



Acupuncture and Herbal Moxibustion for the Treatment of 'BiQiu' (Allergic Rhinitis Symptoms) in a Hong Kong Chinese Medicine Clinic: Protocol for a Randomized Controlled Trial

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Summary

Introduction: 'BiQiu' is a Traditional Chinese Medicine name for the disease with allergic rhinitis symptoms, which is one of the most common health complaints worldwide. Acupuncture has been widely used to treat patients with 'BiQiu' (allergic rhinitis symptoms) in East Asia, but the relevant evidence is insufficient. The study aims to evaluate the clinical effectiveness of acupuncture and/or with herbal moxibustion in Hong Kong population.

Methods: This study is a single-centre, randomized; assessor blinded controlled trial with three parallel arms. The acupuncture groups will receive acupuncture treatment three times per week for a total of 12 sessions in four weeks. Acupuncture combined with herbal

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moxibustion treatment group will receive herbal moxibustion once per week for a total of 4 sessions over four weeks in addition to the same acupuncture treatment. Participants in the waitlist group will not receive any acupuncture or herbal moxibustion treatments during this period. All patients will receive advice on life style, diet and exercise. The primary outcome measures the change in the total nasal symptom score; secondary outcome measures the Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) score and the total IgE in serum.

Results: This study will demonstrate an evidence-based of acupuncture for BiQiu and will be published in a peer-reviewed journal.

Discussion: This trial will provide evidence for the effectiveness of either acupuncture combined with herbal moxibustion or acupuncture alone when compared to waitlist group as a treatment for allergic rhinitis.

Trial registration: ChiCTR-INR-16010047 registered on November 25, 2016.

Keywords: Acupuncture; Allergic rhinitis; BiQiu; Randomized controlled trial; Study protocol

Abbreviations

AR: Allergic Rhinitis

TCM: Traditional Chinese Medicine

TNSS: Total Nasal Symptom Score

G6PD: Glucose-6-Phosphate Dehydrogenase

PASS: Power Analysis and Sample Size

SD: Standard Deviation

ANCOVA: Analysis of Co-Variance

RQLQ: Rhinoconjunctivitis Quality of Life Questionnaire

IL-4: Interleukin-4

IL-5: Interleukin-5

ECP: Eosinophil Cationic Protein

EOS: Eosinophils

CMCTRs: Chinese Medicine Centres for Training and Research

HA: Hospital Authority

Introduction

'BiQiu' is a disease name in Traditional Chinese Medicine (TCM) that firstly originated from "Yellow Emperor's Inner Classic" nearly 2000 years ago [1]. Its common symptoms are sudden and recurrent nasal congestion, itchiness, sneezing and runny nose with thin nasal discharge, which are similar to Allergic Rhinitis (AR). AR is an inflammation of the nasal mucous membranes caused by Immunoglobulin E (IgE) mediated allergic reaction to aeroallergens. The symptoms of AR appear across different life stages, with the highest prevalence recorded in adolescents. It has been estimated that about 10-20% of the world's population has AR, and the number of patients is on the rise [2]. However, AR does not draw enough awareness, and is often misdiagnosed and mistreated [3]. If appropriate treatment is

not received, about 10%-39% of patients would develop bronchial asthma, or even pulmonary heart diseases, etc. It is relatively easy to have a relapse. The patient's daily life, sleep and work may be seriously affected, which is not only harmful to personal health, but also creates significant economic burden for both the individual and the society [4,5].

Currently, the main prevention and treatment approaches for AR include allergen prevention, medication or immunisation. Surgical treatment can also be conducted if necessary. Medication is one of the most commonly used means to mitigate the symptoms. Clinically the medicinal treatments of AR include corticosteroids, antihistamines, mast cell stabilizer, anticholinergics and nasal decongestant drugs, etc., however, the effect generally lasts for a short time and there are often many side effects (such as sedation, nose bleeds, rebound nasal congestion and septal perforation or the risk of anaphylaxis); The symptoms are highly likely to recur. In addition, these medications have to be taken for prolonged periods, thus also prolonging the side effects experienced by the patients [6,7]. Immunisation can change the natural progress of AR by immunity regulation mechanism, but the treatment cycle is long and expensive [8,9]. There is also the potential risk to trigger serious allergic reaction [10]. Surgery is only applicable for some certain complications and comorbidities of rhinitis. It is also traumatic, costly and not easily accepted by patients [11]. Therefore, it is an essential task to identify an effective treatment for AR with low relapse rate and few side effects.

Acupuncture and herbal moxibustion are commonly used for treatment of AR in China. Some clinical studies have shown that acupuncture for treating AR can improve its symptoms, reduce the recurrence rate and improve the quality of life [12-14]. It has been shown that acupuncture could decrease serum IgE, IL-4 and IL-5 levels [15].

Moxibustion generally refers to burning moxa made from dried mugwort on acupoints. But herbal moxibustion here refers to applying the mixture of some specific herbs to paste on acupoints, which is a traditional treatment modality in Traditional Chinese Medicine (TCM). According to the theory of TCM, the basic pathogenesis of 'BiQiu' is mainly inadequate functioning of lung 'Qi', often accompanied by the 'Qi' insufficiency of spleen and kidney. Therefore, the general treatment principle for 'BiQiu' is regulating the function of lung 'Qi', unblocking the meridians and replenishing the 'Qi' of spleen and kidney. Because herbal moxibustion used herbs with properties of warming Yang and stimulating meridians, the channel of 'Qi' flowing inside body, they may exert the treatment effect similar to moxibustion. Such an effect of herbal moxibustion can complement acupuncture, and therefore improve the clinical effectiveness. Studies demonstrated that herbal moxibustion may improve general health, social life and vitality in quality of life [16].

The recently published systematic reviews on the effect of treating AR with acupuncture and herbal moxibustion have also demonstrated that these two methods may have promising treatment effect for AR [17-19]. However, the ratings on the quality of clinical studies were generally low. Some limitations with previous studies include inappropriate sample size, inappropriate outcome assessment measures, a lack of information on random allocation and blinding, and a lack of the standardization of acupuncture treatment procedure, etc [20-22].

To establish the reliable evidence about the effect of acupuncture or herbal moxibustion for AR, we propose to conduct a scientific-rigorous randomized controlled trial to assess the clinical effect

of acupuncture or herbal moxibustion on treating the AR symptoms, namely 'BiQiu' in TCM.

Methods

Aims and hypotheses

The primary aim is to determine the clinical effectiveness of either acupuncture combined with herbal moxibustion or acupuncture alone when compared to waiting list for patients with AR symptoms, measured by the improvement of nasal condition, quality of life, and serum IgE level. The secondary aim is to compare the clinical effectiveness of acupuncture combined with herbal moxibustion to acupuncture alone.

This study is designed to test three hypotheses: (1) Acupuncture combined with herbal moxibustion is clinically effective on treating AR symptoms compared to waiting list; (2) Acupuncture is clinically effective on treating AR symptoms compared to waiting list; (3) Acupuncture combined with herbal moxibustion is more clinically effectively than acupuncture alone on the treatment of AR symptoms.

Design

This study is a prospective, single-centre, three-arm, assessor blinded, randomized controlled trial. The trial participants with AR symptoms will be assigned randomly to the acupuncture and moxibustion group, the acupuncture group and waiting list group according to the ratio of 1:1:1. This trial will follow the Declaration of Helsinki Good Clinical Practice guidelines for trial conduct.

Trial participant

Participant recruitment: From November 2016 to July 2017, an open recruitment for eligible subjects will be carried out by the Nethersole Chinese Medicine Service cum the Chinese University of Hong Kong Chinese Medicine Clinical Training and Research Centre. Promotional flyers will be posted in the United Christian Hospital and Alice HoMiu Ling Nethersole Hospital. The relevant information will also be publicized in newspaper advertisements, electronic direct mail, and the face book of United Christian Nethersole Community Health Service etc. The written informed consent form should be obtained from the subjects before they enter the trial.

Inclusion criteria: Based on the clinical diagnosis of AR in Western medicine, subjects were included upon meeting the following criteria [23]:

- **Medical history:** The subject has a history of AR, which is related to change in temperature and allergens such as pollen, dust mites, etc.,
- **Clinical symptoms:** The subject has the primary symptoms of nasal congestion, runny nose, sneezing and nasal itchiness. Subjects must have two or more of these symptoms
- Aged between 18 - 65
- A Total Nasal Symptom Score (TNSS) \geq 4
- The subject agrees to take part in this study and is fully capacitated, can express personal will and accurately describe symptoms

Exclusion criteria: The subjects will be excluded when they meet one of the following criteria:

- Has undertaken Chinese medicine treatment related to AR over the past month
- Has contracted respiratory infection or acute paranasal sinusitis within the past 14 days
- Has a history of chronic paranasal sinusitis
- Has organic nasal pathological changes or has had nasal surgeries
- Has asthma and other respiratory attack conditions
- Has taken antihistamines, steroids, decongestants (used on the nose, the mouth and the eyes), antibiotics, anti-coagulant and anti-platelet agents in the past month
- Has undertaken specific immune treatment or systemic hormone therapy in the past year
- Has serious cardiac, liver, renal, cerebrovascular conditions, or neural or mental disorders, etc.,
- Pregnant or nursing, or planning to conceive during the course of treatment
- Has Glucose-6-Phosphate Dehydrogenase Deficiency (G6PDD)
- Has wounds at the punctured locations or diabetes mellitus

Randomization and Blinding

The eligible participants will be randomly allocated to one of the three groups, the combination of acupuncture and herbal moxibustion, the acupuncture and the waiting list group, in a 1:1:1 ratio. A randomization list will be generated using computer program (Random Allocation Software Version 1) [24]. Then, grouping cards written with serial number and allocated group will be made. The card will be put into a sealed opaque envelop, which is prepared with serial number on the envelope.

After being evaluated against the inclusion and exclusion criteria, the eligible participant will be asked to sign an informed consent form, and thereafter allocated with a serial number. The envelope with corresponding serial number will be given to the Chinese medicine practitioner. The Chinese medicine practitioner will provide treatment protocols as indicated on the card inside the envelope. The individual treatment protocols will be blinded to the data collector.

Interventions

Acupuncture treatment

The basic pathogenesis of 'BiQiu' is inadequate functioning of lung 'Qi' caused by external or internal pathogenic factors, often accompanied by the 'Qi' insufficiency of spleen and kidney. Therefore, the general treatment principle for 'BiQiu' is regulating the function of lung 'Qi', unblocking the meridians and replenishing the 'Qi' of spleen and kidney. In the fixed acupuncture treatment regimen, LI20 (Yingxiang), GB20 (Fengchi) and EX-HN3 (Yintang) can regulate the function of lung 'Qi' and unblocking the meridians; LI4 (Hegu) and ST36 (Zusanli) can replenish the 'Qi' of spleen. Because herbal moxibustion used herbs with properties of warming effect and also could stimulate meridians, the channel of 'Qi' flowing inside the body, they may exert the treatment effect similar to moxibustion. Such warming effect of herbal moxibustion can complement acupuncture, and therefore improve further the clinical treatment effectiveness.

The following acupuncture points are used for the treatment of 'BiQiu' (AR symptoms): bilateral LI20 (Yingxiang), GB20 (Fengchi), LI4 (Hegu), ST36 (Zusanli) and EX-HN3 (Yintang) (Table 1).

Acupoints	Location
Yingxiang (LI20)	At the midpoint laterals to the border of the ala nasi, in the nasolabial groove.
Fengchi (GB20)	Below the occiput, approximately midway between Fengfu (DU16) and Wangu (GB12), in the hollow between the origins of the sternomastoid and trapezius muscles.
Hegu (LI4)	On the dorsum of the hand, between the 1st and 2nd metacarpal bones, in the middle of the 2nd metacarpal bone on the radial side.
Zusanli (ST36)	Below the knee, 3 cun inferior to Dubi(ST35), one fingerbreadth lateral to the anterior crest of the tibia.
Yintang(EX-HN3)	At the forehead, at the midpoint between the two medial ends of the eyebrow.
Dazhui (GV14)	On the midline at the base of the neck, in the depression below the spinous process of the seventh cervical vertebra.
Feishu (BL13)	On the back, 1.5 cun lateral to the lower border of the spinous process of the 3rd thoracic vertebra.
Shenshu (BL23)	On the back, 1.5 cun lateral to the lower border of the spinous process of the 2nd lumbar vertebra.

Table 1: Summary of the acupoints' location.

'Hua Tuo brand' disposable sterile acupuncture filiform needles of the 0.25x25mm or 0.25x40mm specification will be used. After all sites of acupuncture points are carefully sterilised with 75% alcohol pad, the needles are inserted using the lifting-thrusting and twirling-rotating techniques, until 'deqi' (arrival of 'Qi') sensation is achieved at all acupuncture points. In Chinese medicine, Deqi means the acupuncture needle are modulating the movement of qi along the meridian. It can be felt by the person receiving acupuncture through perception of a complex sensations including heaviness, numbness, soreness, or distension (with The acupuncture practitioner can feel deqi through the feeling of tenseness around the needle. The needle stays inserted for 20 minutes for each session. The acupuncture treatment will be conducted 3 times per week for continuous 4 weeks. There is a total of 12 acupuncture treatment sessions during one month.

Herbal moxibustion treatment

For herbal moxibustion, 'Tianjiu' No.1 (for external use) designed by the Hong Kong Hospital Authority Chinese Medicine Service Department will be used. It will be pasted on the following acupuncture points: GV14 (Dazhui), BL13 (Feishu) and BL23 (Shenshu).

For preparation of the pasted herbal medicines, 240 ml of ginger juice and 200 g of powdered medicine ('Tianjiu' No.1) are mixed into a paste and cut into circular pellets weighing 2-3 g each; these will have a surface area with a diameter of 10mm and about 4-5 mm thick. A 4 cm x 4 cm plaster will be used to fix the medicine onto the abovementioned acupuncture points. After the medicine is patched, the skin will experience mild itchiness and a burning sensation. The patch should not be taken away until 1 hour later, and it will be applied once a week for 4 weeks during the study. Notes on caring for the medicine application areas will be given to the patients.

Every 200 g of powdered medicine ('Tianjiu' No.1) contains *Sinapis semen* (Jiezi) 44.4g; *Corydalis rhizome* (treated Yanhusuo) 22.2g; *Kansui radix* (treated Gansui) 22.2g; *Asarum sieboldii miq* (Xixin) 22.2g; *Ephedrae herba* (Mahuang) 22.2g; *Aconm lateralis radix praeparata* (treated Fuzi) 22.2g; *Cinnamomi cortex* (Rougui) 22.2g; *Caryophylli flos* (Dingxiang) 22.2g.

Health advice

An information sheet on the advised lifestyle, exercise, diet and warnings to avoid possible allergens will be given to the patients. And some explanations may be told face to face.

Intervention assignment

The patients in the acupuncture and herbal moxibustion treatment group will receive the abovementioned acupuncture first, then the herbal moxibustion treatment and health advice during the study. The patients in the acupuncture treatment group will receive the abovementioned acupuncture treatment and health advice. And the patients in the waiting list group will receive only the health advice.

Follow-up visit

Follow-up visits will be conducted for all the patients within one month upon completion of treatment. No treatment targeting 'BiQiu' will be provided during the follow-up visit period.

Outcome Measures

Primary outcome

Total Nasal Symptom Score (TNSS), which is the sum of individual scores for each symptom evaluated by patients [25]. The symptoms include nasal congestion, runny nose, nasal itching and sneezing. Each symptom is to be ranked on a scale of five, according to their level of seriousness, i.e., no symptoms (0), mild (1), moderate (2), heavy (3) and severe (4).

Secondary outcomes

(1) The Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ), which has 28 questions in 7 domains (activity limitation, sleep problems, nose symptoms, eye symptoms, non-nose/eye symptoms, practical problems and emotional function) [26]. Each symptom is to be ranked on a scale of seven, according to their level of seriousness, i.e., not impaired at all (0), almost not impaired (1), slightly impaired (2), moderately impaired (3), quite impaired (4), very impaired (5) and extremely impaired (6). (2) Total IgE in serum (kIU/L). This test will be conducted in the United Christian Nethersole Community Health Service Pathology Laboratory.

All the outcome measurement will be collected before the initiation of treatment, four weeks after treatment beginning and one month after the end of treatment.

The demographic data of subjects, such as age, gender, type's classification of AR and medical history, etc., will be collected at baseline.

Adverse events will be assessed by the registered Chinese medicine practitioner after each treatment, who will examine any possible adverse conditions such as pain, haemorrhage, needle faintness, needle sticking, etc. The redness, heatedness, itchiness, pain or even blisters appearing on the skin after herbal moxibustion will also be recorded. The occurrence and severity of adverse events, the time and handling method, etc., will be noted down in the adverse events (reaction) report (Table 2).

Statistical Analysis

Analysis will be on an intention-to-treat basis. Descriptive statistics will be computed for each of the analysed variables. We will use

analysis of covariance to assess whether clinical differences, if any, are significant. Some baseline measures, including age and medical history, will be used as the covariates. A priori subgroup analyses will be conducted to compare those patients with medical history of AR less than two years to those more than two years. All statistical tests will be two sided, and $p < 0.05$ is considered statistically significant. The statistical software of SPSS 17.0 will be used for analysis.

	Baseline	Treatment phase (weeks)				Follow-up phase (weeks)
		W1	W2	W3	W4	W8
Demographic data	X					
Sign informed consent	X					
Randomisation		X				
TNSS	X				X	X
RQLQ	X				X	X
Total IgE	X				X	X
AEs		X	X	X	X	

Table 2: Time of data collection.

TNSS: Total Nasal Symptom Score; RQL: Rhinoconjunctivitis Quality Of Life Questionnaire; Total IgE: Total Mmunoglobulin E; AEs: Adverse Events; W: Week.

Sampling Size Calculation

Based on a previous study, we presume that the standard deviation of TNSS is 3.6, and the mean difference of TNSS score between the acupuncture group and the waiting list group is 1.8 [27]. We firstly calculated a sample size (N) for an independent t test using the assumed SD and the difference in TNSS mean change between two groups with a power of 80% and 5% false positive errors. The software of PASS was used for the calculation. The Pearson correlation coefficient (R) is estimated as 0.76 based on a previous study [28]. Eventually, we compute with $(1-R^2)$ times N and come up with the sample size required by ANCOVA using a simple formula proposed by George F Borm, and each group needs 27 cases [29]. We estimate that the withdrawal rate could reach 20%, and decide that the required total sample size is 96 (32 in each group).

Termination or Discontinuation Criteria

- The subject takes prohibited drugs (antihistamines, steroids, decongestants, antibiotics, anti-coagulant and anti-platelet agents) or undertakes other therapies that could affect the results of the trial
- The subject has sudden or serious complications over the course of treatment
- The subject runs into serious adverse events or allergic reactions or requests to discontinue with the trial because of adverse events; or that a trial operator considers it necessary to terminate the trial because of adverse events
- The subject has low compliance and fails to execute as required, or fails to persist with the treatment and requests to be withdrawn
- The timely treatment become necessary because the rhinitis worsens; or the subject is considered unsuitable to continue with the trial according to the judgement of the research investigator

Although the patients in the waiting list group are encouraged to not undertake other therapies throughout the trial, in the situation

when these patients feel they cannot tolerate the symptoms, for ethical reason, they are allowed to take drugs. All patients will be monitored throughout the trial and the protocol will follow an intention-to-treat approach. However, from our previous observations in the clinic, patients with AR may feel troubled by the symptoms but they are capable of tolerating it. Most of these patients have suffered AR for a long time and show exceptional tolerance to AR symptoms. The registered TCM practitioner will ask the subject if she or he has ever taken any prohibited drugs or received other therapies during each treatment (3 times per week) and record it. If yes, the patient will be dropped out, but we will continue to collect the pre-specified outcome data. The reasons for discontinuance will be recorded. The impact on the overall study will be considered and noted in the study report.

Quality Control

- Two registered Chinese medicine practitioners will be responsible for the treatment work. All registered Chinese medicine practitioners have ever received five years undergraduate education in Chinese medicine and over two years experience of acupuncture treatment. They will be trained on the process of research and the manipulation of acupuncture and herbal moxibustion treatment so as to ensure the consistency of the treatment. All the treatments will be conducted by Hong Kong's registered Chinese medicine practitioner
- Assessor-blinding is strictly implemented. The designated investigator will conduct clinical rating over the assessment. During the assessment process, the assessor must be kept from knowing the treatment assignment, and the assessor will not involve any treatment during the study
- The researchers will be actively involved in pre-treatment promotion of the study intention and significance, therefore help subjects to stay with the study to reduce drop off cases
- All investigators who have completed good clinical practice training will independently collect the data and assess the effects of the treatments
- A remote data capture system will be used to store data on a password-protected computer that will store recorded data in a secure environment. In principle, clinical information will not be released without the permission of the principal investigator (ZHANG Hongwei), with the exception of an emergency or as necessary for monitoring and auditing by the data monitoring committee

Discussion

The Hong Kong government has established 18 Hospital Authority Tripartite Chinese Medicine Centres for Training and Research (CMCTRs). The CMCTRs aim at facilitating the development of evidence-based medicine in Chinese Medicine, providing professional Chinese Medicine consultation services, and training placements to local Chinese Medicine degree graduates. The centres are operated on a tripartite collaboration model involving the Hospital Authority (HA), a non-governmental organisation and a local university. Designed as a pragmatic randomized controlled trial, another objective of this study is to provide research experience for the further development of clinical trials of Chinese medicine conducted in CM clinics.

In Hong Kong, a predominantly urban environment, persistent AR with intermittent aggravation is the most common presentation in clinic. In Hong Kong, where the climate is warm and humid, and with crowded living conditions, it has been identified that house dust mite and cockroach were the common aetiological agents of AR [30-32].

On the other hand, in central China, the majority of AR patients had perennial AR with or without seasonal aggravation [33].

This trial is designed as patients not being blinded. Since patients of the acupuncture group and the acupuncture plus moxibustion group will receive additional therapies than the patients in the waiting list group, the effectiveness will not be necessary caused by the specific treatment effects. Although many placebo-controlled RCTs of acupuncture have demonstrated the existence of placebo effect during acupuncture treatment, the current study aimed to investigate the total clinical effectiveness of acupuncture or/with herbal moxibustion, not the specific treatment effect. The existence and magnitude of specific treatment effect of acupuncture or herbal moxibustion are related to the acupoint selection and the technique of needling manipulation, which is not the research question in this study.

Total IgE reflects the allergenic response in human body. From previous mechanism study, it is known that acupuncture and herbal moxibustion may adjust the immune function of the human body so as to lower the total IgE level [34,35]. Total IgE test is used to provide an objective indicator besides those subjective assessments.

All subjects will receive health education on lifestyle, encouragement to carry out proper physical activities, adequate sleep, refrain from cold food and avoid contacting allergens, which is a part of ordinary TCM clinical practice. From the view of Chinese medicine, the onset of 'BiQiu' is highly related to lifestyle, which would affect the treatment efficacy if the modification of living style is neglected. So, the Chinese medicine practitioner always makes advices on healthy lifestyle in order to facilitate the treatment. In addition, it would foster the compliance of the participants in the waiting list. The health education in this study is common advice given to patients by Chinese medicine doctors in the clinic. Some general allergens encountered in everyday living, such as those from dusty living environment, contact with cats or dogs, etc., can be delineated from everyday habit and via health education patients may improve their conditions by adjusting their life style accordingly. Although some patients may have eliminated or reduced their symptoms without acupuncture and/or moxibustion treatments, the fluctuation of symptoms in these patients will not pose bias to the study since patients will be properly randomized into the three study groups. The symptoms may be influenced after patients follow health education. But such fluctuation of symptoms is generally in a balanced distribution among three groups after randomization.

Competing Interests

The authors declare that they have no competing interests.

Ethics Approval and Consent to Participate

Written consent will be obtained from each participant. This study was approved by all relevant local ethics review boards: Joint Chinese University of Hong Kong-New Territories East Cluster Clinical Research Ethics Committee Faculty of Medicine The Chinese University of Hong Kong Prince of Wales Hospital on November 2, 2016 (CREC Ref. No.: 2016.452). This trial will follow the Declaration of Helsinki Good Clinical Practice guidelines for trial conduct.

Authors' Contributions

All authors have participated extensively in the design of the study and will perform the clinical trial. Dr. Zhang Hong Wei, Mr. Yung Ting Yiu, Ms. Chen Heng Chun, Mr. Chan Chun Wai and Ms. Lee

Man Hork have drafted the manuscript. Dr. Zhang Hong Wei, Dr. ZIEA Tat Chi, Dr. NG Fung Leung, Dr. Lin ZhiXiu, Mr. Zhang Lang, Mr. Tang Lap Che, Mr. Yung Ting Yiu, Mr. Tam Wai Man and Mr. Law Chak On will supervise and coordinate the clinical trial. Mr. Law Chak On is responsible for recruiting the subjects. Dr. Zhang Hong Wei, Mr. Zhang Lang and Mr. Yung Ting Yiu have given critical review and advice on the manuscript. Mr. Tam Wai Man is responsible for the management of herbal moxibustion drugs. Mr. Chan Chun Wai will participate in assessing the subjects. Ms. Lee Man Hork and Ms. Chen Heng Chun will participate in treating the subjects. Dr. Zhang Hong Wei and Mr. Yung Ting Yiu will participate in randomization and statistical analysis. All authors will proofread the approved final manuscript.

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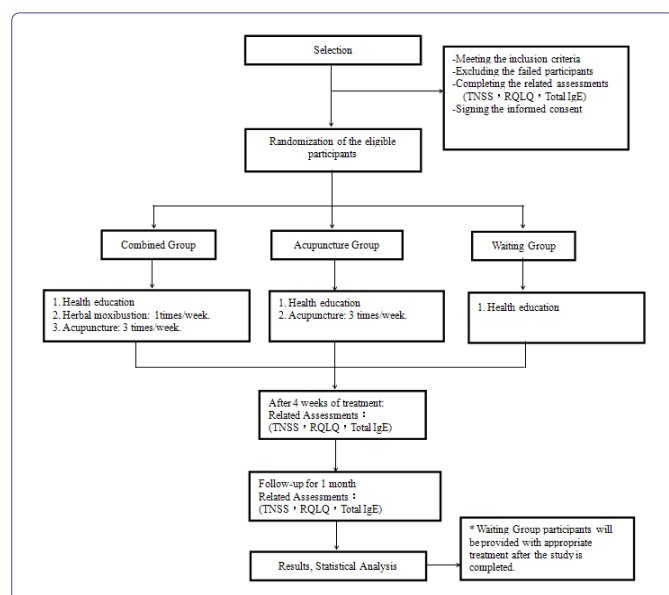
Availability of Data and Materials

The datasets used and/or analyzed during the current study will be available from the corresponding author on reasonable request after study completion.

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Chart of Study Flow



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