

This is a provisional PDF only. Copyedited and fully formatted version will be made available soon.



P O L I S H G Y N E C O L O G Y

# GINEKOLOGIA POLSKA

ORGAN POLSKIEGO TOWARZYSTWA GINEKOLOGICZNEGO  
THE OFFICIAL JOURNAL OF THE POLISH GYNECOLOGICAL SOCIETY

ISSN: 0017-0011

e-ISSN: 2543-6767

## **The therapeutic effect of Neuromuscular electrical stimulation by different pulse widths for overactive bladder in elderly women – a randomized controlled study**

**Authors:** Aiming Lv, Tianzi Gai, Qing Feng, Min Li, Wenhui Deng, Qiubo Lv

**DOI:** 10.5603/GP.a2021.0181

**Article type:** Research paper

**Submitted:** 2020-12-17

**Accepted:** 2021-04-06

**Published online:** 2021-10-05

This article has been peer reviewed and published immediately upon acceptance. It is an open access article, which means that it can be downloaded, printed, and distributed freely, provided the work is properly cited. Articles in "Ginekologia Polska" are listed in PubMed.

## ORIGINAL PAPER/GYNECOLOGY

### **The therapeutic effect of Neuromuscular electrical stimulation by different pulse widths for overactive bladder in elderly women — a randomized controlled study**

Aiming Lv, Tianzi Gai, Qing Feng, Min Li, Wenhui Deng, Qiubo Iv

*Department of Obstetrics and Gynecology, Beijing Hospital, National Center of Gerontology, Institute of Geriatric Medicine, Chinese Academy of Medical Sciences, China*

#### **Corresponding author:**

Qiubo Iv

Department of Obstetrics and Gynecology, Beijing Hospital, National Center of Gerontology, Institute of Geriatric Medicine, Chinese Academy of Medical Sciences, Beijing 100730, P.R. China

e-mail: qiubo2185@126.com

#### **ABSTRACT**

**Objectives:** There have been a number of controversies about which treatment of neuromuscular electrical stimulation (NMES) is more beneficial for overactive bladder (OAB). An attempt to investigate the therapeutic effect of NMES with different pulse widths for OAB in elderly women has been made in this study.

**Material and methods:** The postmenopausal elderly women without pelvic organ prolapse (POP) who received transvaginal NMES in Beijing Hospital from November 2020 to December 2020 were randomly divided into two groups (Group A and Group B). Patients from Group A accepted the treatment with NMES by pulse width of 300  $\mu$ s and patients from Group B accepted the treatment with NMES by pulse width of 200  $\mu$ s. Myoelectric potential of Type I and Type II muscle fibers at pelvic floor and overactive bladder symptom score (OABSS) were valued.

**Results:** There were 46 patients eligible for the study and randomly divided into Group A and Group B, 23 patients for each group. OABSS were significantly reduced in both groups after the treatment of NEMS. And OABSS in Group A (after treated by pulse width of 300  $\mu$ s) were significantly decreased greater than those in Group B (after treated with pulse width of 200  $\mu$ s). Both Group A and Group B had no significant difference in the mean myoelectric potential at pre-resting state when compared before and after the treatment of NEMS. Myoelectric potential of Type I muscle fiber and the maximum myoelectric potential of Type II muscle

fibers were significantly increased after the treatment of NEMS than before the treatment in the two groups, respectively. And myoelectric potential of Type I muscle fiber and the maximum myoelectric potential of Type II muscle fibers in group A (after treated with pulse width of 300  $\mu$ s) were increased significantly much higher than those in Group B (after treated with pulse width of 200  $\mu$ s).

**Conclusions:** Comparing the indicators before and after the treatments of NMES, our study has preliminarily confirmed that NMES has its advantages in treating with OAB. And NMES by pulse width of 300 $\mu$ s were more effective in improving pelvic floor muscle strength than NMES by pulse width of 200 $\mu$ s.

**Key words:** neuromuscular electrical stimulation; overactive bladder; pelvic floor muscles; overactive bladder symptom score; myoelectric potential; pulse width

## INTRODUCTION

According to the Definition of the International Continence Society (ICS), an overactive bladder (OAB) was recognized as a “symptom syndrome suggestive of [lower urinary tract dysfunction](#).” It is specifically defined as “urgency, with or without [urge incontinence](#), usually with frequency and [nocturia](#)” [1]. In China, the prevalence of OAB was 6.0% (5.9% for the male and 6.0% for the female), among which a female more than 50 years old accounted for 46.3% [2]. In the United States, the prevalence of OAB was 16.5% (16.0% for the male, 16.9% for the female) and has a trend of increasing with the age growing among the female (from 2% to 19%), especially among those more than 44 years old [3]. In Europe, epidemiological data indicated that among women over 40 years old, the prevalence of OAB was 16.6% and has been increased with the age growing as well [4]. It can be concluded that postmenopausal women are at a great risk of OAB. Studies have shown that in healthy postmenopausal middle-aged and elderly women, the incidence of OAB was 15–37% [5], among which 20.5% needed clinical intervention [6, 7], exerting great psychological pressure on patients. The pathogenesis of OAB mainly includes non-neurogenic detrusor instability, overactive bladder, dysfunctions of urethra and pelvic floor muscles, abnormal hormone metabolisms and so on. In addition to screening tests, overactive bladder symptom score (OABSS) has been proved to be highly sensitive to the diagnosis of OAB [8]. Traditional treatments for OAB include bladder training, pelvic floor muscle training (PRMT), anticholinergic drug, sacral nerve stimulation (SNS) and surgery. RCT studies have identified

that bladder training [9], PRMT [10, 11] and drug therapy [10] could improve the symptoms of OAB. However, the side effects of drug therapy, such as constipation and dry mouth, has affected the medication adherence, with only 10–30% of the OAB population taking the medication as prescribed for at least one year [12]. SNS and surgery are invasive treatments, with limits in the clinical practice. As a noninvasive treatment, some studies [13–16] have found that neuromuscular electrical stimulation (NMES) could inhibit unstable muscle contractions and spastic musculature, regulate the hypoxic state of the muscles and strengthen the pelvic floor muscle, to improve pelvic floor disorders, such as pelvic organ prolapsed (POP), urinary incontinence and sexual dysfunction. However, there have been a number of controversies about which treatment of NMES is more beneficial for OAB.

### **Objectives**

Our study is aiming to compare the therapeutic effect of NMES with different pulse width for OAB in elderly women, providing evidence for the treatments.

## **MATERIAL AND METHODS**

### **Subjects**

Postmenopausal women with OAB as chief complaint in Beijing Hospital from November 2020 to December 2020 were selected.

### **Inclusion criteria**

- (1) More than 12 months from the last menstrual period;
- (2) Score of "urgent urination" on OABSS questionnaire of overactive bladder (OABSS)  $\geq 2$  points, and total score  $\geq 3$  points. Patients both meet the above two criteria can be enrolled.

### **Exclusion criteria**

- (1) Routine urine test suggested urinary tract infection or ultrasound suggested vesical calculus;
- (2) Pelvic organ prolapse quantification system (POP-Q) suggested the lowest extent in the vagina was  $\geq 0$  cm from the hymenal ring;
- (3) Patients had taken anticholinergic drugs or received behavioral therapy for OAB such as bladder training three months before the enrollment;
- (4) Patients with a pacemaker implanted;

- (5) Patients in the acute stage of vaginal inflammation;
- (6) Patients with malignant tumors;
- (7) Patients suffering from mental illness and unable to cooperate with treatments;
- (8) Transabdominal ultrasound indicated that the residual volume of urine in the bladder was > 50 mL;
- (9) Urination diary indicated that daily water intake was > 2000 mL in average;
- (10) Patients with nervous system diseases;
- (11) Patients with massive space-occupying lesions in pelvis cavity and abdominal cavity;
- (12) patients with a history of urological surgery. Patients meeting any of the exclusion criteria would be excluded.

### **Pre-treatment evaluation**

The same doctor conducted the consultation, gynecological examination, POP-Q examination, and OABSS investigation for both groups. Two other operators were assigned to measure the pelvic floor myoelectric potential for the patients through the Pelvic Floor SEMG Analysis and Biological Feedback Training System (MID A2, Medlander, Nanjing City, China). Four symptoms addressing day-time frequency, night-time frequency, urgency, and urgency incontinence are scored in the Homma OABSS questionnaire (Appendix 1) [17]. The total score is the sum of the four parts.

### **Randomization**

Eligible patients were randomly assigned based on balanced treatment assignments with a computerized randomization allocation sequence via using blocks of 46 opaque, sealed envelopes to include the information of the treatments of NMES with different pulse width (300  $\mu$ s or 200  $\mu$ s) and divided into two groups. Both the patients and the physician in the pre-treatment evaluation were blind to the treatments.

### **Treatments of NMES**

Neuromuscular stimulation Therapy Systems (MID B6, Medlander, Nanjing City, China) was applied in the treatment by two designated operators. With the patient in supine position, an electrode is placed into the vagina (the electrode is placed completely within the hymenal ring). Group A received the treatments with the frequency of 5Hz, pulse width of 300  $\mu$ s, ramp time of 0 second and the duration of 30 minutes. Group B received the treatments with

the frequency of 5Hz, pulse width of 200  $\mu$ s, ramp time of 0 second, the duration of 30 minutes. The treatments were performed in both groups once every 2–3 days for a total of 10 times. The therapeutic magnitude of the current is determined by the patients' feeling of strong muscle contraction or tingling without pain. The maximum safe current was 100 mA.

### **Post-treatment evaluation**

Two of the same operators in the pre-treatment evaluation were assigned to measure the pelvic floor myoelectric potential with the Pelvic Floor SEMG Analysis and Biological Feedback Training System (MID A2, Medlander, Nanjing City, China) and finish the OABSS questionnaire for the second time within two days after all the treatments performed for the patients.

### **Statistical analysis**

The software of EpiData 3.1 was used to input research data and SPSS 32.0 was used for statistical analysis. The quantitative variables within each group were described using means, medians and standard deviations. In addition, the Shapiro-Wilk normality test was applied. For variables with normal distribution in the two groups, Student's *t* test was used to compare between the groups; otherwise, the Mann-Whitney test was used. For paired data in the pre- and post- treatment with normal distribution, paired *t*-test was used; otherwise, Wilcoxon signed rank test was used. The qualitative variables were described with frequencies and percentages and analyzed with Chi-square test. All tests were two sided, and *p*-values < 0.05 were considered statistically different. According to the principle of intent-to-treat analysis (ITT), all the subjects were included in the statistical analysis, whether they received all treatments or not.

## **RESULTS**

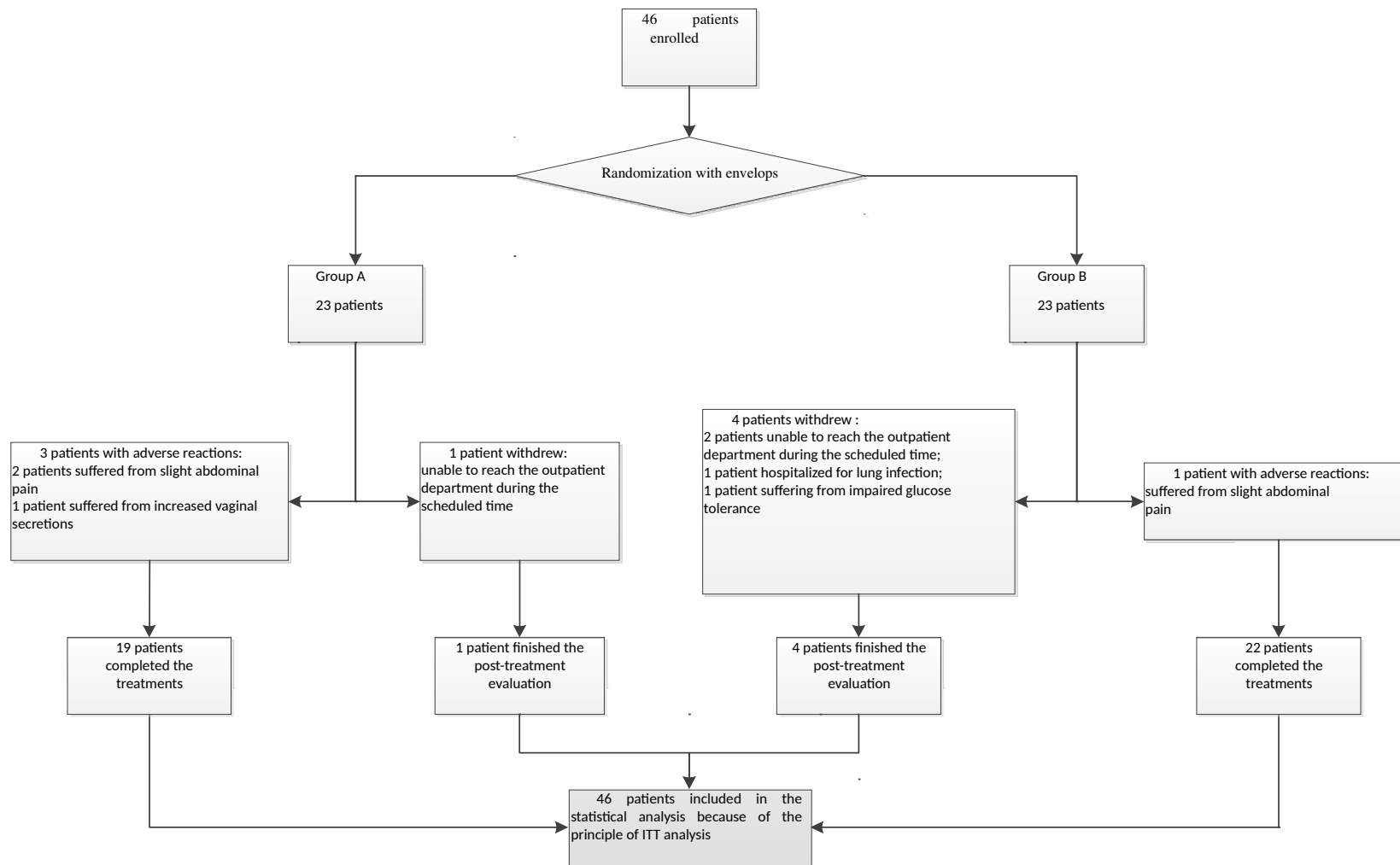
### **Study design**

There were 46 patients eligible for the study and randomly divided into two groups, 23 patients for each group. Group A received treatment of NMES by pulse width of 300  $\mu$ s, and Group B received treatment of NMES by pulse width of 200  $\mu$ s. respectively. A total of five patients (1 from Group A and 4 from Group B) did not complete all the treatments and withdrew from the study, among which three patients (1 from Group A and 2 from Group B) were not able to reach the outpatient department during the scheduled time, one patient (from

Group B) was hospitalized for lung infection, one patient (from Group B) had impaired glucose tolerance (IGT) during the treatments. Finally, 22 patients of Group A and 19 patients of Group B completed all the treatments. The five patients who withdrew from the study also finished post-treatment evaluation within the scheduled time.

During the treatments of NMES, there were three patients (2 from Group A and 1 from Group B) suffered from slight abdominal pain, which disappeared spontaneously 1–3 days later; there was another one patient (from Group A) suffered from increased vaginal secretions, which was confirmed to have bacterial vaginosis later by laboratory tests and recovered after treated with oral metronidazole for one week. All four patients continued the original treatments after the symptoms disappeared. There were no other complaints from the patients.

According to the principle of ITT analysis, all the 46 patients were analyzed statistically, as shown in Figure 1.



**Figure 1.** Flow diagram



### Comparison of the baseline between Group A and Group B

As shown in Table 1, there was no significant difference in baseline between Group A and Group B, including age ( $U = 211.000$ ,  $p = 0.237$ ), BMI ( $t = 0.377$ ,  $p = 0.708$ ), delivery times ( $U = 253.000$ ,  $p = 0.713$ ), cesarean section rate, and forceps delivery rate ( $U = 1.095$ ,  $p = 0.295$ ).

**Table 1. Comparison of the baseline between Group A and Group B**

Baseline	Group A	Group B	U	p
No.	23	23	–	–
Age [years old]	57 (55.58)	56 (54.58)	211.000 <sup>&amp;</sup>	0.237
BMI [kg/m <sup>2</sup> ]	24.34 ± 2.46	24.08 ± 2.37	0.377 <sup>*</sup>	0.708
Delivery times	1 (1.1)	1 (1.1)	253.000 <sup>&amp;</sup>	0.713
Cesarean section rate [%]	7/23	7/23	–	–
Forceps delivery rate [%]	3/23	1/23	1.095 <sup>#</sup>	0.295

BMI — body mass index; <sup>\*</sup>referred to student's t test; <sup>#</sup>referred to chi-square test;

<sup>&</sup>referred to Mann-Whitney U

### Comparison of the indicators before and after the treatments of NMES by pulse width of 300 $\mu$ s in Group A

As shown in Table 2, in Group A, OABSS ( $Z = -4.221$ ,  $p < 0.001$ ) and mean myoelectric potential at pre-resting state ( $Z = -4.198$ ,  $p < 0.001$ ) were significantly decreased after the treatments of NMES by pulse width of 300  $\mu$ s in comparison with those before the treatments. The myoelectric potential of Type I muscle fibers ( $Z = -3.407$ ,  $p = 0.001$ ) and the maximum myoelectric potential of Type II muscle fibers ( $t = -4.577$ ,  $p < 0.001$ ) were significantly increased after the treatments of NMES in comparison with those before the treatments.

**Table 2. Comparison of the indicators before and after the treatments of neuromuscular electrical stimulation by pulse width of 300  $\mu$ s in Group A**

Indicators	Pre-treatment	Post-treatment	Z	p
OABSS	8 (7, 9)	2 (1, 4)	-4.221 <sup>&amp;</sup>	< 0.001
mean myoelectric potential at pre-resting state [ $\mu$ v]	4.45 (2.06, 6.88)	1.10 (0.80, 2.00)	-4.198 <sup>&amp;</sup>	< 0.001
Mean myoelectric potential of Type I muscle fibers (slow-twitch) [ $\mu$ v]	13.12 (11.23, 18.66)	25.02 (22.37, 27.95)	-3.407 <sup>&amp;</sup>	0.001

Maximum myoelectric potential of Type II muscle fibers (fast-twitch) [ $\mu\text{V}$ ]	25.48 $\pm$ 13.81	34.25 $\pm$ 13.00	-4.577*	< 0.001
--	-------------------	-------------------	---------	---------

OABSS — overactive bladder symptom score; \*referred to paired t test; &referred to Wilcoxon rank-sum test

### Comparison of the indicators before and after the treatments of neuromuscular electrical stimulation by pulse width of 200 $\mu\text{s}$ in Group B

As shown in Table 3, in Group B, OABSS ( $Z = -4.217$ ,  $p < 0.001$ ) and mean myoelectric potential at pre-resting state ( $Z = -4.198$ ,  $p < 0.001$ ) were significantly decreased after the treatments of NMES by pulse width of 200  $\mu\text{s}$  in comparison with those before the treatments. However, mean myoelectric potential of Type I muscle fibers ( $Z = -0.396$ ,  $p = 0.692$ ) and the maximum myoelectric potential of Type II muscle fibers ( $t = 0.107$ ,  $p = 0.915$ ) were both not significantly different after the treatments of NMES in comparison with those before the treatments.

**Table 3. Comparison of the indicators before and after the treatments of neuromuscular electrical stimulation in Group B**

Indicators	Pre-treatment	Post-treatment	Z	p
OABSS	9 (6, 10)	5 (2, 6)	-4.217&	< 0.001
mean myoelectric potential at pre-resting state [ $\mu\text{V}$ ]	3.03 (2.18, 5.12)	1.57 (1.20, 2.29)	-4.198&	< 0.001
Mean myoelectric potential of Type I muscle fibers (slow-twitch) [ $\mu\text{V}$ ]	13.40 (10.27, 20.83)	13.14 (10.34, 21.72)	-0.396&	0.692
Maximum myoelectric potential of Type II muscle fibers (fast-twitch) [ $\mu\text{V}$ ]	25.99 $\pm$ 10.07	25.91 $\pm$ 10.84	0.107*	0.915

OABSS — overactive bladder symptom score; \*referred to paired t test; &referred to Wilcoxon rank-sum test

### Comparison of the differences of the indicators before and after the treatments of NMES with different pulse widths between Group A and Group B

As shown in Table 4, before the treatments of NMES, OABSS ( $U = 246.500$ ,  $p = 0.689$ ), mean myoelectric potential at pre-resting state ( $U = 232.500$ ,  $p = 0.482$ ), mean myoelectric potential of Type I muscle fibers ( $U = 255.000$ ,  $p = 0.835$ ) and the maximum myoelectric potential of Type II muscle fiber ( $t = -0.143$ ,  $p = 0.887$ ) had no significant difference between Group A and Group B.

After the treatments of NMES, OABSS ( $U = 142.000$ ,  $p = 0.006$ ) in Group A (treated by pulse width of 300  $\mu\text{s}$ ) was significantly lower than that in Group B (treated by pulse width of 200  $\mu\text{s}$ ). Mean myoelectric potential at pre-resting state ( $U = 190.000$ ,  $p = 0.101$ ) was not significantly different between the two groups after the treatments of NMES with different pulse widths. Mean myoelectric potential of Type I muscle fibers ( $U = 64.000$ ,  $p < 0.001$ ) and the maximum myoelectric potential of Type II muscle fibers ( $t = 2.363$ ,  $p = 0.023$ ) in Group A (treated by pulse width of 300  $\mu\text{s}$ ) were both significantly higher than those in Group B (treated by pulse width of 200  $\mu\text{s}$ ), as shown in Table 5.

We also compare the differences of the indicators before and after the treatments of NMES in Group A (treated by pulse width of 300  $\mu\text{s}$ ) and Group B (treated by pulse width of 200  $\mu\text{s}$ ). As shown in Table 6, the difference of OABSS before and after the treatments of NMES in Group A were significantly greater than that in Group B ( $t = -3.506$ ,  $p = 0.001$ ). The differences of mean myoelectric potential at pre-resting state before and after the treatments of NMES were not significantly different between the two groups ( $U = 184.000$ ,  $p = 0.077$ ). The differences of myoelectric potential of Type I muscle fibers ( $U = 80.000$ ,  $p < 0.001$ ) and the maximum myoelectric potential of Type II muscle fibers ( $t = 5.256$ ,  $p < 0.001$ ) were both significantly greater in Group A than those in Group B.

**Table 4. Comparison of the differences of the indicators before the treatments of neuromuscular electrical stimulation with different pulse widths between Group A and Group B**

Indicators	Group A	Group B	U	P
OABSS	8 (7, 9)	9 (6, 10)	246.500 <sup>&amp;</sup>	0.689
mean myoelectric potential at pre-resting state [ $\mu\text{v}$ ]	4.45 (2.06, 6.88)	3.03 (2.18, 5.12)	232.500 <sup>&amp;</sup>	0.482

Mean myoelectric potential of Type I muscle fibers (slow-twitch) [ $\mu\text{v}$ ]	13.12 (11.23, 18.66)	13.40 (10.27, 20.83)	255.000 <sup>&amp;</sup>	0.835
Maximum myoelectric potential of Type II muscle fibers (fast-twitch) [ $\mu\text{v}$ ]	25.48 $\pm$ 13.81	25.99 $\pm$ 10.07	-0.143 <sup>*</sup>	0.887

OABSS — overactive bladder symptom score; <sup>\*</sup>referred to student's t test; <sup>&</sup>referred to Mann-Whitney U

**Table 5. Comparison of the differences of the indicators after the treatments of neuromuscular electrical stimulation with different pulse widths between Group A and Group B**

Indicators	Group A	Group B	U	P
OABSS	2 (1, 4)	5 (2, 6)	142.000 <sup>&amp;</sup>	0.006
mean myoelectric potential at pre-resting state [ $\mu\text{v}$ ]	1.10 (0.80, 2.00)	1.57 (1.20, 2.29)	190.000 <sup>&amp;</sup>	0.101
Mean myoelectric potential of Type I muscle fibers (slow-twitch) [ $\mu\text{v}$ ]	25.02 (22.37, 27.95)	13.14 (10.34, 21.72)	64.000 <sup>&amp;</sup>	< 0.001
Maximum myoelectric potential of Type II muscle fibers (fast-twitch) [ $\mu\text{v}$ ]	34.25 $\pm$ 13.00	25.91 $\pm$ 10.84	2.363 <sup>*</sup>	0.023

OABSS — overactive bladder symptom score; <sup>\*</sup>referred to student's t test; <sup>&</sup>referred to Mann-Whitney U

**Table 6. Comparison of the differences of the indicators before and after the treatments of neuromuscular electrical stimulation with different pulse widths between Group A and Group B**

Indicators	Group A	Group B	U	p
OABSS	-5.61 $\pm$ 1.95	-3.83 $\pm$ 1.47	-3.506 <sup>*</sup>	0.001
mean myoelectric potential at pre-resting state [ $\mu\text{v}$ ]	-3.45 (-5.30, -1.23)	-0.88 (-2.52, 0.61)	184.000 <sup>&amp;</sup>	0.077
Mean myoelectric potential of Type I muscle	10.45 (2.51, 15.58)	-0.17 (-0.56, 0.85)	80.000 <sup>&amp;</sup>	< 0.001

fibers (slow-twitch) [ $\mu\text{v}$ ]				
Maximum myoelectric potential of Type II muscle fibers (fast-twitch) [ $\mu\text{v}$ ]	$9.71 \pm 8.13$	$-0.08 \pm 3.73$	$5.256^*$	$< 0.001$

OABSS — overactive bladder symptom score; \*referred to student's t test; &referred to Mann-Whitney U

## DISCUSSION

In the treatments of NMES, mean myoelectric potential at pre-resting state is positively correlated with the spasm of pelvic floor muscles, which has been confirmed to be the main cause of OAB [18]. Mean myoelectric potential of Type I muscle fibers and the maximum myoelectric potential of Type II muscle fibers, as the indicators for the functions of the pelvic floor muscles, are both associated with urinary continence. Our study found that after being treated with NEMS by different pulse widths, both Group A (treated by pulse width of 300  $\mu\text{s}$ ) and Group B (treated by pulse width of 200  $\mu\text{s}$ ) had no significant difference in the mean myoelectric potential at pre-resting state, indicating that the treatments may have been no help in reducing the high tension of pelvic floor muscles. However, after being treated with NEMS by different pulse widths, myoelectric potential of Type I muscle fiber and the maximum myoelectric potential of Type II muscle fibers were significantly increased than prior to the treatment of NEMS in the two groups, respectively. And when compared the two groups having been treated with NEMS by different pulse widths, we found that myoelectric potential of Type I muscle fiber and the maximum myoelectric potential of Type II muscle fibers in group A (treated by pulse width of 300  $\mu\text{s}$ ) were increased much higher than those in Group B (treated by pulse width of 200  $\mu\text{s}$ ). In addition, after the treatments of NMES by different pulse widths, OABSS were significantly reduced than before the treatment of NEMS in the two groups, respectively. And when compared the two groups treated with NEMS by different pulse widths, we found that OABSS in group A (treated by pulse width of 300  $\mu\text{s}$ ) were decreased greater than those in Group B (treated by pulse width of 200  $\mu\text{s}$ ), indicating that the patients treated with NEMS by pulse width of 300  $\mu\text{s}$  can improve the ability of urinary continence more effectively than patients treated with NEMS by pulse width of 200  $\mu\text{s}$ .

## **Mechanisms of NMES for OAB**

OAB is composed by the symptoms of frequent, urgent urination or urge incontinence. Clinically, the etiology of OAB still keep unclear. According to the different pathogenesis, OAB can be divided into three categories: detrusor instability, detrusor hyperreflexia, and bladder hypersensitivity, i.e., the initial urine volume of the bladder is less than 100 ml. The pathophysiological changes of OAB include occulted neurogenic bladder, undetected bladder outlet obstruction, urethral-related bladder obstruction, senile urinary epithelial dysfunction, chronic bladder ischemia, chronic bladder inflammation, central sensitization, and autonomic nerve dysfunction [19]. Low-frequency electrical stimulation can increase blood supply of the muscle and its nerve, eliminate fatigue and hypoxia, inhibit excessive nerve sensitivity and reduce muscle hypertonic, so as to improve the symptoms of OAB. In a study of percutaneous electrical stimulation in the anesthetized cats, 30 minutes of electrical stimulation produced long-term post-stimulatory inhibition, and bladder volume increased significantly after treatment, reaching up to  $140.5 \pm 7.6\%$  of the control. In the post-treatment period, the time of bladder contraction was significantly prolonged, reaching up to 200% of the control [20].

## **Analysis for the therapeutic differences with NMES treatments**

With low-frequency pulse current, NMES is able to make alpha-motor unit action potentials (MUAP) in peripheral nerves, which rapidly reach the threshold. As a result, more muscle fibers can participate in the contraction, strengthen the muscle and restore the body's motor function [21]. NMES may improve muscle strength by acting on microrNa-486 /PTEN/FoxO1 pathway and reducing muscle atrophy furtherly [22]. Other studies have shown that NMES could effectively increase the thickness of skeletal muscle [23] and increase muscle strength [24]. Type I muscle fibers accounts for 68–90% of deep pelvic floor muscles, characterized by tetanic contraction and relative indefatigability, whose role is to maintain the basic functions at resting state of the pelvic floor. Type II muscle fibers are mainly distributed in superficial pelvic floor muscles, characterized by periodic and quick contraction and fatigability, whose role is to cope with the exploding force from the outside. Regarding the electrophysiological characteristics of different types of muscle fibers, the pulse width of electrical

stimulation should be different too.

In this study, the treatment of NMES for Group A had an analgesic effect with the release of immunoreactive  $\beta$ -endorphin into the cerebrospinal fluid (1–10 Hz, 300  $\mu$ s, R = 0, the maximum current) [25], closer to electrophysiological characteristics of Type I muscle fibers, which could relax the muscles from the spasm, improve blood supply of the muscle and its nerve, and had analgesia effect. Apart from improving the pelvic floor muscle strength, its main advantage lied in the therapeutic effect for urge incontinence with effectively reducing OABSS [13]. On the other hand, the treatment of NMES for Group B was a kind of analgesic treatment as well, but it was closer to electrophysiological characteristics of Type II muscle fibers with lower pulse width [26]. In conclusion, Type I muscle fibers have been playing a more important role in maintaining the stability of pelvic floor functions.

In this study, it was found that the patients having been treated with NEMS by pulse width of 300  $\mu$ s had more advantages than those patients having been treated with NEMS by pulse width of 200  $\mu$ s in reducing OABSS and increasing myoelectric potential of pelvic floor muscle fibers. The mechanism may be that 300 $\mu$ s was more suitable for OAB patients with long-term high tension, spasm and ischemia of pelvic floor muscle fibers. Therefore, the treatments of NMES should be determined according to the individual situation of the pelvic floor muscle fibers.

### **OABSS in China**

OABSS has been recommended by ICS for evaluating the symptoms of OAB. OABSS was reported by Homma for the first time in 2006 in Japan. Nowadays, it has been adopted in many foreign clinical researches [17, 27] and validated in China as well [28]. It is a self-report questionnaire, creating a single score for all the symptoms — OAB symptom score (OABSS), to quantify the OAB symptoms and evaluate its severity. In this study, after the treatments of NMES, OABSS in Group A and Group B were both significantly reduced, indicating that NEMS may be effective for OAB.

### **Comparison of different treatments for OAB**

The treatments for OAB in clinical practice mainly include behavior therapy (lifestyle changes, PFMT, biological feedback, etc.), drug therapy (Anticholinergic drugs, beta-3 adrenal agonists, estrogen, etc.) [29], sacral neuromodulation, et al.

However, these treatments have been existed with insurmountable limitations in clinical application currently [24].

As the first-line treatment, behavior therapy could effectively improve the adherence of the OAB patients. It is usually recommended to use before or with the drugs. Lifestyle changes, such as reasonable and effective liquid management, avoiding caffeine and soft drinks, reducing fluid intake before sleep, maintaining defecate unobstructed, keeping a healthy weight and stopping smoking, can all improve the symptoms of OAB [30].

Drug therapy is the second-line treatment recommended by ICS. M cholinergic receptor blockers, by competitive inhibiting the acetylcholine in the smooth muscle of bladder and postganglionic cholinergic receptor binding sites, has been used in clinical practice for many years with its effectiveness widely confirmed. Unfortunately, about 80% of the patients had adverse effects of dry mouth. Up to 83% of the patients have stopped using the drug because of intolerance [31]. At present, the most widely studied beta-3 adrenergic agonists have been Mirabelone and Sorabelone. However, drug treatments of OAB cannot increase pelvic floor muscle strength, leaving limitations in treating comprehensive urinary incontinence or pelvic floor dysfunctions combined with the weakened pelvic floor muscle strength.

Sacral nerve stimulation (SNS) is a third-line treatment recommended by ICS. It implants an electrode in the S3 sacral foramen, which is connected to an internal pulse generator under the skin. The internal pulse generator emits pulses to release electric energy from the electrode, thereby stimulating the sacral and pudendal nerves, inhibiting the detrusor contraction and relieving the patient's symptoms. However, due to its high cost and invasion, it is only applicable to patients with severe emergent incontinence who cannot tolerate non-invasive treatments [32].

In the 1860s, Cadwell et al., began to study transvaginal electrical stimulation [33]. Subsequently, it has been proven to achieve therapeutic effects by stimulating the perineal nerve at frequencies below 12 Hz, to inhibit the detrusor muscle, regulate its involuntary contraction and reduce urination times [34]. Electrical stimulation has also been working in a passive way to help OAB patients be aware of their perineal (pelvic floor) muscle contractions, which may in turn help suppress involuntary detrusor contractions [35]. The advantage of NMES in clinical application lies in non-invasion and definite effectiveness. However, the OAB patients still have difficulty com-



plying with the schedule of the outpatient department. Portable electrical stimulation devices that can be used at home may become popular in the future.

### **Limitations**

In this study, the two groups of patients were not double-blind to the treatment. Fortunately, BMI, age, delivery times, OABSS and pelvic floor muscle strength between the two groups were not significantly different before the treatments, making the results of post treatment valuable. In further studies, randomized, double-blind, controlled trials should be designed to validate the therapeutic effectiveness of different treatments of NMES, and to further explore whether it's short-term or long-term effective.

### **CONCLUSIONS**

In conclusion, OAB is a common disease that seriously affects the life quality of postmenopausal elderly women. At present, it has been a hot issue in clinical practice to effectively improve OAB symptoms individually and comprehensively and improve the pelvic floor functions for the patients at the same time. Comparing the indicators before and after the treatments of NMES, our study has preliminarily confirmed that NMES has its advantages in treating with OAB, to improve the life quality of the patients.

### ***Acknowledgements***

We are grateful to Professor Shaowei Wang from Beijing Hospital for his theoretical guidance during the implementation of this research.

### ***Funding***

The study was financed from authors own funds.

### ***Availability of data and materials***

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

### ***Authors' contributions***

Aiming Lv designed the research, analyzed and interpreted the research data, and wrote the manuscript. Tianzi Gai, Qing Feng, Min Li, and Wenhui Deng collected the research data. Qiubo lv designed the study and guiding the writing of the manuscript.

***Ethics approval and consent to participate***

The present study was approved by the Ethics Committee of Beijing Hospital. Informed consent was obtained from all patients.

***Patient consent for publication***

Informed consent was obtained from all patients.

***Conflict of interests***

The authors declare that they have no competing interests. The institution does not develop products with relevant information, apply for patents, and does not provide experimental funds. The institution does not interfere with the decision to publish and share relevant research results in journals.

***Supporting information***

CONSORT Checklist S1 Completed “CONSORT 2010 checklist of information” to include when reporting a randomized trial in this manuscript.

Chinese Clinical Trial Registry Registration number: ChiCTR2000039585

**Appendix 1.** Overactive bladder symptom score (OABSS)

Item	Symptom	frequency/times	Standard-ized score	Score
1. day frequency	How many times of urination from getting up in the morning to going to sleep at night?	≤ 7	0	
		8–14	1	
		≥ 15	2	
2. night-time frequency	How many times of urination from	0	0	
		1	1	
		2	2	

	going to sleep at night to getting up in the morning?	≥ 3	3	
3. urgency	Is there a sudden urge to urinate and an unbearable sensation occurring at the same time?	none	0	
		< 1 time per week	1	
		≥ 1 time per week	2	
		= 1 time per day	3	
		2–4 times per day	4	
4. urgency incontinence	Is there a sudden urge to urinate and an intolerable incontinence?	≥ 5 times per day	5	
		none	0	
		< 1 time per week	1	
		≥ 1 time per week	2	
		= 1 time per day	3	
Total score:		2–4 times per day	4	
		≥ 5 times per day	5	

## REFERENCES

1. Haylen BT, de Ridder D, Freeman RM, et al. International Urogynecological Association, International Continence Society. An International Urogynecological Association (IUGA)/International Continence Society (ICS) joint report on the terminology for female pelvic floor dysfunction. *Neurourol Urodyn.* 2010; 29(1): 4–20, doi: [10.1002/nau.20798](https://doi.org/10.1002/nau.20798), indexed in Pubmed: [19941278](https://pubmed.ncbi.nlm.nih.gov/19941278/).
2. Wang Y, Xu K, Hu H, et al. Prevalence, risk factors, and impact on health related quality of life of overactive bladder in China. *Neurourol Urodyn.* 2011; 30(8): 1448–1455, doi: [10.1002/nau.21072](https://doi.org/10.1002/nau.21072), indexed in Pubmed: [21826714](https://pubmed.ncbi.nlm.nih.gov/21826714/).
3. Stewart WF, Van Rooyen JB, Cundiff GW, et al. Prevalence and burden of overactive bladder in the United States. *World J Urol.* 2003; 20(6): 327–336, doi: [10.1007/s00345-002-0301-4](https://doi.org/10.1007/s00345-002-0301-4), indexed in Pubmed: [12811491](https://pubmed.ncbi.nlm.nih.gov/12811491/).

4. Robinson D, Cardozo L, Milsom I, et al. Oestrogens and overactive bladder. *Neurourol Urodyn*. 2014; 33(7): 1086–1091, doi: [10.1002/nau.22464](https://doi.org/10.1002/nau.22464), indexed in Pubmed: [23868110](https://pubmed.ncbi.nlm.nih.gov/23868110/).
5. Yi J, Tenfelde S, Tell D, et al. Triathlete Risk of Pelvic Floor Disorders, Pelvic Girdle Pain, and Female Athlete Triad. *Female Pelvic Med Reconstr Surg*. 2016; 22(5): 373–376, doi: [10.1097/SPV.0000000000000296](https://doi.org/10.1097/SPV.0000000000000296), indexed in Pubmed: [27403753](https://pubmed.ncbi.nlm.nih.gov/27403753/).
6. Khan AA, Eilber KS, Clemens JQ, et al. Trends in management of pelvic organ prolapse among female Medicare beneficiaries. *Am J Obstet Gynecol*. 2015; 212(4): 463.e1–463.e8, doi: [10.1016/j.ajog.2014.10.025](https://doi.org/10.1016/j.ajog.2014.10.025), indexed in Pubmed: [25446663](https://pubmed.ncbi.nlm.nih.gov/25446663/).
7. Brueseke TJ, Wilkins MF, Willis-Gray MG, et al. Lifetime risk of surgery for stress urinary incontinence or pelvic organ prolapse. *Minerva Ginecol*. 2017; 69(2): 171–177, doi: [10.23736/S0026-4784.16.04011-9](https://doi.org/10.23736/S0026-4784.16.04011-9), indexed in Pubmed: [28001022](https://pubmed.ncbi.nlm.nih.gov/28001022/).
8. Malde S, Kelly S, Saad S, et al. Case-finding tools for the diagnosis of OAB in women: A narrative review. *Neurourol Urodyn*. 2020; 39(1): 13–24, doi: [10.1002/nau.24171](https://doi.org/10.1002/nau.24171), indexed in Pubmed: [31578764](https://pubmed.ncbi.nlm.nih.gov/31578764/).
9. Wallace SA, Roe B, Williams K, et al. Bladder training for urinary incontinence in adults. *Cochrane Database Syst Rev*. 2004(1): CD001308, doi: [10.1002/14651858.CD001308.pub2](https://doi.org/10.1002/14651858.CD001308.pub2), indexed in Pubmed: [14973967](https://pubmed.ncbi.nlm.nih.gov/14973967/).
10. Wein A. Commentary RE: The Standardization of Terminology in Lower Urinary Tract Function: Report From the Standardization Subcommittee of the International Continence Society. *Urology*. 2020; 145: 310–311, doi: [10.1016/j.urology.2020.04.064](https://doi.org/10.1016/j.urology.2020.04.064), indexed in Pubmed: [32333987](https://pubmed.ncbi.nlm.nih.gov/32333987/).
11. Hay-Smith J, Herbison P, Ellis G, et al. Which anticholinergic drug for overactive bladder symptoms in adults. *Cochrane Database Syst Rev*. 2005(3): CD005429, doi: [10.1002/14651858.CD005429](https://doi.org/10.1002/14651858.CD005429), indexed in Pubmed: [16034974](https://pubmed.ncbi.nlm.nih.gov/16034974/).
12. D'Souza AO, Smith MJ, Miller LA, et al. Persistence, adherence, and switch rates among extended-release and immediate-release overactive bladder medications in a regional managed care plan. *J Manag Care Pharm*. 2008; 14(3): 291–301, doi: [10.18553/jmcp.2008.14.3.291](https://doi.org/10.18553/jmcp.2008.14.3.291), indexed in Pubmed: [18439051](https://pubmed.ncbi.nlm.nih.gov/18439051/).

13. Lúcio A, D'ancona CA, Perissinotto MC, et al. Pelvic Floor Muscle Training With and Without Electrical Stimulation in the Treatment of Lower Urinary Tract Symptoms in Women With Multiple Sclerosis. *J Wound Ostomy Continence Nurs.* 2016; 43(4): 414–419, doi: [10.1097/WON.0000000000000223](https://doi.org/10.1097/WON.0000000000000223), indexed in Pubmed: [27014935](https://pubmed.ncbi.nlm.nih.gov/27014935/).
14. Jundt K, Peschers U, Kentenich H. The investigation and treatment of female pelvic floor dysfunction. *Dtsch Arztebl Int.* 2015; 112(33-34): 564–574, doi: [10.3238/arztebl.2015.0564](https://doi.org/10.3238/arztebl.2015.0564), indexed in Pubmed: [26356560](https://pubmed.ncbi.nlm.nih.gov/26356560/).
15. Candy B, Jones L, Vickerstaff V, et al. Interventions for sexual dysfunction following treatments for cancer in women. *Cochrane Database Syst Rev.* 2016; 2: CD005540, doi: [10.1002/14651858.CD005540.pub3](https://doi.org/10.1002/14651858.CD005540.pub3), indexed in Pubmed: [26830050](https://pubmed.ncbi.nlm.nih.gov/26830050/).
16. Silva VR, Riccetto CL, Martinho NM, et al. Training through gametherapy promotes coactivation of the pelvic floor and abdominal muscles in young women, nulliparous and continents. *Int Braz J Urol.* 2016; 42(4): 779–786, doi: [10.1590/S1677-5538.IBJU.2014.0580](https://doi.org/10.1590/S1677-5538.IBJU.2014.0580), indexed in Pubmed: [27564290](https://pubmed.ncbi.nlm.nih.gov/27564290/).
17. Homma Y, Yoshida M, Seki N, et al. Symptom assessment tool for overactive bladder syndrome--overactive bladder symptom score. *Urology.* 2006; 68(2): 318–323, doi: [10.1016/j.urology.2006.02.042](https://doi.org/10.1016/j.urology.2006.02.042), indexed in Pubmed: [16904444](https://pubmed.ncbi.nlm.nih.gov/16904444/).
18. Robinson AJ, Snyder-Mackler L. *Clinical electrophysiology: electrotherapy and electrophysiologic testing*, third edition. Lippincott Williams & Wilkins, Philadelphia 1997.
19. Chen LC, Kuo HC, Chen LC, et al. Pathophysiology of refractory overactive bladder. *Low Urin Tract Symptoms.* 2019; 11(4): 177–181, doi: [10.1111/luts.12262](https://doi.org/10.1111/luts.12262), indexed in Pubmed: [30900373](https://pubmed.ncbi.nlm.nih.gov/30900373/).
20. Yu M, Uy J, Jiang X, et al. An excitatory reflex from the superficial peroneal nerve to the bladder in cats. *Am J Physiol Renal Physiol.* 2017; 313(5): F1161–F1168, doi: [10.1152/ajprenal.00265.2017](https://doi.org/10.1152/ajprenal.00265.2017), indexed in Pubmed: [28855188](https://pubmed.ncbi.nlm.nih.gov/28855188/).
21. Dumitru D, King JC, Zwartz MJ. Determinants of motor unit action potential duration. *Clin Neurophysiol.* 1999; 110(11): 1876–1882, doi: [10.1016/s1388-2457\(99\)00142-x](https://doi.org/10.1016/s1388-2457(99)00142-x), indexed in Pubmed: [10576482](https://pubmed.ncbi.nlm.nih.gov/10576482/).

22. Shen J, Nie X, Huang SY, et al. Neuromuscular electrical stimulation improves muscle atrophy induced by chronic hypoxia-hypercapnia through the MicroRNA-486/PTEN/FoxO1 pathway. *Biochem Biophys Res Commun.* 2019; 509(4): 1021–1027, doi: [10.1016/j.bbrc.2018.12.147](https://doi.org/10.1016/j.bbrc.2018.12.147), indexed in Pubmed: [30654931](https://pubmed.ncbi.nlm.nih.gov/30654931/).
23. Qiu S, Feng J, Xu J, et al. Sonomyography Analysis on Thickness of Skeletal Muscle During Dynamic Contraction Induced by Neuromuscular Electrical Stimulation: A Pilot Study. *IEEE Trans Neural Syst Rehabil Eng.* 2017; 25(1): 59–67, doi: [10.1109/TNSRE.2016.2556687](https://doi.org/10.1109/TNSRE.2016.2556687), indexed in Pubmed: [28141512](https://pubmed.ncbi.nlm.nih.gov/28141512/).
24. Bochkezanian V, Newton RU, Trajano GS, et al. Effect of tendon vibration during wide-pulse neuromuscular electrical stimulation (NMES) on muscle force production in people with spinal cord injury (SCI). *BMC Neurol.* 2018; 18(1): 17, doi: [10.1186/s12883-018-1020-9](https://doi.org/10.1186/s12883-018-1020-9), indexed in Pubmed: [29433467](https://pubmed.ncbi.nlm.nih.gov/29433467/).
25. Han JS. Acupuncture: neuropeptide release produced by electrical stimulation of different frequencies. *Trends Neurosci.* 2003; 26(1): 17–22, doi: [10.1016/s0166-2236\(02\)00006-1](https://doi.org/10.1016/s0166-2236(02)00006-1), indexed in Pubmed: [12495858](https://pubmed.ncbi.nlm.nih.gov/12495858/).
26. Eriksen BC. Electrostimulation of the pelvic floor in female urinary incontinence. *Acta Obstet Gynecol Scand.* 1990; 69(4): 359–360, doi: [10.3109/00016349009036164](https://doi.org/10.3109/00016349009036164), indexed in Pubmed: [2244472](https://pubmed.ncbi.nlm.nih.gov/2244472/).
27. Okui N, Okui M, Horie S. Improvements in overactive bladder syndrome after polypropylene mesh surgery for cystocele. *Aust N Z J Obstet Gynaecol.* 2009; 49(2): 226–231, doi: [10.1111/j.1479-828X.2009.00965.x](https://doi.org/10.1111/j.1479-828X.2009.00965.x), indexed in Pubmed: [19432617](https://pubmed.ncbi.nlm.nih.gov/19432617/).
28. Chou ECL, Hung MJ, Yen TW, et al. The translation and validation of Chinese overactive bladder symptom score for assessing overactive bladder syndrome and response to solifenacin treatment. *J Formos Med Assoc.* 2014; 113(8): 506–512, doi: [10.1016/j.jfma.2012.07.044](https://doi.org/10.1016/j.jfma.2012.07.044), indexed in Pubmed: [25037757](https://pubmed.ncbi.nlm.nih.gov/25037757/).
29. Jiang F, Zhu L, Xu T, et al. Efficacy and safety of solifenacin succinate tablets versus solifenacin succinate tablets with local estrogen for the treatment of overactive bladder in postmenopausal women--a multicenter, randomized, open-label, controlled comparison study. *Menopause.* 2016; 23(4): 451–457, doi: [10.1097/GME.0000000000000574](https://doi.org/10.1097/GME.0000000000000574), indexed in Pubmed: [26757270](https://pubmed.ncbi.nlm.nih.gov/26757270/).

30. Lightner DJ, Gomelsky A, Souter L, et al. 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.000000000000309](https://doi.org/10.1097/JU.000000000000309), indexed in Pubmed: [31039103](https://pubmed.ncbi.nlm.nih.gov/31039103/).
31. Choi H, Bae JH, Oh CY, et al. Clinical Efficacy of Solifenacin in the Management of Diabetes Mellitus-Associated Versus Idiopathic Overactive Bladder Symptoms: A Multicenter Prospective Study. *Int Neurourol J*. 2018; 22(1): 51–57, doi: [10.5213/inj.1834982.491](https://doi.org/10.5213/inj.1834982.491), indexed in Pubmed: [29609421](https://pubmed.ncbi.nlm.nih.gov/29609421/).
32. Noblett K, Siegel S, Mangel J, et al. Results of a prospective, multicenter study evaluating quality of life, safety, and efficacy of sacral neuromodulation at twelve months in subjects with symptoms of overactive bladder. *Neurourol Urodyn*. 2016; 35(2): 246–251, doi: [10.1002/nau.22707](https://doi.org/10.1002/nau.22707), indexed in Pubmed: [25546568](https://pubmed.ncbi.nlm.nih.gov/25546568/).
33. CALDWELL KP. The electrical control of sphincter incompetence. *Lancet*. 1963; 2(7300): 174–175, doi: [10.1016/s0140-6736\(63\)92807-1](https://doi.org/10.1016/s0140-6736(63)92807-1), indexed in Pubmed: [14017856](https://pubmed.ncbi.nlm.nih.gov/14017856/).
34. Messelink EJ. The overactive bladder and the role of the pelvic floor muscles. *BJU Int*. 1999; 83 Suppl 2: 31–35, doi: [10.1046/j.1464-410x.83.s2.7.x](https://doi.org/10.1046/j.1464-410x.83.s2.7.x), indexed in Pubmed: [10210602](https://pubmed.ncbi.nlm.nih.gov/10210602/).
35. Amaro JL, Gameiro MO, Kawano PR, et al. Intravaginal electrical stimulation: a randomized, double-blind study on the treatment of mixed urinary incontinence. *Acta Obstet Gynecol Scand*. 2006; 85(5): 619–622, doi: [10.1080/00016340500495058](https://doi.org/10.1080/00016340500495058), indexed in Pubmed: [16752244](https://pubmed.ncbi.nlm.nih.gov/16752244/).