff Lingyan Jiang, along with the statistician Wenchao Qiu steer the Data and Safety Monitoring Committee.

Composition of the data monitoring committee, its role and reporting structure {21a}

An independent Data and Safety Monitoring Committee oversees the entire process and reviews the information collected from these participants. The Committee includes a neurologist, a scientific administrative staff along with the statistician. The detailed charter of this committee can be found in the supplementary file.

Adverse event reporting and harms {22}

Adverse events will be monitored closely when the participants are in the treatment room, and relevant information will be collected from participants if the adverse events occur in their house. Clinicians will be informed of the condition of the participants and appropriate advice or treatment will be given to them after assessment. Adverse events will be recorded in the participants' file and the investigator's record.

Frequency and plans for auditing trial conduct {23}

Trial conduct will be independently audited every two weeks. This includes reviewing the current enrolment, allocation, eligibility practise, and other procedures. The aim of the audit is to increase the adherence of eligible participants and minimize opportunities to have side effects, to increase the completeness and credibility of the results collected.

Plans for communicating important protocol amendments to relevant parties (e.g. trial participants, ethical committees) {25}

N/A

Dissemination Plans {31a}

Findings from this study will be submitted to the repository of Chinese Clinical Trial Registry and to a journal in the field to publish. These findings will be delivered to participants and the public to help healthcare providers to make a proper decision on BPH patients' treatment.

Discussion

It is expected that the result of the proposed trial will provide objective evidence that acupuncture along with moxibustion is as effective as or superior or inferior to conventional medicinal therapy in alleviating symptoms of benign prostatic hyperplasia by performing the procedure on selected acupoints.

Acupuncture is a traditional therapeutic method for a large variety of medical issues. For thousands of years, it has been widely used for many chronic illnesses. But the effect depends on the selection of the right acupoints and right way of performing acupuncture. Though electroacupuncture is very popular due to the ease in implementation and its consistent effect, manually performing it is still necessary. First of all, the location of acupoints varies between subjects and the feeling of "Teh Qi" is indispensable for the confirmation of selecting the right position and subsequently ensuring its therapeutic effect. Secondly, different manoeuvers result in different outcomes depending on whether they are depleting or replenishing "Qi".

Based on the TCM theory that benign prostatic hyperplasia is the result of weakened “Qi” of the kidney, therapies aim to increase “Qi” after performing acupuncture. On the back, both “shenshu” and “pangguangshu” are important for increasing “Qi” of the kidney. In the front of the body, “qihai” and “zhongji” are well known acupoints for increasing “Qi” of the kidney. “Shuidao” literally means a conduit of water. In TCM, it refers to the facilitation of expelling of the urine. Therefore, acupuncture of these points will synergistically improve the symptoms of benign prostatic hyperplasia.

Moxibustion is another way of increasing “Qi” and “Yang” due to its nature of providing energy to the body. When acupoints absorb energy from the burning moxa, it promotes the function of the meridian which the acupoints belong to. In the same way, it will synergistically increase “Qi” of the kidney when stimulated by both acupuncture and moxibustion. Based on results of previous small scaled studies on both acupuncture and moxibustion on different acupoints from ours [28–32], it is expected that the proposed combination therapy will be as effective as conventional medical therapies if not superior to them in ameliorating prostatic hyperplasia symptoms.

So far, there are a number of clinical trials completed to compare the efficacy of different herbal decoctions to conventional medicinal therapies in managing benign prostatic hyperplasia, significant improvement of symptoms was observed in patients managed with herbal decoctions [33–35]. However, it is impossible to prescribe the same herbs to all patients with benign prostatic hyperplasia due to slight difference in the nature of their conditions. The composition of the decoctions is nearly the same except a couple or a few herbs that target the conditions which are not the same between patients. Therefore, it is hard to run a randomized clinical trial with the same herbal recipe. Acupuncture, on the contrary, is relatively easy to prescribe the same combinations of acupoints. This poses our study design more compliant with randomized controlled clinical trials.

The present study also has its own limitations. First of all, all patients are recruited from the same hospital. There might be certain bias in patient selection. In the present study, only moderate to severe patients are recruited. Secondly, due to the relatively small size of participants (less than 100 in each group based on the significant superiority of the combined therapy to conventional medicines), blinding is not performed using a centralized computer and patients in the acupuncture group actually know that they are managed with acupuncture and moxibustion. Thirdly, patients have been managed with conventional medicines before starting acupuncture. The therapeutic effect of these medicines might last for a short period in the combined therapy group. However, this will be minimal after 10 weeks management with acupuncture and moxibustion.

In conclusion, the present study is expected to show evidence that acupuncture and moxibustion are as effective as or superior to conventional medicines in managing benign prostatic hyperplasia with few side effects.

Trial Status

This trial will start recruiting participants from 1st April 2020 and is estimated to complete by 1st March 2022. The current version of the protocol is V1.1 as on 5th March 2020 when the study was registered.

Abbreviations

All abbreviations have been fully spelled when they first appear in the text.

Declarations

Ethics approval and consent to participate

The proposed study has been approved by the Human Research Ethics Committee of Shanghai Fourth People' Hospital (approval ID: 2020011-001). Written informed consent will be obtained from participants after introducing the procedure and the relevant benefits and risks.

Acknowledgements

We would like to thank Prof Lize Xiong for his advice and support.

Authors' contributions {31b}

HB, HL, and QY1 contributed equally to the conception and design of the study, QY2 contributes to the recruitment and randomization of participants, HB is responsible for the management of participants, MZ and JP are responsible for following up participants and collecting data, WQ is responsible for statistical analysis, HB and HL drafted the manuscript.

Funding {4}

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Availability of data and materials {29}

After completing the trial, the final dataset and statistical codes will be available upon reasonable request.

Ethics approval and consent to participate {24}

The proposed study has been approved by the Human Research Ethics Committee of Shanghai Fourth People' Hospital (approval ID: 2020011-001). Written informed consent will be obtained from participants after introducing the procedure and the relevant benefits and risks to participants.

Consent for publication {32}

Not applicable.

Competing interests {28}

The authors declare that there is no conflict of interests.

Authors' information (optional)

N/A

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Figures

	Study period																			
	Enrolment	Allocation	Post allocation																	Clost-out
Timepoint	-D2	D0	D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	D11	D12	D13	D14	D15	D16	D17	D18	D19
Enrolment																					
Eligibility screen	X																				
Informed consent	X																				
Allocation		X																			
Interventions																					
Acupuncture+moxibustion			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Conventional medicines			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Assessments																					
IPSS	X									X		X								X	X
AMS	X									X		X								X	X
CCMQ	X									X		X								X	X
Post-voiding residue urine	X									X										X	X
Qmax/Qave	X									X										X	X
VV	X									X										X	X
Voiding time and time to max flow	X									X										X	X
Times of urgency/24h	X									X										X	X
voiding frequency/24h	X									X										X	X
nocturnal frequency/24h	X									X										X	X
urge urinary incontinence frequency/24h	X									X										X	X

Figure 1

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