

Review

Acupuncture for Treatment of Overactive Bladder

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HIGHLIGHTS

- Overactive bladder (OAB) has a high prevalence and has a negative impact on patients' quality of life.
- Given the widespread individual and social problems, comprehensive treatment of OAB is necessary.
- Acupuncture as one of the complementary and alternative medicine methods, is a simple and low-risk way which can play an effective role in the treatment of OAB.

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ABSTRACT

Overactive bladder (OAB) is defined as bladder storage dysfunction, which results in a frequent and sudden urge to urinate. OAB is a prevalent disorder, and its symptoms have a detrimental effect on health-related quality of life and increase social problems. Treatment of OAB includes first-line behavioral therapies and second-line anti-muscarinic drugs. However, the rate of drug discontinuation due to drug side effects is high. Acupuncture is considered an effective therapy to suppress contractions and excessive detrusor muscle activity, improve bladder adaptation, maintain normal urination, and improve pathological changes in bladder tissue based on several preclinical and clinical investigations. Therefore, as one of the complementary and alternative medicine methods, acupuncture can play a pivotal role in the treatment of patients with OAB.

Keywords: Acupuncture; Overactive bladder; Urinary incontinence; Treatment

Introduction

As defined by the International Continence Society, overactive bladder (OAB) is associated with bladder storage dysfunction, which results in frequent and sudden urge to urinate (1, 2). The need to urinate may be uncontrollable, and urination may happen involuntarily, known as urinary incontinence (1). The patients with an

OAB suffer the following symptoms:

- Feeling a sudden urge to urinate that is difficult to control,
- Unintentional loss of urine, usually eight or more times a day
- Nocturia, defined as waking up to urinate more than

twice each night.

The presence or absence of urinary incontinence can usually be observed with increasing periods of nocturia without urinary tract infection or any other significant pathology (3). OAB symptoms have a detrimental effect on health-related quality of life and increase social problems (2, 4, 5). Moreover, it is estimated that 16-26 billion US \$ is spent annually in the United States on urinary incontinence management (6). The prevalence of OAB varies between 5.2% to 22% and increases with advancing age in adults (7, 8). In general, 17% of Americans suffer from OAB syndrome, and about half of adult women experience urinary incontinence (1).

The primary pathophysiological process involved in OAB is an involuntary contraction of the bladder smooth muscles even when the volume of urine is low (9). These involuntary contractions create an urgent need for urination.

Several underlying comorbidities are able to predispose the patients to OAB, including (8):

- Diabetes
- Urinary tract infections
- Neurological disorders such as stroke and multiple sclerosis
- Hormonal changes during menopause in women
- Bladder abnormalities such as tumors or bladder stones, and
- Obstructive urinary diseases due to an enlarged prostate, constipation, or previous treatments for other types of incontinence.

These comorbidities are associated with an increased risk of OAB, with high rates of urinary incontinence in affected patients. Additionally, numerous risk factors have been identified to be correlated with symptoms of OAB. For instance, excessive caffeine or alcohol consumption, and medications that increase the urine volume or require a large amount of fluid intake lead to overexpressed OAB symptoms (10). In addition, elderly patients with decreased cognitive function and difficulty in ambulation are more susceptible to experiencing OAB symptoms and urinary incontinence because of the inability to reach the toilet quickly (11).

Taken together, given the widespread individual and social problems and the large economic burden of OAB, its comprehensive treatment is of utmost importance. Treatment of OAB includes first-line behavioral therapies such as control of water intake, delay urination training, pelvic floor exercises, and lifestyle adjustments (12). Second-line therapies consist of drug management with anti-muscarinic drugs such as oxybutynin, solifenacin, tolterodine, and phosphotrocin (13). Mirabegron is a new class of drugs, a beta-3 adrenergic receptor agonist that has had a positive impact on the management of OAB (11).

Regarding the treatment of OAB, according to the American Urological Association, the rate of drug

discontinuation as a result of side effects ranges from 54% to 71%, depending on the types of drugs administered and the side effects that occurred (14). Third-line treatments include invasive techniques such as botulinum toxin injection and nerve modulation, which are generally intended for patients who were not successfully managed with second-line drugs (15).

Nowadays, patients are more inclined to seek alternative medicine to treat OAB symptoms. Acupuncture is considered one of several alternative therapies that have been suggested for OAB management (16). Acupuncture has been used for more than 2000 years, and its application is increasing dramatically as an alternative treatment method, especially in Asia-Pacific (17). The World Health Organization has recommended this modality as an acceptable treatment option for bladder dysfunction (18). Electroacupuncture, a form of acupuncture characterized by the flow of a small electric current between pairs of acupuncture needles, is regarded as a common treatment for OAB in traditional Chinese medicine (19). This technique is considered an effective therapy to suppress contractions and excessive detrusor muscle activity, improve bladder adaptation, maintain normal urination, and improve pathological changes in bladder tissue (1, 19). Herein, we provide a brief overview concerning the impact of acupuncture on the management of OAB.

Preclinical and clinical investigations

Although the exact mechanism of action regarding the impact of acupuncture in controlling the OAB symptoms is not fully understood thus far, it is hypothesized that acupuncture can send signals to the spinal cord through sensory ganglia and interneurons, therefore regulating the activity of motor neurons in the brainstem that controls autonomic functions, including urinary activity. Stimulation of the sacral region may suppress bladder contraction and alter the function of bladder activity-related neurons in and around the urinary center of the pons via the gamma-aminobutyric acidergic (GABAergic) system (20).

Sato et al., investigated the bladder function in rats and concluded that administration of acupuncture-like stimulation to the perineum with a needle inhibits rhythmic involuntary contractions (21). When the pudendal and pelvic nerves were transected bilaterally, this inhibition was not observed. In another study, Wang et al., observed that suppression of bladder contractions in rats happens immediately after stimulation of the sacral area with needle acupuncture (20). This effect was related to the alteration of neuron profiles involved in bladder activity in and around the Barrington nucleus. The authors concluded that acupuncture has a significant effect on bladder activity. It has been reported that the stimulation points used in this study are consistent with classical acupuncture bladder channel points in traditional Chinese medicine (Figure 1). Besides, the use of GABA

agonists before acupuncture shortened the persistence of acupuncture effects, meaning that acupuncture may act through the GABA receptor system.

Meng et al., induced bladder hyperactivity in rabbit models by a cholinergic stimulus (22). In their study, one group underwent acupuncture, and the other group was treated by anticholinergics, and urodynamic tests were applied for the assessment of the endpoints. The final results showed that the rate of bladder emptying improved significantly in the acupuncture group. In this context, Davidson et al., investigated the effect of acupuncture on interstitial cell activity in mice with partial bladder outlet obstruction (23). According to their results, interstitial cell activity plays a pivotal role in the onset of bladder contractile activity and acts as a coordinator of bladder muscle contractions, resembling a pacemaker to produce depolarizing currents in adjacent smooth muscle. Acupuncture causes a decrease in the number of biological markers in interstitial cell activities and intracellular calcium ion concentration, which initially is increased in OAB.

In the bladder, P2X3 receptors on the detrusor muscle act as motor receptors; nonetheless, it seems that they play a sensory role as well (24). Their sensory function is to fill and empty a physiological bladder and act as a pain receptor in pathological conditions. There is evidence of increased P2X3 receptor expression in the urothelium of patients with OAB, and the role of P2X3 receptors in the urgency and pathophysiology of OAB has become the focus of intense attention. Feng et al., have investigated the role of this receptor in the OAB and the effect of acupuncture on this receptor in mice (24). The results

have demonstrated that electroacupuncture improves OAB symptoms by blocking P2X3 receptors. The effect of electroacupuncture was attenuated after P2X3 receptor block via intravenous administration of AF-353.

These preliminary studies have examined acupuncture as an alternative or adjunctive therapy for OAB and demonstrated clinical efficacy with a biochemical mechanism of action (MOA), in pharmacology, MOA refers to the specific biochemical interaction through which a drug substance produces its pharmacological effect. A mechanism of action usually includes mention of the specific molecular targets to which the drug binds, such as an enzyme or receptor,. However, the limitations of the available studies and the existence of contradictory outcomes in some cases make it impossible to reach definitive conclusions.

Several studies reviewing the clinical trials in humans have concluded that OAB symptoms improve with acupuncture, and some studies have reported objective improvements in the urodynamic investigations (1, 3, 18). It should be noted that many comparative studies have shown that the benefits of acupuncture in OAB treatment are comparable to anti-muscarinic drugs. Concerning the acupuncture method, the depth of needle placement, the acupuncture points used, and the treatment duration were heterogeneous among the studies. Sandra L reported that Women who received bladder specific acupuncture treatments showed significant improvements in bladder capacity, urgency, frequency, and quality of life as compared with women who received placebo acupuncture treatment (25). Also, Aydoğmuş in 2014 compares the effect of acupuncture versus solifenacin for treatment

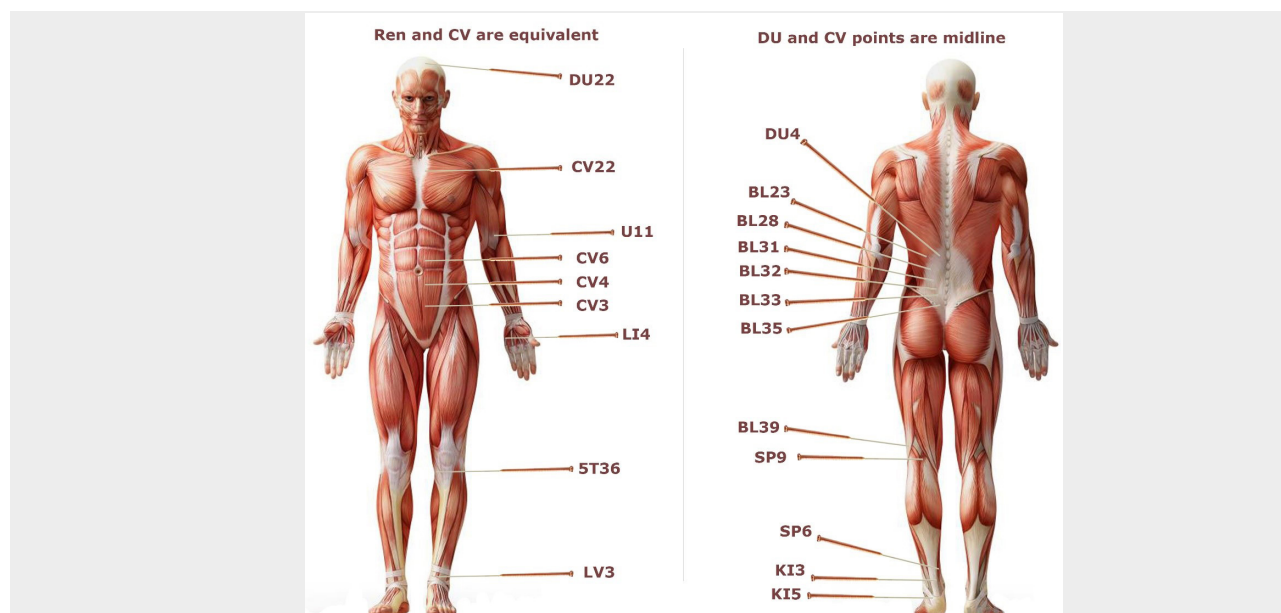


Figure 1. Classical acupuncture bladder channel points

of overactive bladder reported. In patients with OAB in whom anticholinergic treatment is contraindicated, acupuncture is effective and may be considered another treatment option (26).

A meta-analysis that compared the effectiveness of electroacupuncture with drug therapy of OAB (tolterodine and solifenacin) confronted many obstacles to reach definitive conclusions due to substantial heterogeneity among the studies (3). However, the authors reported that electroacupuncture possibly improved patients' quality of life and stated that further studies are required to provide robust evidence about the effects of acupuncture in the treatment of OAB. The United States Department of Health and Human Services and Quality Research Agency conducted a comprehensive review of OAB treatment in women (17). They concluded that acupuncture produces impressive results in reducing the number of urination episodes and symptoms of urgency. All in all, according to the clinical trials and systematic reviews, acupuncture has a potential clinical therapeutic efficacy on OAB.

Recommended methods of acupuncture

Depending on the method used, several small, sterile needles are inserted along the meridian lines and acupuncture points to reduce pain with various mechanisms based on western and eastern acupuncture (1, 3, 17). In various studies, the agreed points for treatment of OAB are as follows: KI3, KI5, SP6, SP9, BL23, BL28, BL31, BL32, BL33, BL39, CV4, ST36, LI4, DU22, REN4. There are needles with different materials, including steel, silver, and gold needles, in the market. The needles are different in terms of length and diameter; the needles used in acupuncture are thin and usually have a diameter of 0.25-0.3 mm. No major incisions or wounds are made in the skin during the needle insertion.

The diameter of inserted needles and depth of penetration in acupuncture is much less than the injection cases and varies depending on the type of disease and the target points. Insertion of the needles into the lumbar tissue results in a fragile pain called a chi sensation, which is in the form of numbness or tingling or a weak electrical shock. Usually, thin needles (25*25) are used. The needles stay in place for 20 to 30 minutes, and patients are advised to attend 10 to 12 sessions of treatment.

Acupuncture has limited side effects that need to be reviewed after each session. Some of the most important ones include bruising and bleeding, a burning sensation at the needle site, hypotension due to the needle penetration, and rare infection (1). In general, acupuncture is considered a safe, uncomplicated, and low-risk method.

Conclusions

OAB has a high prevalence and has a negative impact on patients' quality of life. As one of the complementary and

alternative medicine methods, acupuncture is a low-risk and straightforward modality that can play a pivotal role in the treatment of OAB. Given that drugs, as the first-line treatment, have several side effects with insufficient effects in some cases, complementary medicine methods such as acupuncture can aid in the management of patients with OAB.

Authors' contributions

All authors contributed equally.

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Conflict of interest

The author declares that there are no conflicts of interest.

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Ethical statements

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Data availability

Data will be provided on request.

Abbreviations

GABA Gamma-aminobutyric acidergic
OAB Overactive bladder

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