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RESEARCH ARTICLE

Efficacy of non-pharmacological interventions in patients with overactive bladder: A protocol for systematic review and network meta-analysis

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Abstract

Background: Some meta-analyses have proved the superiority of non-pharmacological interventions in overactive bladder (OAB), but the best choice is still controversial.

Aim: To assess the most effective interventions in female with OAB.

Methods: Studies for relevant randomized controlled trials which compare different kinds of non-pharmacological interventions in females with OAB will be retrieved from 8 databases including PubMed, Cochrane Library, Web of Science, Embase, China National Knowledge Infrastructure, Wanfang Database, VIP Database and China Biology Medicine disc, from inception to 1 January 2021. After screening titles and abstracts, detailed data including participates, interventions and outcomes will be extracted according to the eligible criteria. Then, Cochrane risk-of-bias tool will be used to assess the quality of the literature. The pairwise meta-analysis will be conducted by STATA. Network meta-analysis will be performed to compare and rank the effects of different non-pharmacological interventions, in terms of alleviation of symptoms, by OpenBUGS, R and STATA.

Results: This network meta-analysis will present the best available evidence about non-pharmacological interventions for OAB to both relieve symptoms and improve life quality.

KEYWORDS

female, network meta-analysis, nursing, overactive bladder

Hong Zhou and Wenzhen Chen are the co-first author.

Systematic review registration: INPLASY202110016

1 | INTRODUCTION

Overactive bladder (OAB) is a common chronic urological disorder characterized by urinary urgency, frequency and nocturia, with or without urge urinary incontinence (Shaw & Wagg, 2020). Besides, patients suffering OAB are liable to bother sleep, impact normal social activities and decrease sexuality and impair self-esteem, which extremely exacerbates the quality of life (Brucker et al., 2020). Though the overall prevalence and aetiologies of OAB are similar in males and females (Corcos et al., 2017; Peyronnet et al., 2019; Zhu et al., 2019), there are still specific differences in the two genders. First, females are more likely to be bothered by urinary incontinence while males usually suffer from frequent micturition (Eapen & Radomski, 2016). Second, body mass index is a risk factor of females whereas prostate problems are common aetiologies of males (Eapen & Radomski, 2016). Third, females tend to consult doctors than males; thus, from the analyses, costs for females were almost five times for males (Reynolds et al., 2016). Overall, it is necessary to make a separate analysis of female patients with OAB.

Given the bothersome symptoms, high prevalence and huge cost of OAB in females, it is of great importance to find effective methods for OAB. Several clinical interventions have been used to alleviate the symptoms of OAB including non-pharmacological interventions (first- and third-line therapies), medication management (second-line therapy) and surgery (Corcos et al., 2017; Lightner et al., 2019). However, medication management has a sequence of adverse reactions, which are dry mouth, headache, constipation and vision irregularity that caused limited compliance (Kim & Lee, 2016). Surgical therapies are invasive, involving risks and complications. Due to the concern about the side effects of medicine and complications of the surgery (Kim et al., 2017; Liedl et al., 2017), multiple non-pharmacological interventions are receiving extensive attention as a vital part of treating OAB. Several meta-analyses have been conducted to compare the effectiveness and safety of non-pharmacological strategies on the symptoms of OAB, including bladder training (Cao et al., 2016), acupuncture (Mak et al., 2019), electric stimulation (Booth et al., 2018; Fernandez et al., 2017; Wang et al., 2020) and behavioural therapy (La Rosa et al., 2020). Up to our knowledge, there is only one study that showed the combination is the most effective treatment (Firinci et al., 2020). Thus, the best non-pharmacological treatment for OAB is still elusive, but we assume clinically that bladder training may well be the best as the first-line recommendation (Corcos et al., 2017).

Based on these grounds, to present the remarkable proof for OAB in females, a network meta-analysis should be conducted to summarize the evidence of various non-pharmacological treatments, which allows the estimation of the relative effectiveness and rank ordering of the interventions.

2 | METHODS

2.1 | Registration

The protocol was registered in the International Platform of Registered Systematic Review and Meta-analysis Protocols (INPLASY202110016) and designed by the recommendation of the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) (Moher et al. 2015). Ethics approval and consent do not apply to this study as there are no patients involved.

2.2 | Eligibility criteria

Type of studies. Only peer-reviewed randomized controlled trials (RCTs) will be included. The language will be restricted to English or Chinese.

Type of participants. The population of interest is females, aged 18 and older, with a diagnosis of primary OAB. Secondary OAB does not meet the inclusion. Additionally, because the diagnosis of urinary system diseases are not based on a single symptom, people associated with urinary incontinence, frequency of urinary and other symptoms will be taken into consideration (Homma et al., 2011). However, urinary tract infection or other obvious pathology ought to be excluded, in which circumstances anti-infective treatment is the priority.

Type of interventions and comparators. The systematic review will concentrate on studies with non-pharmacological interventions. Interventions will include but not limited to these: lifestyle modification (e.g. fluid intake, smoking cessation, weight loss), nerve stimulation (e.g. posterior tibial nerve stimulation, transcutaneous sacral, transvaginal stimulations, transcutaneous electrical nerve stimulation), acupuncture therapy (e.g. manual acupuncture, electroacupuncture, moxibustion, acupressure) and behavioural therapy (e.g. pelvic floor muscle training, bladder training). The types of the control group will include usual care, medication therapy or placebo. Figure 1 gives example to illustrate a potential network plot.

Types of outcomes. The primary outcome of interest is the relief of urinary symptoms. A voiding diary will be appropriate to assess the efficacy which is commonly made up of micturition, urgency, and urinary incontinence. OAB-related questionnaires and quality of life questionnaires, as the secondary outcomes will be taken into account (Leron et al., 2018).

2.3 | Exclusion criteria

The following studies will be excluded: (1) Study types as following: non-randomized controlled trials such as reviews, cohort trials, case reports and corresponding. (2) Duplicates or studies without objective data. (3) The full text of the literature is not accessible to obtain. (4) Participants ≤18 years old or with males.

2.4 | Search strategy

The search will be undertaken in electronic databases from set up to 1 January 2021. Eight electronic databases will be searched including PubMed, Cochrane Library, Web of Science, Embase, China National

Knowledge Infrastructure, Wanfang Database, VIP Database and China Biology Medicine disc. According to the requirements of each database, the search strategy will be adjusted. The initial search strategy for PubMed is shown in Table 1.

2.5 | Data extraction

Endnote will be applied to manage all literature from electronic databases. After deleting the duplicates, two researchers will independently review the titles and abstracts of studies in compliance with the eligibility criteria. Data will be extracted as follows: (1) demographic information: age, sample size, name of interventions; (2) study information: title, first author, publication year and publication nation; (3) outcome information: name of outcomes (incontinence episodes/24 hr, urgency episodes/24 hr, voiding episodes/ 24 hr, nocturia/24 hr, mean voiding volume/time), data of outcomes in baseline and endpoint. Moreover, a third referee will make the decision in case of doubts or disagreements. The selection process will be carried out in the PRISMA flow chart as Figure 2.

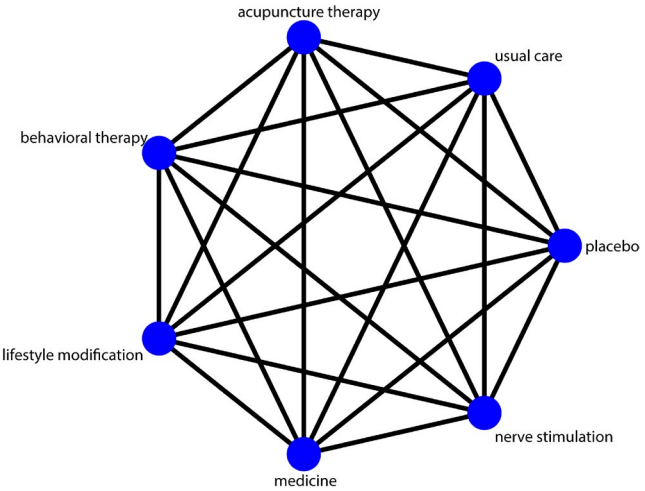

FIGURE 1 Network plot of possible direct comparisons

2.6 | Risk of bias in individual studies

Cochrane risk-of-bias tool (ROB 2.0) as a reference will be used to evaluate the quality by two reviewers (Sterne et al., 2019). The following five domains will be considered: (1) bias arising from the randomization process, (2) bias due to deviations from intended interventions, (3) bias due to missing outcome data, (4) bias in the measurement of the outcome and (5) bias in the selection of the reported result. Each domain will be classified into 3 levels: High risk, some concern or low risk. Any disagreements between reviewers will be resolved by discussion or consultation with a third reviewer.

2.7 | Data synthesis and statistical methods

Pairwise meta-analysis. Pairwise meta-analysis for direct comparisons will be conducted by STATA. Given that our outcomes are continuous data, the effect size of the non-pharmacological interventions will assess with the standardized mean difference (SMD) and 95% confidence intervals (CIs). Statistical heterogeneity across studies will be evaluated with P and I^2 statistics. If the *p*-value is ≥0.1

TABLE 1 Draft search strategy of PubMed

Search number	Search Details	Results
1	"urinary bladder, overactive"[MeSH Terms]	4,812
2	"overactive bladder"[Title/Abstract]	6,585
3	"overactive urinary bladder"[Title/Abstract]	90
4	"OAB"[Title/Abstract]	3,239
5	"bladder overactivity"[Title/Abstract]	535
6	"urinary urgency"[Title/Abstract]	1,020
7	"bladder instability"[Title/Abstract]	370
8	"detrusor overactivity"[Title/Abstract]	2,696
9	"overactive detrusor"[Title/Abstract]	169
10	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9	10,657
11	Randomization	1,244,746
12	"random"[All Fields]	387,446
13	"randomized"[All Fields]	873,890
14	"randomly"[All Fields]	348,621
15	"rct"[All Fields]	25,282
16	#11 OR #12 OR #13 OR #14 OR #15	1,424,699
17	#10 AND #16	1,727

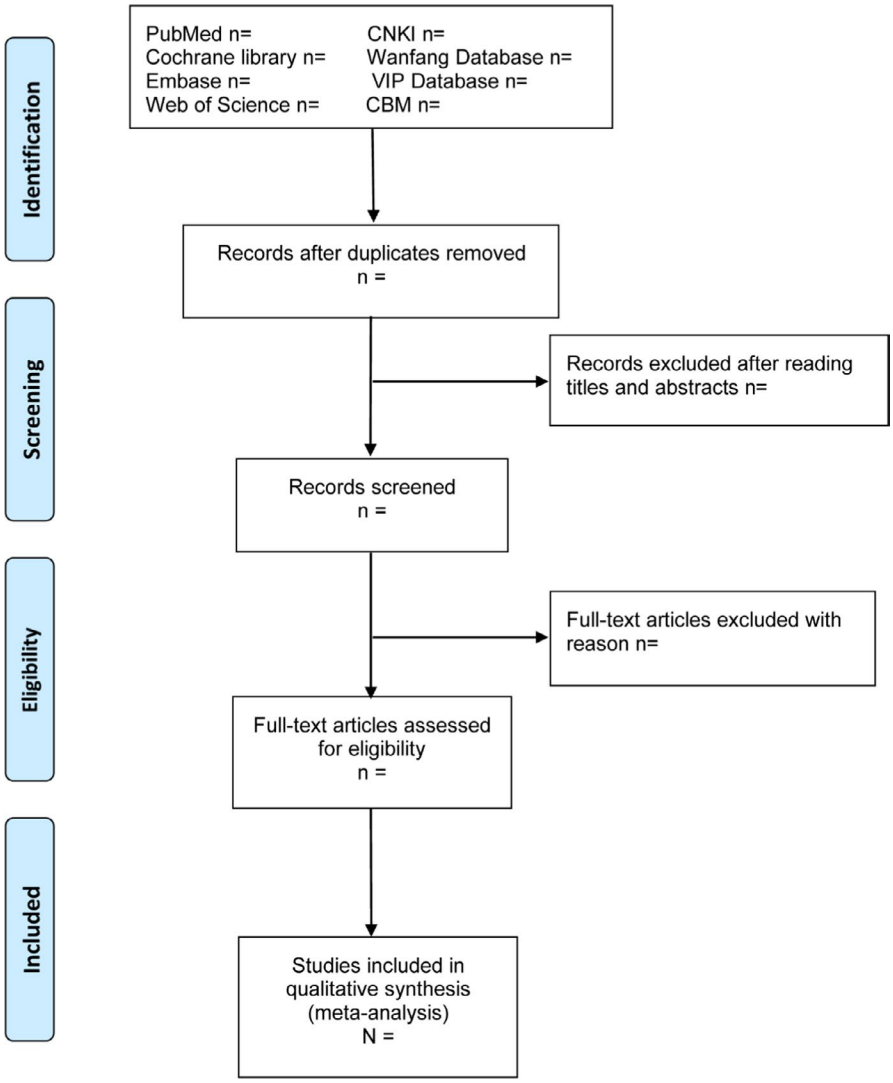

FIGURE 2 PRISMA flow diagram of the study selection process

and I^2 ≤50%, a fixed model will be synthesized. If not, the random-effects model will be used. Subgroup and sensitivity analysis will be carried out if it is necessary.

Network meta-analysis. Bayesian network meta-analysis will be used in our study. All data will be analysed by Open BUGS, R and STATA. Node splitting analysis by R is used to estimate the appropriateness of the model. STATA will be designed for surface under the cumulative ranking curves (SUCRA) and league figure to rank the non-pharmacological interventions in OAB after SMD or OR calculated by Open BUGS. Direct and pooled I^2 will be assessed by R. Potential publication bias will also be evaluated through funnel plots.

2.8 | Grading the quality of evidence

Grades of Recommendations, Assessment, Development and Evaluation (GRADE) profiler 3.6 will be used to appraise the quality of evidence for outcomes by two reviewers. Five aspects of GRADE (limitations in study design, inconsistency, indirectness, imprecision and publication bias) are applied to assess the quality of intervention effect in this study. The quality of the evidence will be rated as high, moderate, low or very low according to the standards of GRADE.

3 | DISCUSSION

OAB with notable morbidity is one of the most common diseases in females that cause functional decline and a significant reduction in quality of life. Several studies have demonstrated the aetiology that age, metabolic, affective disorder, pelvic floor dysfunction, urinary microbiota and subclinical autonomic nervous system dysfunction would be associated with OAB (Peyronnet et al., 2019; Zhu et al., 2019). As estimated, the expenses of OAB in females were $18.8 billion much higher than in males ($6.1 billion) (Reynolds et al., 2016). As a consequence, the management of OAB in females is still considered to be complex and challenging.

According to the framework for the management of OAB presented by the guideline, there are a variety of treatment options

for OAB. Particularly, behavioural therapy and life modification, the first-line treatment option for OAB, are widely used in patients with OAB (Lightner et al., 2019). Nerve stimulation also has been recommended as a third-line therapy option (Pratt & Suskind, 2018). And some reviews suggested acupuncture, nerve stimulation and pelvic floor muscle therapy provide symptomatic improvement, strength functional bladder capacity and consequently maintain normal urination (Chan et al., 2018; Pekbay et al., 2019; Sonmez et al., 2021). Nonetheless, inconsistent evidence has been reported about non-pharmacological interventions yet. Hence, it is hard to investigate the superiority approach of different non-pharmacological interventions. To solve the problem, this study will be the first quantitatively comparing different non-pharmacological interventions and generate evidence using a network meta-analysis to rank, interpret and present an evidence mapping. The findings are expected to best match the clinical practice for females with OAB.

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Not applicable.

CONFLICT OF INTEREST

The author(s) declare that they have no conflict of interests.

AUTHOR CONTRIBUTIONS

Data curation: HZ, CWF, WZC; Formal analysis: WZC, JW; Funding acquisition: JW; Investigation: HZ, YZY; Methodology: CWF, YZY, BYW; Project administration: WZC, JW; Resources: HZ, YZY; Software: WZC, BYW; Supervision: JW, CWF; Writing—original draft: HZ, WZC; Writing—review and editing: WZC, CWF. HZ and WZC contributed equally to this work. All authors have read and approved the manuscript for publication. All authors have agreed on the final version and meet at least one of the following criteria [recommended by the ICMJE (https://www.icmje.org/recommendations/)]: substantial contributions to conception and design, acquisition of data or analysis and interpretation of data; drafting the article or revising it critically for important intellectual content.

ETHICAL APPROVAL

Not applicable.

CONSENT FOR PUBLICATION

Not applicable.

DATA AVAILABILITY STATEMENT

All the data will be available and reported in our future study with regard to this protocol.

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