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REVIEW

Acupuncture for Women with Overactive Bladder: Perspective of Traditional Chinese Medicine and Related Mechanism

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Purpose: Overactive bladder (OAB) syndrome is one of the most common diseases in urology and affects quality of life. Although the current treatment for OAB is based on oral medications, there are limitations and many patients have difficulty accepting drug-induced adverse effects. This review aimed to analyze the efficacy of acupuncture and its related mechanisms and provide a preliminary therapeutic regimen.

Methods: Two authors independently searched PubMed, Embase, and Cochrane Library up to April 2022. They searched related English literature and extracted the data under a standard form based on the search strategy. Clinical trials which included OAB women with the treatment of acupuncture were included. Common acupuncture alone without other pharmacotherapy, external treatments was in the treatment group. The control interventions may include any active treatments, sham placebo, or no establishment of a control group. Outcomes included 3-day or 24-hour voiding diary, overactive bladder symptom score, etc. The Cochrane risk of bias tool was also used to assess the methodological quality of the randomized controlled trials (RCTs).

Results: We analyzed five RCTs and one comparative study on acupuncture for OAB to review and discuss the acupoint location, treatment course, and retention time based on clinical evidence and treatment ideas in traditional Chinese medicine. Additionally, we used the available evidence to reveal and discuss the acupuncture mechanisms for OAB. Acupuncture may regulate bladder function by inhibiting C-fibers, modulating nerve growth factors and reducing spontaneous contractions of the detrusor muscle.

Conclusion: Combined with the available evidence, the combination of local acupoints and distal acupoints should be necessary to consider, especially the lumbosacral acupoints, the small abdomen acupoints and the lower limb acupoints. Among them, acupuncture at SP4, CV4 and KI3 are strongly recommended. The treatment course of acupuncture should be no less than 4 weeks and maintain the frequency of acupuncture no less than once a week. The duration of each session should be no less than 20 minutes. In addition, investigations remain necessary to verify acupuncture's efficacy and precise mechanism for OAB treatment in further exploration.

Keywords: female, treatment course, acupoint location, retention time, urology, therapeutic regimen

Introduction

Overactive bladder (OAB) is a common chronic bladder dysfunction that is clinically characterized by frequent, urgent, and increased nocturia.[1] OAB prevalence increases with age, affecting approximately 30% of people over 65 and 7% ~26% of the worldwide population.[2,3] The overall OAB prevalence in females is significantly higher than in males.[4] Frequent and urgent urination syndrome can seriously disrupt patients' daily lives and even lead to sexual dysfunction and psychological disorders due to prolonged treatment.[5,6]

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OAB treatment includes behavioral therapy, medication, invasive techniques, and neuroelectric stimulation.[7] Anticholinergic drugs are common therapeutic agents, but cognitive impairment limits their use in older patients with OAB. Side effects, such as dry mouth, severely reduce patient compliance with medication and seriously compromise their efficacy.[8] Additionally, invasive treatment is often associated with urinary retention and urinary tract infections, making it difficult for patients to choose.[9] Moreover, peripheral nerve stimulation's long-term efficacy and safety remain to be monitored.[10]

Therefore, many clinicians explore alternative OAB treatment methods. Traditional Chinese medicine (TCM) is increasingly recognized internationally. Acupuncture has broader applications in lower urinary tract symptoms.[11,12] Many reviews focused more on discussing its efficacy.[13,14] However, there is insufficient discussion of the acupoint location, retention time, treatment duration, depth of needling, and involved mechanisms. Hence, we differ from previous review articles by focusing more on analyzing these aspects of TCM and Western medical mechanisms and conclude a preliminary therapeutic regimen to enrich clinical applications and elucidate the features of acupuncture for OAB.

Materials and Methods

Search Strategy

We made the strategy of PubMed, Embase and Cochrane Library to search studies (up to April 2022). We also examined the trails from previous reviews to make the search more comprehensive. The language of the publications was limited to English. The following search terms were used: acupuncture, acupuncture treatment, electroacupuncture, acupuncture therapy, warm needling, laser acupuncture, overactive bladder, overactive bladder syndrome, bladder overactive, overactive detrusor, bladder instability, urinary bladder, clinical trial, trial, clinical study, controlled study, and randomized. Searching items listed below are used in Table 1.

Table 1 PubMed Search Strategy

No.	Searching Item
#1	Acupuncture[Title/Abstract]
#2	Acupuncture treatment[Title/Abstract]
#3	Electroacupuncture[Title/Abstract]
#4	Acupuncture therapy[Title/Abstract]
#5	Warm needling[Title/Abstract]
#6	Laser acupuncture[Title/Abstract]
#7	Or/#1-#6
#8	Overactive bladder[Title/Abstract]
#9	Overactive bladder syndrome[Title/Abstract]
#10	Bladder overactive[Title/Abstract]
#11	Overactive detrusor[Title/Abstract]
#12	Bladder instability[Title/Abstract]
#13	Urinary bladder[Title/Abstract]
#14	Or/#8-#13
#15	Clinical trial[Publication Type]
#16	Trial[Publication Type]
#17	Clinical study[Publication Type]
#18	Controlled study[Publication Type]
#19	Randomized [Publication Type]
#20	Placebo[Publication Type]
#21	Or/#16-#21
#22	#4 and #14 and #21

Inclusion Criteria

(1) Types of studies: Clinical trials involving acupuncture for OAB were included, and the qualified papers were limited to the English language.

(2) Types of participants: Women with a diagnosis of OAB by clinical and/or instrumental methods were included, regardless of their ethnicity, country, and course.

(3) Types of interventions: Common acupuncture (including acupuncture, electroacupuncture, warm needling, laser acupuncture) alone without other pharmacotherapy, external treatments in the treatment group regardless of acupoint position, treatment frequency, and course.

(4) Types of comparisons: The control interventions may include any active treatments or sham placebo. Or there was no establishment of a control group in the trail.

(5) Types of outcomes: 3-day voiding diary or 24-hour voiding diary as the primary outcomes were recorded. The overactive bladder symptom score (OABSS), Incontinence Impact Questionnaire (IIQ-7), Urogenital Distress Inventory (UDI-6), etc. were also used as secondary outcomes.

Data Collection and Analysis

Selection of Studies

Two authors screened articles independently according to the search strategy (Table 1) and sorted out the results. Duplicate studies were eliminated. Some studies were excluded after analyzing the title and abstract. Furthermore, studies that did not meet the inclusion criteria were eliminated after analyzing the full text. The procedure is shown in Figure 1.

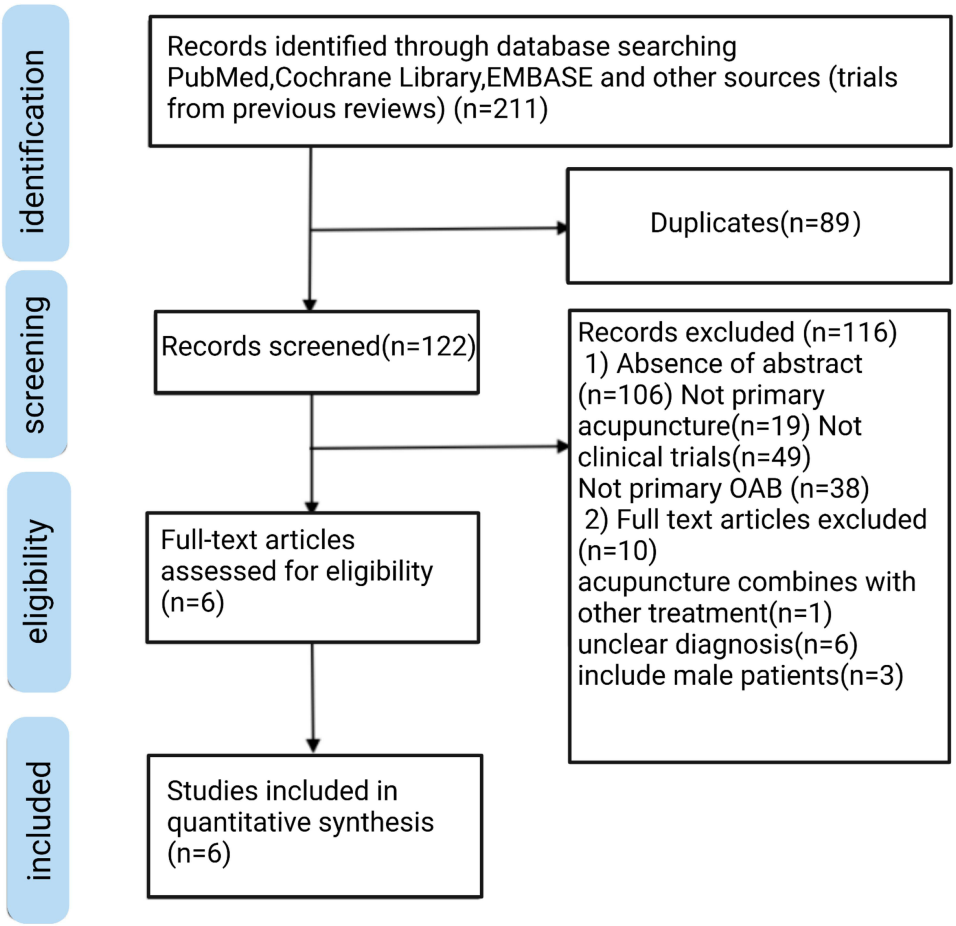

Figure 1 Flow chart of the study search.

Data Extraction

Two authors extracted the data independently. Extraction contents included the first author's name, sample treated by acupuncture, acupoints, duration, outcomes and conclusion. Extracted data was compared by two authors to be accurate and complete.

Assessment of Risk of Bias

The Cochrane risk of bias tool was used to assess the RCTs in Table 2. It includes seven domains: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting and other bias. The studies were then classified into three levels of bias: low, unclear, and high, which were used to classify the RCTs. Disagreements were resolved by discussion between the authors.

Results

The International Continence Society officially defined the concept of OAB in 2002.[21] Previously, the concept of OAB was not uniform, and we have combined the patient's symptoms and diagnosis by reading the full text to think that these patients from one study conform to OAB characteristics.[20] Finally, we included 6 clinical studies in English, with 241 females treated with acupuncture or laser acupuncture. Basic characteristics such as patient age are mentioned in Table 3.

This review revealed 6 studies that used conventional acupuncture,[15,17–20] 1 used laser acupuncture.[16] The retention time for each treatment is 20~30 min and most tend to 20 min. The session varies from 1 to 8 times, except in the trial of Chang et al.[16] The vast majority of treatment sessions are over 4 weeks long. Of these, 3 studies had a 4-week treatment course.[17–19]

Plenty of acupoint selections have been used in OAB, including 8 meridians' 20 different acupoints. We used different colors in Figure 2 to represent the acupoints on different studies. In this review, the most commonly chosen meridians for OAB treatment are bladder meridian and ren meridian. The acupoint with the highest frequency is SP6 (Sanyinjiao), which occurs 6 times. Other acupoints are CV4 (Guanyuan) and KI3 (Taixi), corresponding to 5 and 4 times, respectively.

From these 6 studies in Table 3, the final results all indicate acupuncture in OAB is effective and safe. In Hargreaves' s study,[15] 88.4% of women had a satisfaction with the efficacy of acupuncture. However, the authors did not mention the specifics of the efficacy of the acupuncture plus standard care group. Chang et al[16] showed OABSS score decreased significantly after 3rd, 6th, and 9th sessions of acupuncture, compared with the placebo group. In acupuncture group, IIQ-7 score decreased significantly from baseline in week 3 and week 6, and UDI-6 also decreased after 6th and 9th interventions. They had significant differences compared with the placebo group. In a 4-week study,[17] and acupuncture had an advantage over the placebo group in improving the women's quality of life and symptom scores. Also, women in both acupuncture and pharmacological groups of Yuan et al's study had significant reduction in OAB symptoms at week

Table 2 Risk of Bias for Included Randomized Controlled Trials

Reference	Sequence Generation	Allocation Concealment	Blinding of Participants and Personnel	Blinding of Assessment	Incomplete Outcome	Selective Outcome Report	Other Source of Bias
Hargreaves 2021[15]	Low	Low	High	High	High	Unclear	Unclear
Chang 2020[16]	Low	Unclear	Low	Unclear	Low	Low	Unclear
Aydoğmuş 2014[17]	Low	Unclear	Low	Unclear	High	Unclear	Unclear
Yuan 2015[18]	Low	Low	High	Low	High	Low	Low
Emmons 2005[19]	Low	Low	Low	Low	Low	Unclear	Low

Table 3 Summary of the Included Studies

References	Sample	Characteristics	Treatment	Acupoints	Outcomes	Conclusion
Hargreaves 2021[15]	16	54.5±16.23 years 8.4 voids/ day;3.16 leakage episodes per day;1.39 episodes of nocturia	Standard care (individually tailored advice regarding bladder health, pelvic floor exercises and lifestyle adjustment) plus acupuncture, 30 min, 6 sessions for 8 weeks	CV3 (Zhongji), CV4 (Guanyuan), CV5 (Shimen), ST25 (Tianshu), SP6 (Sanyinjiao), SP9 (Yinlingquan), KI3 (Taixi), KI7 (Fuliu)	Voids per day 8.4±1.57 vs 7.87±2.84 in week 8 and 8.80±2.40 in week 14; leakage episodes per day 3.16±3.20 vs 2.70±2.95 in week 8 and 2.53 ±3.00 in week 14; nocturia 1.39±1.36 vs 1.39 ±1.36 in week 8 and 1.13±1.15 in week 14; ICIQ-SF score 11.00±4.73 vs 9.4±5.2 in week 8 and 10.2±5.1 in week 14	The majority of participants found the protocol acceptable and completed all aspects of the study. Acupuncture treatment appeared to be safe and well-tolerated and feasible.
Chang 2020[16]	15	56.4±14.3 years 10 wet OAB and 5 dry OAB	Subjects in the verum laser acupuncture group received a total energy of 6 joule at each acupoint with frequency prescribed, 611Hz~1102Hz, 9 sessions for 3 weeks	KI3 (Taixi), SP6 (Sanyinjiao), CV4 (Guanyuan), CV6 (Qihai), BL33 (Zhongliao), BL34 (Xialiao), GV20 (Baihui)	OABBS 8.7±1.8 vs 4.7±2.4 in week 1 and 3.4±1.9 in week 2 and 3.1±1.6 in week 3 (p<0.01); UDI-6 6.0±2.5 vs 3.5±1.9 in week 1 and 2.3±1.8 in week 2 and 2.4 ±1.6 in week 3 (p<0.05); IIQ-7 9.9 ± 5.7 vs 4.2±2.3 in week 1 and 4.2±3.2 in week 2 and 3.0±2.5 in week 3 (p<0.05)	Laser acupuncture can alleviate OAB symptoms and improve quality of life and could be an effective therapy for women with OAB.
Aydoğmuş 2014[17]	28	38±12.9 years all OAB dry	Acupuncture, 20 min, 8 session for 4 weeks	LI4 (Hegu), GV22 (Xinhui), SP6 (Sanyinjiao), ST36 (Zusanli), LR3 (Taichong), GV29 (Yintang), CV4 (Guanyuan), KI3 (Taixi), KI5 (Shuiquan)	NFG,0.92pg/mL (range 0.70–2.45) vs 0.07 (range 0.01–2.82); symptom scores 21 (range 14–21) vs 5 (range 2–20); quality of life scores 2.0 (1–3) vs 2.0 (range 0–3), all the results had been significantly improved after treatment (p<0.01)	In patients with OAB in whom anticholinergic treatment is contraindicated, acupuncture may be considered another treatment option.

(*Continued*)

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Table 3 (Continued).

References	Sample	Characteristics	Treatment	Acupoints	Outcomes	Conclusion
Yuan 2015[18]	118	57.5±12.1 years 2.2 incontinence episodes/day	Acupuncture, 20 min, 4 sessions for 4 weeks	SP6 (Sanyinjiao), SP9 (Yinlingquan), KI3 (Taixi), CV4 (Guanyuan)	At week 4, the number of urgency episodes per 24 h in the intervention group decreased by 3.1 (−47.7%), urgency incontinence episodes by 1 (−45.5%), daytime frequency by 4.2 (−30.0%), nocturia episodes by 1.5 (−37.5%) and the volume voided per micturition increased by 68 mL (40.0%), while in the control group, the number of urgency episodes per 24 h decreased by 3.5 (−50%), urgency incontinence episodes by 1.2 (−48%), daytime frequency by 4.3 (−32.6%), nocturia episodes by 1.3 (−36.1%) and the volume voided per micturition increased by 70 mL (43.2%).	Acupuncture is safe with significant improvements in patient assessment of overactive bladder symptoms and may be considered a clinically alternative treatment for overactive bladder in female adult.
Emmons 2005[19]	38	53±13 years 30.4 voids/3 days; 16.2 urge episodes/3 days	Acupuncture, 20 min, 4 sessions for 4 weeks	SP6 (Sanyinjiao), BL39 (Weiyang), BL28 (Pangguangshu), CV4 (Guanyuan)	A 59% reduction in number of incontinent episodes; a 14% reduction in urinary frequency ($p=0.013$); a 30% reduction in the proportion of voids associated with urgency ($p=0.016$), and a 13% increase in both maximum voided volume and maximum cystometric capacity ($p=0.01$); an 54% reduction in the urinary distress inventory and incontinence impact questionnaire scores ($p<0.01$)	Women who received 4 weekly bladder specific acupuncture treatments had significant improvements in bladder capacity, urgency, frequency, and quality of-life scores as compared with women who received placebo acupuncture treatments.
Chang 1988[20]	26	35±17 years symptom duration 9 months->10 years	Acupuncture, 20 min, 1 session	SP6 (Sanyinjiao)	Acupuncture improved maximum cystometric capacity ($p<0.01$) and decreased peak urinary flow rate ($p<0.02$).	Acupuncture could be used as a simple and effective method to treat female patients with frequency, urgency and dysuria.

Abbreviations: OABSS, the overactive bladder symptom score; IIQ-7, incontinence impact questionnaire; UDI-6, urogenital distress inventory short form; NGF, nerve growth factor.

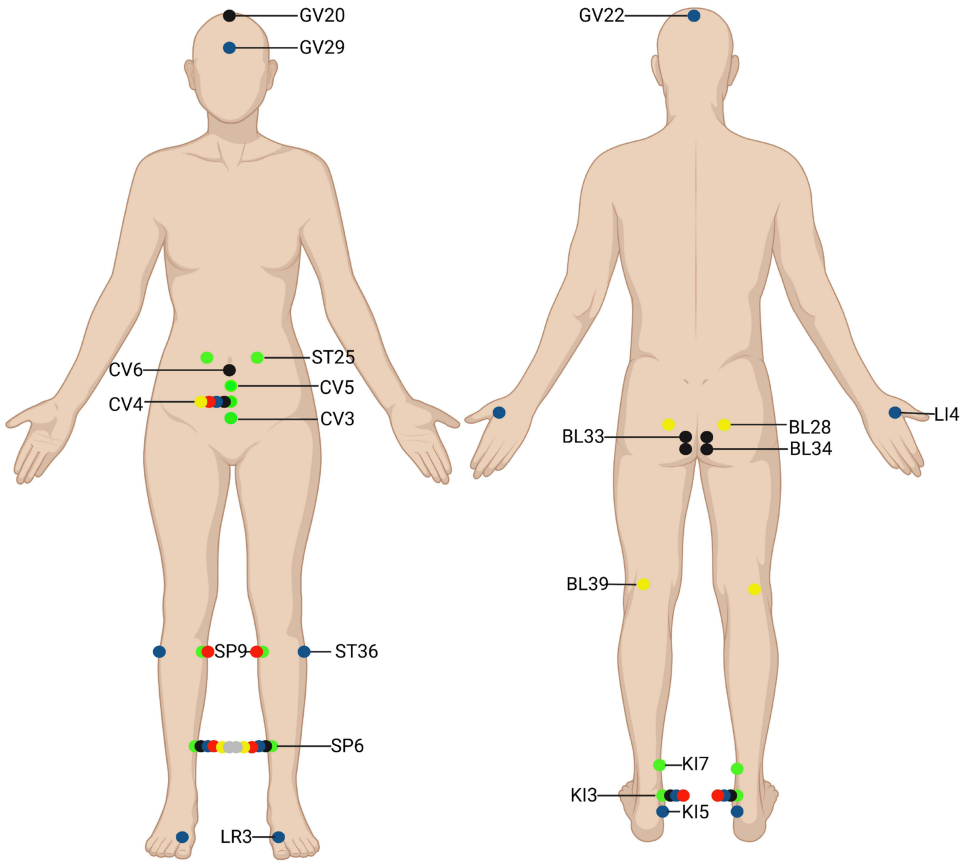

Figure 2 The location and distribution of the acupoints.
Notes: The green, black, blue, red, yellow, and gray circles represent the acupoints selected by Hargreaves et al, Chang et al (2020), Aydoğmuş et al, Yuan et al, Emmons et al and Chang et al (1988), respectively (Created with BioRender.com.).

4, however they were without a significant difference between each group.[18] Another 4-week study by Emmons et al[19] finally recruited 38 women in acupuncture group. The results showed that acupuncture significantly relieved OAB voiding symptoms, including urinary incontinence and frequency and increased maximum urinary output and bladder capacity. Unlike other studies, Chang et al[20] performed only one acupuncture treatment on 26 female patients, and their results showed acupuncture had significant improvement in maximum cystometric capacity.

All of these studies showed no serious adverse effects of acupuncture treatment. And the inevitable possibility of minor local bleeding after needle removal is understood by the patient.

Discussion

Advantages and Ideas for Acupuncture of OAB in TCM

OAB is not life-threatening, but its influence of the life quality plays an important role in determining patient treatments.[22] The negative impact of OAB on daily activities, mental health, sexual function, and marital satisfaction has been well documented and has been highlighted in many studies.[23] Women with OAB are middle-aged or older who may have frailty or other chronic illnesses.[24] In terms of treatment, first-line treatment options represented by behavioral therapy have limited clinical efficacy in improving the patient's symptoms.[25] Oral medication or other therapies can have adverse effects that are difficult for patients to accept. As a component of TCM, many patients recognize acupuncture for treatment.[15,17] A preliminary analysis of its influencing factors related to TCM was briefly analyzed based on the above clinical efficacy and advantage of acupuncture in OAB treatment.

Acupoint Location

The included acupoint retrieval modalities in this review are proximal and distal acupuncture point retrieval. Figure 2 shows that acupoints, such as BL33, BL34, CV3, and CV4, are mainly concentrated in the lumbosacral region and the small abdomen near the bladder. From a TCM perspective, a feeling of deqi after insertion into the body is experienced as soreness, numbness, swelling, or other reactions.[26] The local acupoints can be promoted to effectively regulate the flow of qi at this time, thereby allowing the release of excessive local qi in the bladder.[27,28] On the other hand, CV3, CV4, and CV5 are all adjacent to the bladder organ, and the nerves under them originate from the inferior ventral nerve T10 to L1, which mainly innervates the bladder and urethra.[29] The CV3 is in the T12-L1 spinal cord segment, where the bladder nerves partially overlap. The parasympathetic sacral center is located in S2-S4 of the sacral medulla and has a pro-urinary function. Acupuncture at the CV4 stimulates the parasympathetic nerve and modulates the detrusor and internal urethral sphincter, thereby eliciting the urinary reflex.[30] BL33 is in the sacral region, near the 3rd posterior sacral foramen, under which the gluteus maximus muscle starts and the posterior branch of the third sacral nerve pass. BL34 is near the caudal end of the sacrum, underlain by the gluteus maximus muscle, the nerve of the caudal, and the pubic region. BL34 is in the projection area of the bladder on the body surface, and its acupuncture sensation can spread to the bladder, urethra, and perineum. From the opinion of Chang et al,[16] stimulation of BL33 and BL34 may be related to the theory of sacral neuromodulation.

Distal acupoint selection is to perform acupuncture at a site farther from the disease location, which is based on the meridian theory.[31] Figure 2 shows the selected acupoints in the head, such as GV20 and GV29, and extremity end acupoints, such as KI15, KI13, etc., for OAB treatment. Interestingly, most of these acupoints belong to the meridians of du and kidney. Concurrently, acupoints of the meridian of du, such as GV20, GV22, and GV29, can regulate mental symptoms.[32] In addition, studies have shown that the use of percutaneously inserted acupuncture needles into the SP6, connecting to an electric current and repetition with electrical stimulation of the tibial nerve, seems to prolong the bladder detrusor contraction interval.[33,34] McGuire et al[35] demonstrated that acupuncture stimulation at SP6 may affect the nerve impulses of the voiding center to inhibit the uninhibited detrusor muscle contraction. KI3, KI5, and KI7 are all close to the tibial nerve.

Treatment Course

The duration of acupuncture OAB treatment is not uniform as shown in Table 3. Most duration times are 4 weeks. Acupuncturists mostly use their experience and the patient's schedule to pre-determine the treatment course, with a long refractory and chronic disease duration when treating diseases, and acute conditions may need a shorter course of acupuncture.[36] OAB is a chronic disease mostly suffered by middle-aged and elderly females, and a longer treatment cycle should be developed according to TCM ideas. Hargreaves et al[37] considered that acupuncture for OAB was usually 1 session per week to achieve a course of 4–12 sessions, and acupuncture also has a continual therapeutic effect and may be more clinically relevant for long-term efficacy measurement. However, the current evidence in the literature remains inadequate concerning the specific duration of acupuncture treatment for OAB. Additionally, the included literature in this review had 1–3 times/week. Zhao et al[38] randomly included 60 patients, divided into groups of 3 times per week and 2 times per week. They observed the effect of different treatment frequencies of electroacupuncture therapy on the effect of female stress urinary incontinence (SUI). After 12 treatments, incontinence symptoms and quality of life scores significantly improved in both groups ($p < 0.01$), and the overall effectiveness of the 3-times-a-week group was 90.0% (27/30), which was better than the 76.7% (23/30) of the 2-times-a-week group ($p < 0.05$). This suggests that lower urinary tract symptoms in women may require more frequent acupuncture treatment per week. However, due to inadequate evidence, further research is needed on acupuncture duration and frequency for OAB treatment.

Retention Time

The amount of effective stimulation in acupuncture treatment is an important criterion for efficacy.[39] The stimulation duration positively correlated with the amount of effective stimulation within a certain range. However, prolonged duration of stimulation may lead to ineffective stimulation or adverse effects. Needle retention times may differ for different diseases, and the same disease has not yet been standardized, requiring a long process.[40] Most studies favor a

retention time of 20 min for acupuncture, which seems to come from the experience as it stands now, and no studies concentrated on different retention times of OAB treatment. Therefore, the search for the optimal retention time for acupuncture in OAB treatment or other diseases is significant to standardize the operation and improve treatment efficacy.

The Mechanism of Acupuncture for OAB May Be Through the Regulation of Related Pathways

Acupuncture may reduce spontaneous contractions of the detrusor muscle by regulating ICCs. Cajal interstitial cells (ICCs) are regulators of bladder smooth muscle contractile activity, with a range of excitation-related channels on ICCs, such as $Ca2^+$ channels, hyperpolarization-activated cyclic nucleotide-modulated ion (HCN) channels, and voltage-dependent K^+ channels, which are closely associated with epithelial-afferent nerve, as well as nerve-smooth muscle signaling.[41] ICCs initiate bladder contractile activity, act as pacemakers to generate depolarizing currents into adjacent smooth muscle, and coordinate bladder muscle contraction.[42] The role of ICCs appears more prominent in pathological states than in physiological states, such as OAB.[43] Several researchs showed increased numbers of ICCs in the bladder of OAB compared to normal.[44–46]A study has investigated acupuncture on the activity of ICCs of rats with partial bladder outlet obstruction-induced OAB.[47] They revealed that acupuncture inhibited bladder overactivity, downregulated HCN2 mRNA and protein expression, and reduced HCN2 channels while decreasing the intracellular free $Ca2^+$ concentration in bladder ICCs. Lu et al[48] compared EA on the bladder tissue of rats with neurogenic bladder with those acupoints of CV3 and CV4 and found that EA significantly inhibited the mRNA and protein high expression of HCN1-4 channels. Additionally, HCN channel inhibition at the BL32 was superior to that at the CV3 and CV4 in the study. HCN channels are closely related to the autoregulation and excitability of ICCs and may also increase intracellular $Ca2^+$ concentration by activating the T-type voltage-dependent $Ca2^+$ channel concentration.[45] Intracellular $Ca2^+$ is closely related to the contractile activity of the detrusor muscle. The mechanism may inhibit HCN channels, reduce the free intracellular $Ca2^+$ concentration, decrease the excitability of ICCs, and inhibit detrusor activity.

Acupuncture may reduce OAB symptoms by modulating nerve growth factor (NGF). The levels of NGF in the urine are a potential biomarker for OAB diagnosis.[49] NGF plays an important part in preventing the pathological process of secondary spinal cord injury.[50] Increased NGF localized to the spinal cord injury facilitates the growth of injured axons and has important regulatory control over central and peripheral neurons. Several studies detected higher baseline NGF in OAB patients than in healthy controls in the urine. Urinary NGF levels were also higher in OAB patients with urge incontinence, which emphasized the potential value of urinary NGF in identifying OAB.[51–53] Aydoğmuş et al[17] revealed significantly decreased NGF levels in the acupuncture therapy. NGF/creatinine levels decreased from 1.26 to 0.6 pg/mL and from 0.99 to 0.07 pg/mL. This was also attempted by Lin et al,[54] but the enzyme-linked immunosorbent assay kit readings were too low and lacked practical significance. The amount of NGF in the urine samples was probably too small to be detected for other reasons. Therefore, continuing to enrich the evidence in this area remained necessary to confirm the role of acupuncture in NGF regulation.

Acupuncture may regulate bladder function by inhibiting C-fibers. Bladder C-fibers have an important role in OAB. The bladder afferent nerves include myelinated Aδ-fibers and unmyelinated C-fibers.[55] Among them, Aδ-fibers excite and transmit impulses to the pontine voiding center via the midbrain's spinal cord, brainstem, and periaqueductal gray matter, thereby producing urinary urge.[56] Contrastingly, C-fibers have a higher mechanical threshold than Aδ-fibers.[57] The C-fiber-mediated neural pathway activates and affects the voiding process when inflammation or injurious chemical stimuli are present in the bladder. Hino et al[58] demonstrated the correlation between acupuncture modulation of bladder contractile function and C-fibers and revealed that acupuncture stimulation could inhibit bladder contraction in OAB rats, significantly reducing urination intervals. However, the bladder of OAB rats was not improved by acupuncture when the bladder was perfused with capsaicin (a C-fiber-disrupting substance) in advance. Several studies revealed that increased c-fos gene expression in the sacral medullary voiding center indicates excessive afferent C-fiber activity.[59,60] Yu et al[61] demonstrated that acupuncture inhibited the OAB state in rats with spinal cord transection by decreasing the c-fos expression in the sacral medullary voiding center, which attenuated C-fiber activity.

Limitations and Conclusion

This review included 6 English-language studies in strict accordance with the search strategy of our review. Our study limitations included small sample size and low quality of evidence. This review aimed to analyze the role of acupuncture in female patients with OAB from the TCM aspects and related mechanisms and initially provide a management for acupuncture for OAB. However, the arguments for the mechanisms associated with acupuncture for OAB may not be sufficient and remain to be further explored due to inadequate evidence.

This review is the first to discuss the therapeutic role of acupuncture in OAB from a relevant TCM perspective and possible mechanisms, which provide potential trends for future research and help clinicians treat OAB by acupuncture. Based on the evidence in the literature, the women troubled by OAB may benefit from the acupuncture therapy, and considering the location of acupoints, the duration of needle retention, and the duration of course are necessary in treating OAB by acupuncture. The mechanism of acupuncture on OAB may relate to neuromodulatory, such as local nerve modulation and neuronal activity regulation in the brain. Both the efficacy and mechanism still should be researched in future studies. Finally, from these present evidence, we made a preliminary therapeutic regimen:

(a) In the selection of acupoints, the combination of local acupoints and distal acupoints should be paid attention to, especially the lumbosacral acupoints, the small abdomen acupoints and the lower limb acupoints. Among them, acupuncture at SP4, CV4 and KI3 are strongly recommended.
(b) The treatment course of acupuncture should be no less than 4 weeks and maintain the frequency of acupuncture no less than once a week.
(c) The duration of each session should be no less than 20 min.

Data Sharing Statement

Data supporting this article are all in this article.

Acknowledgments

Figure 2 is created with BioRender.com.

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Disclosure

The authors report no conflicts of interest in this work.

References

1. Hutchinson A, Nesbitt A, Joshi A, Clubb A, Perera M. Overactive bladder syndrome: management and treatment options. *Aust J Gen Pract*. 2020;49(9):593–598. doi:10.31128/AJGP-11-19-5142
2. Pagoria D, O'Connor RC, Guralnick ML. Antimuscarinic drugs: review of the cognitive impact when used to treat overactive bladder in elderly patients. *Curr Urol Rep*. 2011;12(5):351–357. doi:10.1007/s11934-011-0198-9
3. Coyne KS, Sexton CC, Kopp ZS, Ebel-Bitoun C, Milsom I, Chapple C. The impact of overactive bladder on mental health, work productivity and health-related quality of life in the UK and Sweden: results from EpiLUTS. *BJU Int*. 2011;108(9):1459–1471.
4. Irwin DE, Milsom I, Hunskaar S, et al. Population-based survey of urinary incontinence, overactive bladder, and other lower urinary tract symptoms in five countries: results of the EPIC study. *Eur Urol*. 2006;50(6):1306–1314.
5. Scarneciu I, Lupu S, Bratu OG, et al. Overactive bladder: a review and update. *Exp Ther Med*. 2021;22(6):1444.
6. Zilberlicht A, Haya N, Feferkorn I, Goldschmidt E, Kaldawy A, Abramov Y. Somatic, psychological, and sexual triggers for overactive bladder syndrome in women. *Neurourol Urodyn*. 2018;37(1):163–168.
7. Robinson D, Cardozo L. Managing overactive bladder. *Climacteric*. 2019;22:654.
8. Araklitis G, Robinson D, Cardozo L. Cognitive Effects of Anticholinergic Load in Women with Overactive Bladder. *Clin Interv Aging*. 2020;15(8):1493–1503.
9. Murphy AM, Krlin RM, Goldman HB. Treatment of overactive bladder: what is on the horizon? *Int Urogynecol J*. 2013;24(1):5–13.
10. Bhide AA, Tailor V, Fernando R, Khullar V, Digesu GA. Posterior tibial nerve stimulation for overactive bladder—techniques and efficacy. *International Urogynecology Journal*. 2020;31(5):865–870. doi:10.1007/s00192-019-04186-3

11. Arnouk A, De E, Rehfuss A, Cappadocia C, Dickson S, Lian F. Physical, Complementary, and Alternative Medicine in the Treatment of Pelvic Floor Disorders. *Curr Urol Rep*. 2017;18(6):47. doi:10.1007/s11934-017-0694-7
12. Muchtar NJ, Helianthi DR, Nareswari I. Effectiveness of Electroacupuncture for Management of Young Patients with Overactive Bladder at 1-Year Follow-Up. *Med Acupunct*. 2021;33(2):169–174. doi:10.1089/acu.2020.1462
13. Zhao Y, Zhou J, Mo Q, Wang Y, Yu J, Liu Z. Acupuncture for adults with overactive bladder: a systematic review and meta-analysis of randomized controlled trials. *Medicine*. 2018;97(8):e9838. doi:10.1097/MD.0000000000009838
14. Forde JC, Jaffe E, Stone BV, Te AE, Espinosa G, Chughtai B. The role of acupuncture in managing overactive bladder; a review of the literature. *International Urogynecology Journal*. 2016;27(11):1645–1651. doi:10.1007/s00192-015-2935-y
15. Hargreaves E, Harding C, Clarkson C. Acupuncture in addition to standard conservative treatment for overactive bladder; a feasibility trial for a randomized controlled study. *Neurourol Urodyn*. 2021;40(7):1770–1779. doi:10.1002/nau.24741
16. Chang Y-W, Lo T-S, Chang H-N, Shiao Y-H, Yeh Y-C. Laser Acupuncture Alleviates Symptoms and Improves Quality of Life in Women with Overactive Bladder: a Double-Blind, Pilot Randomized Controlled Trial. *Evid Based Complement Alternat Med*. 2020;2020:1705964. doi:10.1155/2020/1705964
17. Aydogmus Y, Sunay M, Arslan H, Aydın A, Adiloğlu AK, Şahin H. Acupuncture versus solifenacin for treatment of overactive bladder and its correlation with urine nerve growth factor levels: a randomized, placebo-controlled clinical trial. *Urol Int*. 2014;93(4):437–443. doi:10.1159/000358202
18. Yuan Z, He C, Yan S, Huang D, Wang H, Tang W. Acupuncture for overactive bladder in female adult: a randomized controlled trial. *World J Urol*. 2015;33(9):1303–1308. doi:10.1007/s00345-014-1440-0
19. Emmons SL, Otto L. Acupuncture for overactive bladder: a randomized controlled trial. *Obstet Gynecol*. 2005;106(1):138–143. doi:10.1097/01.AOG.0000163258.57895.ec
20. Chang PL. Urodynamic Studies in Acupuncture for Women with Frequency, Urgency and Dysuria. *J Urol*. 1988;140(3):563–566. doi:10.1016/S0022-5347(17)41719-8
21. Wein AJ, Rovner ES. Definition and epidemiology of overactive bladder. *Urology*. 2002;60(Suppl 5):7–12. doi:10.1016/S0090-4295(02)01784-3
22. Lightner DJ, Gomelsky A, Souter L, Vasavada SP. Diagnosis and Treatment of Overactive Bladder (Non-Neurogenic) in Adults: AUA/SUFU Guideline Amendment 2019. *J Urol*. 2019;202(3):558–563. doi:10.1097/JU.0000000000000309
23. Bradley CS, Nygaard IE, Hillis SL, Torner JC, Sadler AG. Longitudinal associations between mental health conditions and overactive bladder in women veterans. *Am J Obstet Gynecol*. 2017;217(4):430.e1–430.e8. doi:10.1016/j.ajog.2017.06.016
24. Ouslander JG. Geriatric considerations in the diagnosis and management of overactive bladder. *Urology*. 2002;60(Suppl 5):50–55. doi:10.1016/S0090-4295(02)01795-8
25. Allahdin S, Oo N. An overview of treatment of overactive bladder syndrome in women. *J Obstet Gynaecol*. 2012;32(3):217–221. doi:10.3109/01443615.2011.649317
26. Kwon OS, Kim J, Choi K-H, Ryu Y, Park J-E. Trends in deqi research: a text mining and network analysis. *Integr Med Res*. 2018;7(3):231–237. doi:10.1016/j.imr.2018.02.007
27. Lee S, Chae Y, Kim S-N, et al. Short term effects by acupuncture to SP3 on the autonomic blood flow control. *Neurol Res*. 2010;32(Suppl sup1):37–42. doi:10.1179/016164109X12537002793887
28. Kuo T-C, Lin C-W, Ho F-M. The soreness and numbness effect of acupuncture on skin blood flow. *Am J Chin Med*. 2004;32(1):117–129. doi:10.1142/S0192415X04001825
29. Zhong P, Zeng H, Huang M, Chen L, Fu W. Combined acupuncture and moxibustion therapy for the treatment of neurogenic bladder and bowel dysfunction following traumatic spinal cord injury: a case report. *Explore*. 2021;21:244–245.
30. Fu YQ. Clinical observation on deep-oblique acupuncture with long needle at Guanyuan (CV 4) for urinary retention. *Zhongguo Zhen Jiu*. 2013;33(12):1071–1075.
31. Katekawa L, Iwasaki AC, Shinkai RS, de Campos TT. Acupuncture applied at local or distal acupoints reduces pain related to temporomandibular disorders in female patients. *Int J Prosthodont*. 2021;34(4):428–432.
32. Luo Z, Hu X, Chen C, et al. Effect of Catgut Embedment in Du Meridian Acupoint on Mental and Psychological Conditions of Patients with Gastroesophageal Reflux Disease. *Evid Based Complement Alternat Med*. 2020;2020:5415813.
33. Scaldazza CV, Morosetti C, Giampieretti R, Lorenzetti R, Baroni M. Percutaneous tibial nerve stimulation versus electrical stimulation with pelvic floor muscle training for overactive bladder syndrome in women: results of a randomized controlled study. *Int Braz J Urol*. 2017;43(1):121–126.
34. Manríquez V, Guzmán R, Naser M, et al. Transcutaneous posterior tibial nerve stimulation versus extended release oxybutynin in overactive bladder patients. A prospective randomized trial. *Eur J Obstet Gynecol Reprod Biol*. 2016;196(1):6–10.
35. McGuire E, Morrissey S, Zhang S, Horwinski E. Control of reflex detrusor activity in normal and spinal injured non-human primates. *J Urol*. 1983;129(1):197–199.
36. Ha L, Liu X, Liu Y, et al. Scheme optimization of acupoints compatibility and influence factors of the effect. *Medicine*. 2021;100(50):e27883.
37. Hargreaves E, Baker K, Barry G, et al. Acupuncture for treating overactive bladder in adults. *Cochrane Database Syst Rev*. 2020;2020(1):CD013519.
38. Zhao L, Wang SY. Efficacy impacts of the different treatment frequencies on female stress urinary incontinence. *Zhongguo Zhen Jiu*. 2013;33(12):1088–1090.
39. Wang H, Zhao M, Zhang JW, et al. The Efficacy of Acupuncture on Patients with Erectile Dysfunction: a Review. *Evid Based Complement Alternat Med*. 2022;2022:4807271.
40. Litscher G. History of Laser Acupuncture: a Narrative Review of Scientific Literature. *Med Acupunct*. 2022;32(4):201–208.
41. McCloskey KD. Interstitial cells in the urinary bladder–localization and function. *Neurourol Urodyn*. 2010;29(1):82–87.
42. Davidson RA, McCloskey KD. Morphology and localization of interstitial cells in the Guinea pig bladder: structural relationships with smooth muscle and neurons. *J Urol*. 2005;173(4):1385–1390.
43. Vannucchi MG, Traini C. The telocytes/myofibroblasts 3-D network forms a stretch receptor in the human bladder mucosa. Is this structure involved in the detrusor overactive diseases? *Ann Anat*. 2018;218(7):118–123.
44. Kubota Y, Kojima Y, Shibata Y, Imura M, Sasaki S, Kohri K. Role of KIT-Positive Interstitial Cells of Cajal in the Urinary Bladder and Possible Therapeutic Target for Overactive Bladder. *Adv Urol*. 2011;2011:816342.

45. Deng T, Zhang Q, Wang Q, Zhong X, Li L. Changes in hyperpolarization-activated cyclic nucleotide-gated channel expression and activity in bladder interstitial cells of Cajal from rats with detrusor overactivity. *Int Urogynecol J*. 2015;26(8):1139–1145.
46. Juszczak K, Maciukiewicz P, Drewa T, Thor PJ. Cajal-like interstitial cells as a novel target in detrusor overactivity treatment: true or myth? *Cent European J Urol*. 2014;66(4):413–417.
47. Feng QF, Hou YH, Hou WG, Lin ZX, Tang KM, Chen YL. The effects of acupuncture on bladder interstitial cells of Cajal excitability in rats with overactive bladder. *Evid Based Complement Alternat Med*. 2013;2013:261217.
48. Lu JY, Ying XW, Chen XL, Tu WZ, Li SS, Jiang SH. Effects of electroacupuncture at different acupoints on the histomorphology of neurogenic bladder and the expression of hyperpolarization-activated cyclic nucleotide-gated channels in interstitial cells of Cajal in a rat model of suprasacral spinal cord injury. *Ann Palliat Med*. 2020;9(6):3830–3838.
49. Antunes-Lopes T, Cruz F. Urinary Biomarkers in Overactive Bladder: revisiting the Evidence in 2019. *Eur Urol Focus*. 2019;5(3):329–336.
50. Riccio A, Pierchala BA, Ciarallo CL, Ginty DD. An NGF-TrkA-mediated retrograde signal to transcription factor CREB in sympathetic neurons. *Science*. 1997;277(5329):1097–1100.
51. Liu HT, Kuo HC. Urinary nerve growth factor level could be a potential biomarker for diagnosis of overactive bladder. *J Urol*. 2008;179(6):2270–2274.
52. Liu HT, Chancellor MB, Kuo HC. Decrease of urinary nerve growth factor levels after antimuscarinic therapy in patients with overactive bladder. *BJU Int*. 2009;103(12):1668–1772.
53. Kim JC, Park EY, Seo SI, Park YH, Hwang TK. Nerve growth factor and prostaglandins in the urine of female patients with overactive bladder. *J Urol*. 2006;175(5):1773–1776.
54. Lin ZX, Chan NHT, Kwan YK, et al. A randomized controlled trial to assess the effectiveness and safety of acupuncture for overactive bladder: a study in Hong Kong population. *Chin Med*. 2020;15(10):108.
55. Kadekawa K, Majima T, Shimizu T, et al. The role of capsaicin-sensitive C-fiber afferent pathways in the control of micturition in spinal-intact and spinal cord-injured mice. *Am J Physiol Renal Physiol*. 2017;313(3):F796–F804.
56. Dmochowski RR, Appell RA. Advancements in pharmacologic management of the overactive bladder. *Urology*. 2000;56(6 Suppl 1):41–49.
57. Ito T, Sakakibara R, Yamamoto T, et al. Urinary dysfunction and autonomic control in amyloid neuropathy. *Clin Auton Res*. 2006;16(1):66–71.
58. Hino K, Honjo H, Nakao M, Kitakoji H. The effects of sacral acupuncture on acetic acid-induced bladder irritation in conscious rats. *Urology*. 2010;75(3):730–734.
59. Wang Y, Hassouna MM. Neuromodulation reduces c-fos gene expression in spinalized rats: a double-blind randomized study. *J Urol*. 2000;163(6):1966–1970.
60. De Ridder D, Chandiramani V, Dasgupta P, Van Poppel H, Baert L, Fowler CJ. Intravesical capsaicin as a treatment for refractory detrusor hyperreflexia: a dual center study with long-term followup. *J Urol*. 1997;158(6):2087–2092.
61. Yu JN, Ma XJ, Liu ZS, et al. Effect of electroacupuncture at Ciliao (BL 32) on c-fos expression in the sacral segment of spinal cord in rats with detrusor hyperreflexia. *Zhen ci yan jiu*. 2010;35(3):204–207.