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Research paper

Acupuncture for the treatment of overactive bladder: A protocol for systematic review and meta-analysis of randomized controlled trials

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ABSTRACT

Introduction: This review aims to evaluate the current evidence for the efficacy of acupuncture in the management of overactive bladder.
Methods: Fourteen databases will be searched from their inception, including PubMed, MEDLINE, AMED, EMBASE, the Cochrane Library, six Korean Medical databases (Korean Studies Information Service System, DBPIA, the Korean Institute of Science and Technology Information, the Research Information Service System, KoreaMed, and the Korean National Assembly Library), the China National Knowledge Infrastructure (CNKI), the Chongqing VIP Chinese Science and Technology Periodical (VIP), and Wanfang. Only randomized clinical trials using acupuncture with or without electrical stimulation for overactive bladder will be considered. The selection of the studies, data extraction, and assessment will be performed independently by two researchers. The risk of bias will be assessed with the Cochrane risk of bias.
Dissemination: The systematic review will be published in a peer-reviewed journal. The review will also be disseminated electronically and in print. Updates of the review will be conducted to inform and guide healthcare practice and policy.
Trial registration number: PROSPERO 2014:CRD42014010377.

1. Introduction

Overactive bladder (OAB) is a clinical diagnosis characterized by the presence of bothersome urinary symptoms including urgency, frequency, nocturia and urgency incontinence [1]. Most studies of OAB, including studies from the International Continence Society (ICS) [2] and the American Urological Association (AUA) guidelines [1], exclude individuals with symptoms related to urinary tract infections or other obvious pathology, such as neurological conditions [3]. OAB is highly prevalent, estimates in a cross-sectional population-representative survey have revealed that 10.9% and 14.6% of men and 22.5% and 33.7% of women in the UK and Sweden, respectively, experience OAB [4]. Although OAB symptoms with and without incontinence place a considerable burden on quality-of-life, quality-of-sleep, and mental health in both men and women [5], medical options (both medication and behavioral approaches) are only partially effective [6–8].

Acupuncture is defined as a method of relieving symptoms or curing illness by placing needles into the skin at particular points, known as acupoints, on the body. Needles can be stimulated electrically (electroacupuncture), and heat and moxibustion can be applied through the needle [9].

A trial of 4 weekly acupuncture sessions showed the efficacy of treatment compared with sham acupuncture in 95 female subjects with OAB [10]. Electroacupuncture at SP 6, referred to by urologists as percutaneous posterior tibial nerve stimulation (PTNS), is commonly examined for its effects on OAB [11].

A trial of electroacupuncture at SP6 has demonstrated the efficacy of this intervention compared with sham acupuncture in 220 subjects with OAB [12], Other studies suggest that acupuncture compares favorably to tolterodine [13] and is a viable long term therapy [14].

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Acupuncture is known to have analgesic [15], neuromodulation or hormonal effects [16] via peripheral and central mechanisms [9,17]. Among the possible mechanisms, acupuncture and also PTNS may act as methods of neuromodulation in controlling OAB, as evidenced by purinergic signaling in the lower urinary tract [18,19]. The mechanism of action of acupuncture induced the stimulation of neuromodulation of the bladder is not precisely understood. Mechanical stimulation seems to produce signaling via the sensory ganglia and interneurons to the spinal cord which modulates the activity of the motor neurons in the brain stem that control autonomic function, including urogenital activity, such as the detrusor and sphincter muscles. However, reliable evidence has not been found.

Current pharmacotherapy for the OAB is only partially effective with respect to efficacy, tolerability, and long-term compliance [8]. Several studies support acupuncture [10,20] and PTNS [13,14,21–23] as effective treatment options of OAB symptoms.

Several reviews of OAB or urinary incontinence have focused on acupuncture [24] or included acupuncture as one of the treatment modalities [25–27]. However, these reviews were either not systematic, out dated or did not follow the formal recommendations of a systematic review [28]. Therefore, their conclusions are unreliable. Hence, there is a great need for a systematic review of acupuncture for OAB that presents current evidence in an unbiased manner.

This review aims to systematically evaluate evidence pertaining to the efficacy of acupuncture for treating OAB from RCTs.

2. Methods

2.1. Study registration

The protocol of this systematic review has been registered on PROSPERO 2014 (registration number: CRD42014010377).

2.2. Data sources

The following databases will be searched from their inception to the current date: PubMed, MEDLINE, AMED, EMBASE, the Cochrane Library, Korean Medical Databases (Korean Studies Information Service System, DBPIA, the Korean Institute of Science and Technology Information, the Research Information Service System, KoreaMed, and the Korean National Assembly Library), the China National Knowledge Infrastructure (CNKI), the Chongqing VIP Chinese Science and Technology Periodical (VIP), and Wanfang. Articles identified through reference lists of included studies and relevant systematic reviews will be considered for inclusion based on their title. Our search strategy will include the main keywords ‘acupuncture’ and ‘overactive bladder’ (Supplements 1). Study selection will be documented and summarized in a Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) compliant flow chart (http://www.prisma-statement.org).

2.3. Eligibility criteria

2.3.1. Population

We will include populations with a diagnosis of OAB regardless of age, gender, and race. Only studies in which there are an external set of criteria will be used to screen participants for the condition (e.g., criteria from the International Urogynecological Association (IUGA)/ICS joint report on the terminology for female pelvic floor dysfunction [2], AUA [1], and the ICS [29]).

2.3.2. Interventions

Studies that evaluate any type of invasive acupuncture with or without electrical stimulation will be included. The treatments considered must involve needle insertion at acupuncture points, pain points or trigger points and must be described as acupuncture. Control interventions may include treatments such as general conventional care (drugs, exercise, education, behavioral approach, etc.), sham treatment (interventions mimicking ‘true’ acupuncture/true treatment but deviating in at least one aspect considered important by acupuncture theory, such as skin penetration or correct point location), waiting list, or no-treatment. We will exclude studies in which one form of acupuncture is compared with a different form of acupuncture. Studies investigating other methods of stimulating acupuncture points without needle insertion (e.g., acupressure, pressed studs, and laser stimulation) will be excluded.

2.3.3. Outcome measures

2.3.3.1. Primary outcomes.

- Total treatment efficacy: the number of patients whose OAB symptoms improve
- Quality of life: measured using a validated questionnaire, for example, the International Consultation on Incontinence Questionnaire (ICIQ) [30], Medical Outcomes Study Short-Form 20 [31], or the King's Health Questionnaire [32].

2.3.3.2. Secondary outcomes.

- Urinary function: change in urgency, frequency, nocturia and urgency incontinence.
- Impact of symptoms: measured by validated questionnaires, such as the Urinary incontinence questionnaire and urogenital distress inventory [33] and the psychosocial adjustment to illness scale [34].
- Change in symptoms: measured by a 100 mm Visual Analogue Scale (VAS).
- Adverse events.
- Participant withdrawal.

2.3.4. Study design

Only RCTs will be included and must clearly report randomization in their manuscript or title. Observational, cohort, case-control, case series, qualitative studies, uncontrolled trials and laboratory studies will be excluded.

2.4. Data extraction

All articles will be read by two independent reviewers who extract data from the articles according to predefined criteria. The extracted data will include the first author, year of publication, country, sample size, age and gender of the participants, acupuncture intervention, control intervention, main outcomes and adverse effects. The extracted data will be tabulated (Supplement 2) for future analysis. Details regarding the acupuncture and control interventions will be extracted on the basis of the revised Standards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA) [35] (Supplement 3).

2.5. Risk of bias assessment

Quality assessment will be performed using the tool for ‘risk of bias’ assessment from the Cochrane Handbook for Systematic

reviews of Interventions (Supplement 4) [36]. The following characteristics will be assessed: (1) random sequence generation (2) allocation concealment (3) blinding of participants and personnel (4) blinding of outcome assessment (5) incomplete outcome data (6) selective outcome reporting and (7) other sources of bias (we will evaluate baseline imbalance). This review will use 'L, U and H' as a key for these judgments, where 'Low' (L) indicates a low risk of bias, 'Unclear' (U) indicates that the risk of bias is uncertain, and 'High' (H) indicates a high risk of bias. Disagreements will be resolved by discussion among all authors. The risk of bias assessment for included studies will be summarized in a table, and the results and implications will be critically discussed.

2.6. Data synthesis

All statistical analyses will be conducted using the Cochrane Collaboration's software program, Review Manager (RevMan), V.5.3 for Windows (Copenhagen, The Nordic Cochrane Center). Differences between the intervention and control groups will be assessed. In the analysis of clinical efficacy, categorical data will be assessed in terms of risk ratio (RR), and continuous data will be assessed in terms of standardized mean difference (SMD) for considering the consistency. Categorical and continuous variables will be expressed as efficacy values with 95% confidence intervals (CIs). If the meta-analyses exhibit heterogeneity (defined as results of tests of heterogeneity that indicate a value of $p < 0.1$ by chi square test and Higgins $I^2 \geq 50\%$), subgroup analyses will be explored to determine the cause of clinical heterogeneity. A random effects model will be used to assess combined effect size from efficacy variables because clinical heterogeneity is highly expected across the included studies from the diversity of interventions, study design, and other conditions. Publication bias will be assed using funnel plots and Egger's regression method [37]. If missing data are detected, we will request any missing or incomplete information from the original study investigators. Subgroup analyses will be conducted according to different control interventions (sham acupuncture *vs* conventional medication), the type of acupuncture (Asian *vs* Western or PTNS), type of stimulation (manual *vs* electric), acupuncture points (one or two points *vs* multiple points), the design of the trial (acupuncture *vs* sham acupuncture; acupuncture *vs* conventional medication; and acupuncture combined with conventional medication *vs* conventional medication) and country where the study conducted (Asian *vs* Western). Where appropriate, a sensitivity analysis will be performed to evaluate the robustness of the meta-analysis results. To determine consistency with other meta-analyses and meta-regressions, the primary quality measure will be a binary measure of allocation concealment [38].

3. Dissemination

To date, one systematic review of urinary incontinence has been published [24]. The authors concluded that results supporting acupuncture as an effective treatment for urinary incontinence in the 4 databases searched were limited. Our systematic review will update and provide a detailed summary of the current evidence related to the efficacy of acupuncture in treating the symptoms of patients with OAB. This evidence will be useful to practitioners, patients and health policy-makers regarding the use of acupuncture in OAB treatment.

Conflict of interest statement

The authors declare that they have no potential conflict of interest.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.eujim.2016.08.161.

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