



# Efficacy of Acupuncture Versus Sham Acupuncture in Treating Overactive Bladder: a Randomized Controlled Trial



Ma D<sup>1</sup>, Cao F<sup>1</sup>, Tang J<sup>1</sup>, Chen Y<sup>1</sup>, Liu Q<sup>1</sup>, Pang R<sup>1</sup>  
1. Guang'anmen Hospital, China Academy of Chinese Medical Sciences

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## Hypothesis / aims of study

Overactive bladder (OAB) is a common condition in adult and the prevalence increases significantly with age. Although OAB is not life-threatening, it has a significantly negative impact on quality of life (QoL). Not only do the bothersome OAB symptoms limit the patients' physical, social and sexual activities, but also may cause the mental disorders.

The management of OAB remains a challenge, even though a number of treatment options are available. While behavior therapy and pharmacotherapy are generally employed as initial treatment, the efficacy is diminished by poor adherence [1]. For refractory OAB, percutaneous tibial nerve stimulation, onabotulinumtoxin A, and sacral neuromodulation are considered as the optional treatments, but the complications and costs limit their clinical use.

Acupuncture has been recognized as an effective therapeutic approach for various urological diseases. There is, however, limited evidence to support acupuncture's efficacy and safety in treating OAB. Thus, this study aims to assess the effectiveness and safety of acupuncture for OAB compared with sham acupuncture.

## Study design, materials and methods

Patients with OAB symptoms (a score of more than 3 points on the OABSS and a score of more than 2 points on question 3) for more than 3 months were recruited and randomly divided into either acupuncture or sham acupuncture group at a 1:1 ratio, utilizing random numbers produced by JMP version 16 (SAS Institute. Inc., Cary, NC).

In terms of acupuncture intervention, the selected acupoints include bilateral BL33 (Zhong Liao), BL35 (Hui Yang), ST36 (Zu San Li), and SP6 (San Yin Jiao). After inserting the needles, the handles of the needles at BL33 and BL35 are attached to an electro-acupuncture apparatus to provide 30 minutes of disperse-dense wave electrical stimulation at a frequency of 4/20 Hz for 30 min, three times per week for 8 weeks. Regarding sham acupuncture procedure, the points located at 20mm outward to bilateral BL33, BL35, SP36 and SP6 are inserted superficially. The same portable electro-stimulator and electrode connection with the acupuncture group are applied, but no real current is outputted due to broken internal wires. To blind the participants, the electro-stimulator provides same visual signal (a flashing light) and sound with the acupuncture group.

The two co-primary outcomes will be the change in the mean numbers of micturition per 24 h from baseline to week 8 (end of intervention) and week 20 (follow-up) respectively, which are calculated based on 3-day bladder diaries. Secondary outcomes included the change in mean urgency, daytime micturition and nocturia episodes per 24 h, which were also calculated based on 3-day bladder diaries, OABSS, Overactive Bladder Questionnaire Short Form (OAB-q SF) from baseline to week 8 and week 20 respectively. Additionally, the urinary nerve growth factor (NGF), brain derived neurotrophic factor (BDNF) and monocyte chemoattractant protein-1 (MCP-1) were measured at baseline and week 8 as the secondary outcomes. All adverse events during the study were recorded clearly and evaluated as the safety assessment.

Table 1. Baseline demographic and OAB characteristics.

	Acupuncture (N = 30)	Sham-Acupuncture (N = 30)	P value
Age, Mean (SD)	54.33 (15.07)	57.10 (11.53)	0.428
Sex, N (%)			
Male	16 (53.3%)	22 (73.3%)	0.108
Female	14 (46.7%)	8 (26.7%)	
BMI, Mean (SD)	24.35 (4.92)	25.33 (3.56)	0.383
Current Smoker, N (%)	3 (10%)	9 (30%)	0.104
Current Drinker, N (%)	4 (13.3%)	4 (13.3%)	1.000
Wet OAB , N (%)	21 (70%)	21 (70%)	1.000
Hypertension, N (%)	12 (40%)	11 (36.7)	1.000
Diabetes, N (%)	4 (13.3%)	4 (13.3%)	1.000
Micturition/24 h, Mean (SD)	12.65 (4.30)	11.74 (3.76)	0.391
Daytime micturition/24 h, Mean (SD)	10.38 (3.48)	9.43 (2.65)	0.242
Nocturia episodes/24 h, Mean (SD)	2.27 (1.16)	2.31 (1.44)	0.896
Urgency episodes/24 h, Median (IQR)	4.50 (6.75)	3.50 (6.08)	0.684
OABSS, Mean (SD)	10.27 (2.57)	10.23 (2.71)	0.961
OAB-q SF, Mean (SD)			
Symptom bother score	62.56 (22.87)	60.78 (22.94)	0.765
HRQL score	33.64 (20.18)	38.92 (15.10)	0.256
NGF/Cr (pg/mg), Median (IQR)	3.28 (4.50)	2.70 (2.64)	0.115
BDNF/Cr (pg/mg), Median (IQR)	5.69 (7.81)	4.03 (4.57)	0.093
MCP-1/Cr (pg/mg), Median (IQR)	2.24 (4.36)	1.50 (2.76)	0.511

BMI = body mass index; SD = standard deviation; IQR = Interquartile Range; OAB-q SF =Overactive bladder quality of life short-form questionnaire; OABSS = Overactive Bladder Symptom Score; HRQL = Health-Related Quality of Life;

## Results and interpretation

Between Mar, 2022, and Aug, 2023, a total of 68 patients with OAB were enrolled, and 60 patients were included in the interim analysis of the trial. At baseline, no statistically significant differences are detected in patients' characteristics between the two groups.

After 8 weeks, the acupuncture group presents a significant decrease in the mean numbers of micturition per 24 h compared to the baseline (-2.78, 95%CI [-4.62 to -0.94], P < 0.01), but the sham-acupuncture group (-0.81, 95%CI [-2.56 to 0.94], P=0.36) does not. In terms of comparison between groups, the acupuncture group exhibited a significant improvement compared to sham one (-1.97, 95%CI [-2.96 to -0.97], P < 0.01). Compared to sham acupuncture group, the acupuncture group also demonstrates significant improvements in urgency episodes per 24 h (-3.33 [IQR 4.75] vs -1.00 [IQR 1.42], P < 0.05), daytime micturition per 24 h (-2.02±1.45 vs -0.54±1.41, P < 0.01) , nocturia episodes per 24 h (-0.76±0.76 vs -0.27±0.66, P=0.01), OABSS(-3.47 ± 2.73 vs -1.27 ± 1.60, P < 0.01), OAB-q SF symptom bother score (-26.89±21.41 vs -13.44±11.95, P < 0.01), and OAB-q SF HRQL score (23.13±16.90 vs 12.87±9.36, P < 0.01). Moreover, the levels of urinary NGF and BDNF in acupuncture group show a significant decrease after 8-week treatment, which is not found in the control group. Although the level of urinary MCP-1 also shows a slight decrease in acupuncture group, no statistically difference is detected. Additionally, the improvement effect of acupuncture on most outcomes can last 20 weeks.

Table 2. Outcome

Outcome	8 Weeks		P value	20 Weeks		P value
	Acupuncture (N=30)	Sham-Acupuncture (N=30)		Acupuncture (N=30)	Sham-Acupuncture (N=30)	
Micturition						
CFB (95% CI)	-2.78 (-4.62, -0.94)	-0.81 (-2.56, 0.94)	< 0.01	-2.23 (-4.11, -0.35)	-0.84 (-2.60, 0.92)	0.03
DID (95% CI)	-1.97 (-2.96, -0.97)			-1.19 (-2.27, -0.11)		
Urgency episodes						
CFB (95% CI)	-3.33 (-4.17, -2.17)	-1.00 (-1.50, -0.50)	< 0.01	-2.84 (-4.17, -1.17)	-1.00 (-1.50, 0.50)	< 0.01
DID (95% CI)	-2.00 (-3.01, -1.00)			-1.34 (-2.67, -0.66)		
Daytime micturition						
CFB (95% CI)	-2.02 (-3.53, -0.51)	-0.54 (-1.83, 0.77)	< 0.01	-1.68 (-3.21, -0.14)	-0.53 (-1.82, 0.77)	0.02
DID (95% CI)	-1.48 (-2.22, -0.74)			-1.00 (-1.83, -0.16)		
Nocturia episodes						
CFB (95% CI)	-0.76 (-1.23, -0.28)	-0.27 (-0.89, 0.36)	0.01	-0.55 (-1.04, -0.07)	-0.31 (-0.94, 0.32)	0.30
DID (95% CI)	-0.49 (-0.86, -0.12)			-0.19 (-0.56, 0.18)		
OABSS						
CFB (95% CI)	-3.47 (-5.08, -1.85)	-1.27 (-1.86, -0.67)	< 0.01	-2.95 (-4.59, -1.30)	-1.20 (-2.69, 0.29)	< 0.01
DID (95% CI)	-2.2 (-3.35, -1.05)			-1.75 (-2.87, -0.63)		
OAB-q SF						
Symptom bother score						
CFB (95% CI)	-26.89 (-38.23, -15.55)	-13.44 (-24.73, -2.15)	< 0.01	-24.34 (-35.88, -12.80)	-11.37 (-22.87, 0.12)	0.01
DID (95% CI)	-13.44 (-22.40, -4.48)			-12.62 (-22.48, -2.76)		
HRQL score						
CFB (95% CI)	23.13 (16.82, 29.44)	12.87 (9.38, 16.37)	< 0.01	25.67 (15.79, 35.54)	10.95 (2.19, 19.71)	0.02
DID (95% CI)	10.26 (3.20, 17.32)			10.99 (2.21, 19.76)		

CFB = Change from Baseline; DID = Difference in Difference; CI = Confidence Interval.

## Interpretation

The interim analysis of this study indicates that acupuncture can not only improve patients' OAB symptoms and QoL, but also the urine biomarkers of OAB significantly compared to sham acupuncture group. The potential mechanism may be the regulation effect of acupuncture on sacral nerve and pudendal nerve, which can decrease muscarine receptors binding capacities and down-regulate the VR1 expression in sacral micturition center.

## Conclusions

Acupuncture is an effective and safe approach for OAB patients that is capable of improving both subjective and objective outcomes. Additionally, there is a correlation between acupuncture treatment and changes in urinary NGF and BDNF levels among OAB patients.

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