

BMJ Open Acupuncture for adults with overactive bladder: a systematic review protocol

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ABSTRACT

Introduction: Overactive bladder (OAB) is a symptom syndrome defined by the International Continence Society (ICS) as 'the presence of urinary urgency (both daytime and nighttime), usually accompanied by increased frequency and nocturia with or without urge urinary incontinence in the absence of a urinary tract infection or other obvious pathology'. Clinical studies indicate that acupuncture could reduce micturition over 24 h, urgency episodes over 24 h, and improve quality of life among people with OAB. This systematic review protocol details the proposed methods for evaluating the effectiveness and safety of acupuncture for OAB.

Methods and analysis: The following databases will be searched for relevant studies: the Cochrane Central Register of Controlled Trials (CENTRAL), the Cochrane Incontinence Group Trials Register, MEDLINE, EMBASE, Chinese Biomedical Literature Database (CBM), Chinese Medical Current Content (CMCC), Chinese Scientific Journal Database (VIP database), Wan-Fang Data, and China National Knowledge Infrastructure (CNKI) and will hand search a list of medical journals as a supplement. Any randomised controlled trials in English or Chinese without restriction of publication status will be included with treatment of OAB. Outcomes will mainly include number of micturition episodes over 24 h, number of urgency episodes over 24 h and number of incontinence episodes over 24 h. Two reviewers will independently screen the titles, abstracts or even full texts, and extract data. Two other reviewers will assess study quality. Revman 5.1 software will be used to conduct meta-analysis and calculate the risk ratio for dichotomous data. Weighted mean difference or standard mean difference will be calculated for continuous data. The Cochrane collaboration's tool will be used to assess the risk of bias.

Dissemination: This systematic review protocol will provide information on acupuncture therapy for OAB. The results will be disseminated through peer-reviewed publication or conference presentations.

Protocol registration: PROSPERO
CRD42014010181.

INTRODUCTION

Description of the condition

Overactive bladder (OAB) is a symptom syndrome defined by the International

Continence Society (ICS) as 'the presence of urinary urgency (both daytime and nighttime), usually accompanied by increased frequency and nocturia with or without urge urinary incontinence in the absence of a urinary tract infection or other obvious pathology'.^{1,2} OAB has a serious impact on the quality of life of patients.^{3,4} It can cause anxiety and depression, and it influences patients' social interactions and sexual function.³⁻⁶

Description of the intervention

Acupuncture is a branch of traditional Chinese medicine (TCM) that encompasses many methods, such as body acupuncture, scalp acupuncture, auricular acupuncture, warm needling, fire needling and elongated needling. Acupuncture has been used to treat urinary incontinence since ancient times in China. The HuangdiNeijing (The Yellow Emperor's Canon of Medicine) says 'For needling, the reinforcing methods should be used for urinary incontinence and the reducing method for urinary retention'.⁷

How the intervention might work

Acupuncture works by stimulating points with needles. In TCM theory, acupuncture is thought to regulate qi circulation. For OAB, needling at points on the kidney or bladder meridians could reinforce qi and promote the recovery of bladder function.^{8,9} In Western medicine, the mechanism of acupuncture is as yet unknown.

Why it is important to perform this review

The American Urological Association (AUA) recommends a three-line therapy for OAB.³ The first-line therapy is behavioural therapy, such as delayed voiding bladder training, pelvic floor muscle training, lifestyle modifications and management of fluid intake. These therapies are suitable for all OAB patients; however, patients need to invest much time and effort to achieve good effects.¹⁰⁻¹² The second line of therapy is

oral anticholinergic drugs such as tolterodine, solifenacin and oxybutynin. Although drug therapy is non-invasive, side effects such as dry mouth, constipation, headache and vision abnormality may affect quality of life.^{12–15} The third line of therapy refers to neural regulation such as sacral nerve stimulation; however, this treatment is limited because it is invasive and can cause adverse reactions such as infection.^{3 16}

Acupuncture is an alternative therapy for OAB; it is minimally invasive and causes few side effects.^{17–20} Several clinical studies have shown that acupuncture could reduce micturition over 24 h, urgency episodes over 24 h, and improve quality of life.^{21–25} Two systematic reviews have also been found on acupuncture for urinary incontinence and stress urinary incontinence.^{8 9} Both reviews reported favourable effects of acupuncture on symptoms, but neither of them determined its effect for insufficient evidence. No systematic review has been found about acupuncture for OAB; it is therefore important to establish whether acupuncture is a good choice for OAB patients who do not want surgery, and whether it is as effective as other therapies.

The objective of this proposed systematic review is to determine the effectiveness and safety of acupuncture for OAB in adults. The following comparisons will be addressed:

1. Acupuncture versus placebo or no treatment.
2. Acupuncture versus any other treatment.

METHODS

Criteria for included studies

Type of studies

Randomised controlled trials (RCTs) in English or Chinese will be included without restriction of publication type. Quasi-RCTs will be excluded as they are not truly randomised, and there is a greater risk of selection bias in trials in which allocation is not adequately concealed.

Type of participants

Participants of any race or gender with a diagnosis of OAB (according to the definition of the ICS and the guidelines of the AUA³) will be included. Participants must be at least 18 years old.

Type of interventions

The following acupuncture methods will be included: body acupuncture, electro-acupuncture, scalp acupuncture, warm acupuncture, elongated needling, and auricular acupuncture. The control interventions of included studies may include placebo, sham acupuncture (minimal, non-point), waiting list, no treatment, and any active treatment³ (ie, bladder retraining, pharmacological therapies, neurologic stimulation, surgery).

Laser acupuncture, dry needling, cupping and acupressure will be excluded. Laser acupuncture and dry

needling are not routine or traditional acupuncture methods, and cupping and acupressure are different therapies from acupuncture in TCM.⁹ Studies with the following comparisons will also be excluded:

1. Acupuncture plus another therapy versus the same other therapy plus drug therapy
2. Acupuncture plus a therapy versus another different therapy
3. One kind of acupuncture versus another kind of acupuncture

Studies comparing acupuncture plus a therapy versus the same therapy will be included.

Type of outcome measures

Primary outcomes

1. Number of micturition episodes over 24 h
2. Number of urgency episodes over 24 h
3. Number of incontinence episodes over 24 h

Secondary outcomes:

1. Pads used over 24 h
2. Number of nocturnal awakenings related to OAB over 24 h
3. Maximum cystometric capacity (mL)
4. Quality of life (quality of life assessment using any of the available validated instruments, such as Distress Inventory (UDI-6), the Incontinence Impact Questionnaire (IIQ-7),²⁶ OAB Questionnaire (OAB-q)²⁷ and the Incontinence Quality of Life Scales (IQOL)²⁸)
5. Safety (measured by incidence and severity of adverse effects)

Search methods for the identification of studies

A search strategy will be designed and conducted according to the Cochrane handbook guidelines.²⁹

Electronic searches

We will search the following databases from inception to July 2014:

1. The Cochrane Incontinence Group Trials Register
2. MEDLINE
3. EMBASE
4. The Cochrane Central Register of Controlled Trials (CENTRAL)
5. Chinese Biomedical Literature Database (CBM)
6. Chinese Medical Current Content (CMCC)
7. China National Knowledge Infrastructure (CNKI)
8. Wan-Fang Data
9. Chinese Scientific Journal Database (VIP)

Table 1 presents the full list of search terms to be used.

Searching other resources

The following medical journals published out of the time span of the databases will be manually searched in libraries: *Acupuncture Research* (1976–July 1998), *Chinese Acupuncture and Moxibustion* (1981–July 1998), *Journal of Clinical Acupuncture and Moxibustion* (1985–July 1998) and *Shanghai Journal of Acupuncture and Moxibustion* (1982–July 1998).

Table 1 Ovid MEDLINE search strategy

N	Search items
1	randomized controlled trial.pt.
2	controlled clinical trial.pt.
3	randomized.ab.
4	randomly.ab.
5	placebo.ab.
6	drug therapy.fs.
7	trial.ab.
8	groups.ab.
9	or/1–8.
10	exp animals/ not humans.sh.
11	9 not 10
12	exp acupuncture therapy.
13	acupuncture.mp.
14	acupressure.tw.
15	(acupoint or electroacupuncture or electro-acupuncture).mp.
16	elongated needle.mp.
17	warming needle.
18	auricular acupuncture.
19	or/12–18.
20	OAB.tw.
21	(overactive bladder or overactive bladder syndrome or bladder overactive or urge inconvenience or overactive detrusor or urinary bladder, overactive or detrusor overactivity, bladder instability, detrusor instability).tw.
22	or/20–21
23	11 and 19 and 22

This search strategy will be suitable for other electronic databases.

In addition, for studies without the full text, we will try to contact the authors for the full text.

Data collection and analysis

Selection of studies

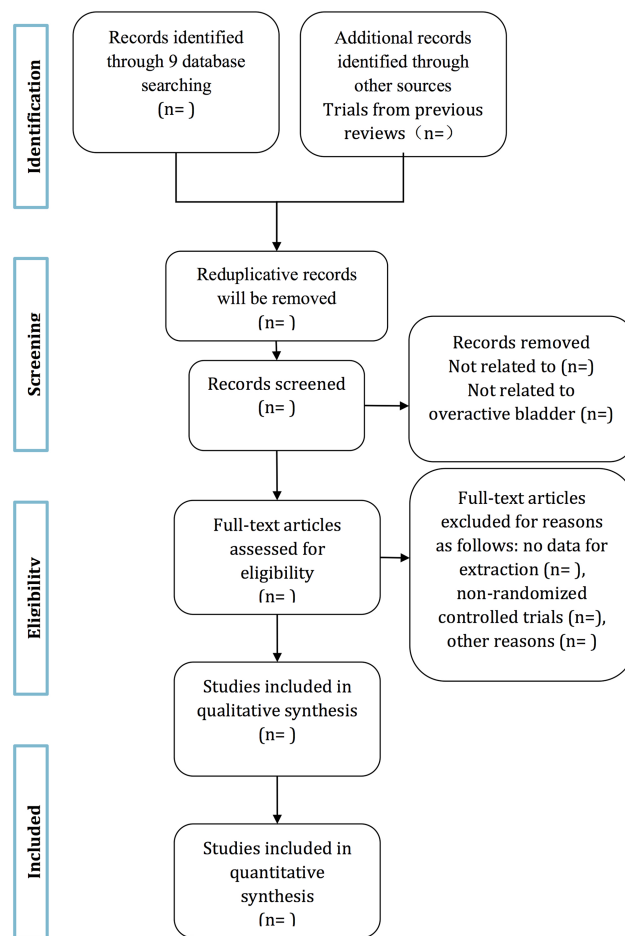
Two reviewers (QM and YW) will screen the studies at the same time independently. If any disagreement occurs, a decision will be made through discussion or consultation with a third author (ZL). Details of the study selection procedure are shown in [figure 1](#). Excluded studies will be listed in a table with reasons.

Data extraction

Before data extraction, a standard form containing specified outcomes will be created after discussion among all reviewers. Two reviewers (QM and YW) will extract data independently using this standard form. When data in included studies have been collected but not reported, reviewers will seek clarification from the author. If the reviewers have different opinions, the issue will be resolved through discussion or consultation with a third author (ZL).

Risk of bias assessment

The reviewers will independently assess six domains of bias (sequence generation, allocation concealment,

**Figure 1** Process of the systematic review.

blinding or masks, incomplete data assessment, selective outcome reporting, and other sources of bias).²⁹ The studies will then be classified into three levels of bias: low, unclear, and high risk of bias. Differences in opinion will be resolved by discussion or consultation with a third author (ZL).

Measures of treatment effect

Analysis will be based on available data of included studies. For dichotomous data, the risk ratio (RR) will be calculated with 95% CI. For continuous variables, we will use means and SDs to calculate a mean difference (MD) with 95% CI.

Unit of analysis issues

The unit of analysis is the individual participant (unit to be randomised for interventions to be compared).

Dealing with missing data

For studies with missing data, the reviewers will try to obtain the information by contacting the study investigators. If the investigators cannot be contacted, we will base our analysis on the available data.

Assessment of heterogeneity

Higgins I^2 statistics will be used to test inconsistencies among the included trials. The cut off point of I^2

statistics is 50%.²⁹ $I^2 > 50\%$ will indicate the existence of significant heterogeneity among studies.²⁹ In this case, a meta-analysis will be conducted to find the source of heterogeneity. Subgroup analysis will be conducted according to the source of heterogeneity.

Assessment of reporting biases

A funnel plot will be used to evaluate publication bias if more than 10 studies are included.

Data synthesis

Revman 5.1 software will be used to conduct meta-analysis and calculate the RR, and 95% CI for dichotomous data. Weighted mean difference (WMD) or standard mean difference (SMD) and 95% CI will be calculated for continuous data. If the same outcome measurement tool and unit was used, the WMD and 95% CI will be calculated, or otherwise the SMD and 95% CI. If the included studies have existing heterogeneity (the p value is < 0.05), the RR, WMD or SMD will be calculated by the random-effect model. Otherwise, a fixed-effect model will be used.

Subgroup analysis and investigation of heterogeneity

There is no pre-subgroup plan. If data are available, factors like acupuncture methods, existence of detrusor overactivity (DO) and sex of patients will be taken into account.

Sensitivity analysis

The sensitivity analysis will be used to assess whether the sample size and missing data impact the results of this review. If there are adequate studies (no less than three studies), we will conduct a sensitivity analysis to check the robustness of conclusions and assess the impact of methodological quality.

Ethics and dissemination

This review does not need ethical approval, as data used here are not individual or private. The results will provide a general overview and evidence of effectiveness and safety of acupuncture for OAB. They will also have implications for clinical practice and further research.

DISCUSSION

Studies have shown that acupuncture is effective for relieving the symptoms of OAB; however, its effect has not been scientifically evaluated.^{21–25} We present a protocol of a systematic review to determine the effectiveness and safety of acupuncture for OAB. The conclusions drawn from this review will benefit policy makers, patients and clinicians seeking effective and minimally invasive methods for treating OAB.

This study might have some limitations. Specifically, different forms of acupuncture therapies and qualities of methodology may cause significant heterogeneity. Because of the language barrier, only English and

Chinese medical database will be included. Hence, some relevant studies in other languages might be missed.

Contributors QM and YW contributed to the conception of the study. The manuscript of the protocol was drafted by QM and YW, and was revised by ZL. QM and YW will also independently screen the potential studies and extract data from included studies. JY and YY will assess the risk of bias, and finish data synthesis. ZL will arbitrate any disagreements and ensure that no errors occur during the review. All authors have approved the publication of the protocol.

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