

A randomized controlled trial of neuromuscular electrical stimulation for chronic urinary retention following traumatic brain injury

Yong-bing Zhang, MB^a, Yan-na Cheng, MB^{b,*}

Abstract

Background: This study aimed to evaluate the effectiveness of neuromuscular electrical stimulation (NMES) therapy for chronic urinary retention (CUR) following traumatic brain injury (TBI).

Methods: This 2-arm randomized controlled trial (RCT) enrolled 86 eligible patients with CUR following TBI. All included patients were randomly allocated to a treatment group (n=43) or a sham group (n=43). The administration of NMES or sham NMES, as intervention, was performed for an 8-week period treatment, and 4-week period follow-up. In addition, all subjects were required to undergo indwelling urinary catheter throughout the study period. The primary outcome was assessed by the post-voiding residual urine volume (PV-VRU). The secondary outcomes were evaluated by the voided volume, maximum urinary flow rate (Q_{max}), and quality of life, as assessed by Barthel Index (BI) scale. In addition, adverse events were also recorded during the study period. All primary and secondary outcomes were measured at baseline, at the end of 8-week treatment, and 4-week follow-up.

Results: At the end of 8-week treatment, the patients in the treatment group did not achieve better outcomes in PV-VRU ($P=.66$), voided volume ($P=.59$), Q_{max} ($P=.53$), and BI scores ($P=.67$), than patients in the control group. At the end of 4-week follow-up, there were also no significant differences regarding the PV-VRU ($P=.42$), voided volume ($P=.71$), Q_{max} ($P=.24$), and BI scores ($P=.75$) between 2 groups. No adverse events occurred in either group.

Conclusions: In summary, the findings of this study showed that NMES therapy may not benefit patients with CUR following TBI.

Abbreviations: BI = barthel Index, CUR = chronic urinary retention, ITT = intention-to-treat, NMES = neuromuscular electrical stimulation, PV-VRU = post voiding residual urine volume, Q_{max} = maximum urinary flow rate, RCT = randomized controlled trial, TBI = traumatic brain injury, UR = Urinary retention.

Keywords: chronic urinary retention, effectiveness, neuromuscular electrical stimulation, safety, traumatic brain injury

1. Introduction

Urinary retention (UR) is a very tricky disorder, involving inability to voluntarily urinate for patients with traumatic brain injury (TBI).^[1–4] It is defined as a post-void residual (PVR) urine volume of >100 mL for 2 consecutive occasions.^[5–6] Such disorder often categorized into acute UR and chronic UR. Acute UR is the condition with sudden and painful inability to void through having a full bladder.^[7–9] Chronic urinary retention (CUR) is a different condition that often associates with painless and increased volume of residual urine.^[10–12] Patients with such disorder often manifest with complete lacking voiding,

incomplete bladder emptying or overflow incontinence.^[13–14] These patients with UR are often managed with catheterization.^[8,15–16] Unfortunately, such management can induce urinary tract infection or even renal dysfunction if they cannot be treated with adequate management.^[17–19] Thus, it is very necessary to figure out the proper bladder management to improve patients' functional outcomes.

Management for CUR mainly consists of a variety of interventions, including a wide range of medications, indwelling urinary catheter, bladder training, high energy transurethral microwave thermotherapy, laser therapy, acupuncture, and electroacupuncture.^[20–29] However, most of them have limited efficacy and even a lot of adverse events.^[20–29] Electrical stimulation is reported to treat CUR disorder and has achieved a satisfying effect.^[30–31] However, there is still limited data and insufficient evidence to support this therapy, especially the effectiveness of neuromuscular electrical stimulation (NMES) therapy for the treatment of CUR following TBI. Therefore, in this randomized controlled trial (RCT), we hypothesized that the effectiveness of NEMS would be superior to the sham NMES for CUR following TBI.

2. Methods

2.1. Ethical consideration

This 2-arm RCT was approved by the Medical Ethical Committee of Yan'an People's Hospital and Yanan University Affiliated Hospital.

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The authors have no conflicts of interest to disclose.

^a Department of Neurosurgery, Yan'an People's Hospital, ^b Department of Nephrology, The Affiliated Hospital of Yan'an University, Yan'an, China.

* Correspondence: Yan-na Cheng, Department of Nephrology, The Affiliated Hospital of Yan'an University, No. 250 Beiguan St, Yan'an, Shaanxi 716000, China (e-mail: yannacheng2010@yeah.net).

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2.2. Design

All patients were recruited from Yan'an People's Hospital and Yanan University Affiliated Hospital from January 1, 2017 to May 30, 2018. Totally, 86 patients with CUR following TBI were included and were randomly allocated to the treatment group ($n=43$) or the control group ($n=43$). Patients in the treatment group were administered with NMES, while the subjects in the control group underwent sham NMES. Patients in both groups were treated for a total of 8 weeks and 4 weeks period follow-up. All outcomes were measured at baseline, at the end of 8-week treatment, and 4-week follow-up.

2.3. Inclusion and exclusion criteria

2.3.1. Inclusion criteria. Both men and women aged 18 to 75 years old with TBI were considered in this study. In addition, they were all diagnosed with CUR according to the Diagnosis Criteria of International Continence Society.^[32] CUR in this study was defined as an elevated PVR >300 mL, and persisted for at least 6 months documented on 2 or more separate occasions. Furthermore, all patients had more than 6 months duration of TBI, normal consciousness, completed self-communication, and signed written informed consent.

2.3.2. Exclusion criteria. Patients were excluded if the CUR was caused by other diseases (such as stroke, bladder stones, tumors, diabetes, spinal problems, etc) except the TBI; CUR before the TBI; had history of psychological disorder; taken other medications that affected the CUR; pregnancy or breastfeeding; received electroacupuncture, electrical stimulation, or NMES 1 month prior to the study. In addition, patients were excluded if they also received other therapies for CUR duration of the study period.

2.4. Randomization and blinding

An independent statistician performed computer-generated block randomization by using the SAS software (version 9.3; SAS Institute, Inc., Cary, NC). A total of 86 patients were randomly allocated to a treatment group and a control group, each group 43 patients. All allocation information was concealed in numbered opaque, sealed envelopes. Patients and practitioners, outcome assessors and data analysts were all blinded to the randomization assignment and allocation.

2.5. Intervention

Patients in both groups received indwelling urinary catheter throughout the study. In addition, patients in the treatment group also underwent NMES therapy, while the subjects in the control group received sham NMES intervention. NMES therapy was applied by a portable NMES stimulator (Globus ACTIVA 600 Pro, Globus, Italy) alongside a sacral nerve (S3) and attached 2 sets of electrode pads to the skin surface.^[33] Each patient in the treatment group was administered with 50 Hz frequency, 250 μ s pulse duration, and 10s on and 30s off. Each individual was treated 30 min daily, once weekly for a total of 8 weeks. The subjects in the control group received sham NEMS at the same location, same NMES device, and same intervention schedule as the treatment group, but with power off.

2.6. Outcome evaluation

The primary outcome was measured by post voiding residual urine volume (PV-VRU).^[34] It was detected by collecting the

residual urine from the catheter after the subjects' automatic micturition. The secondary outcomes were assessed by the voided volume and maximum urinary flow rate (Q_{max}).^[35] In addition, quality of life was evaluated by Barthel Index (BI) scale.^[36–37] The scale ranges from 0 to 20, with lower scores indicating higher disability.^[36–37] The adverse events were recorded during the study period. All outcomes were measured at baseline, at the end of 8-week treatment, and 4-week follow-up.

2.7. Statistical analysis

All data were analyzed by a statistician using the SAS software (version 9.3; SAS Institute, Inc., Cary, NC) using intention-to-treat (ITT) approach. The t test or Mann-Whitney U test was conducted to analyze the difference of continuous data between 2 groups. The Chi-square test or Fisher exact test was applied to analyze the difference of categorical data between 2 groups. The level of statistical significance was set at $P < .05$.

3. Results

A total of 139 eligible patients with CUR following TBI were initially entered for the assessment (Fig. 1). However, 53 of them were excluded after the initial assessment, because of the failure to meet the inclusion criteria, and refusing to enter the study. Therefore, 86 patients were included and were equally and randomly allocated to the treatment group and the control group. Of them, 41 and 40 subjects in the treatment group and control group respectively completed all the treatment. At the follow-up phrase, 3 and 4 patients were lost to follow-up in the treatment group and the control group, respectively, although all patients in both groups entered the final data analysis by using ITT approach.

The characteristics of all included patients at baseline are demonstrated in Table 1. No significant differences regarding all characteristic values were detected between 2 groups.

At the end of 8 weeks treatment, patients who received NMES did not show better outcomes in PV-VRU ($P=.66$, Table 2), voided volume ($P=.59$, Table 3), Q_{max} ($P=.53$, Table 3), and BI scores ($P=.67$, Table 3), than patients who received sham NMES.

At the end of 4-week follow-up, there were still no significant differences in PV-VRU ($P=.42$, Table 2), voided volume ($P=.71$, Table 3), Q_{max} ($P=.24$, Table 3), and BI scores ($P=.75$, Table 3) between 2 groups.

During the period of 8-week treatment and 4-week follow-up, no adverse effects related to the NMES or sham NMES intervention occurred in either group. No death related to the interventions was also recorded in either group.

4. Discussion

This study with period of 8-week treatment, and 4-week follow-up firstly investigated the effectiveness and safety of NMES for the treatment of patients with CUR following the TBI among Chinese population. The results of this study did not show that NMES can relieve symptoms of patients with CUR after TBI, as well as can improve their quality of life after 8 weeks of treatment.

Several previous related studies have explored the effectiveness of electrical stimulation for patients with CUR.^[30–31,38–41] Although few of those studies achieved encouraging outcome results,^[30–31,41] none of them specifically addressed the effectiveness of NMES in patients with CUR after TBI.

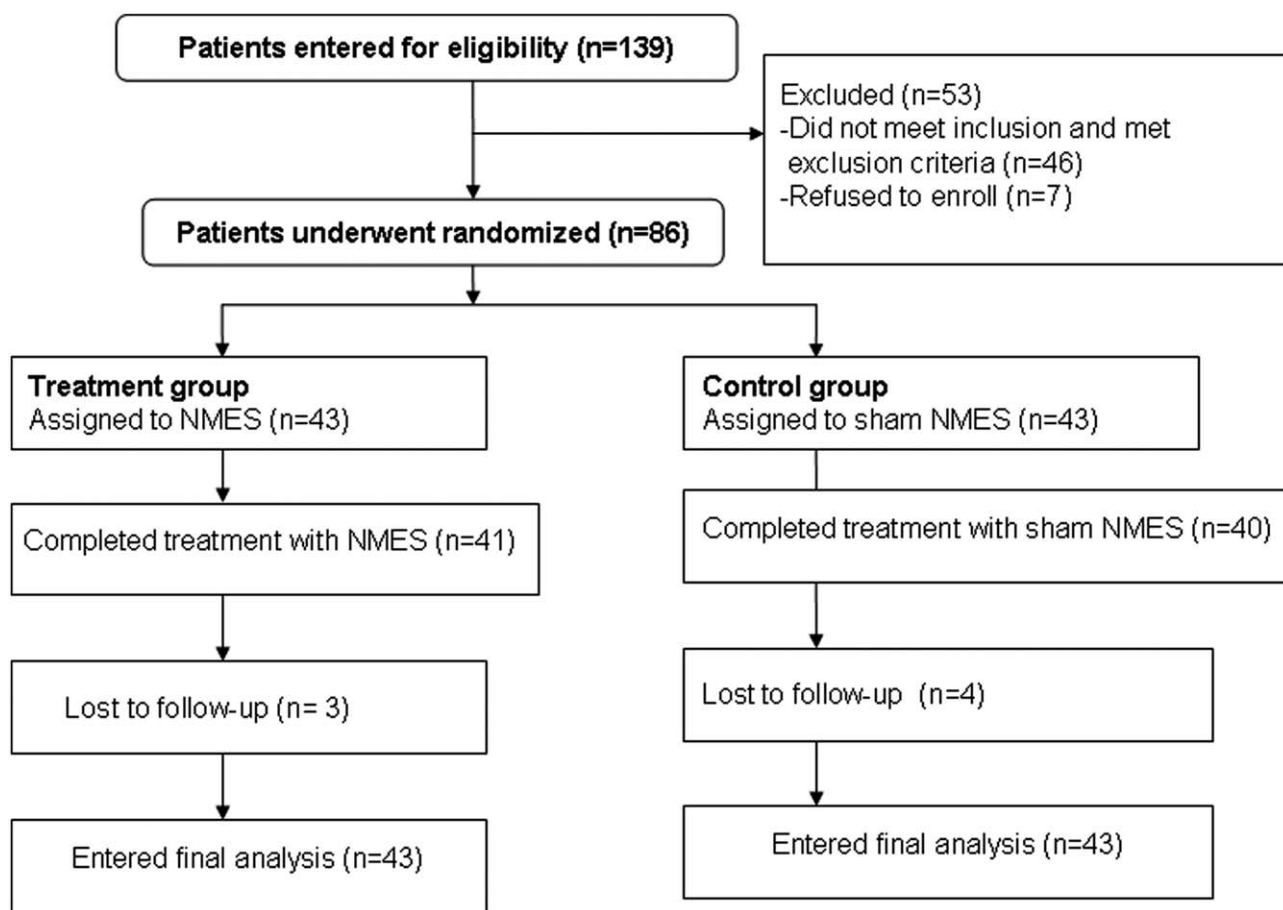


Figure 1. Flow of patient selection.

Table 1
Patient characteristic at baseline.

Characteristics	Treatment group (n = 43)	Control group (n = 43)	P
Mean age (year)	47.6 (9.8)	44.3 (11.5)	0.15
Sex			
Male	34 (79.1)	31 (72.1)	0.45
Female	9 (20.9)	12 (27.9)	–
BMI (kg/m ²)	22.7 (1.6)	23.1 (2.2)	0.33
Duration of TBI (month)	8.9 (2.4)	9.1 (2.7)	0.72
Duration of CUR (month)	6.8 (1.7)	7.0 (1.4)	0.55
Causes of TBI			
Car accident	18 (41.9)	22 (51.2)	0.39
Vehicle crashes	15 (34.9)	13 (30.2)	0.65
Falls	9 (20.9)	6 (14.0)	0.40
Others	1 (2.3)	2 (4.7)	0.56
Co-morbidities			
Hypertension	6 (14.0)	9 (20.9)	0.40
Constipation	11 (25.6)	14 (32.6)	0.48
Hyperlipidaemia	13 (30.2)	10 (23.3)	0.47
Osteoarthritis	5 (11.6)	8 (18.6)	0.37
Gastritis	7 (16.3)	4 (9.3)	0.34
PV-VRU	297.6 (107.5)	307.2 (113.6)	0.69
voided volume (ml)	264.5 (10.3)	268.9 (11.1)	0.13
Q _{max}	6.7 (3.1)	7.0 (3.4)	0.67
BI	9.1 (2.4)	9.7 (2.7)	0.28

Data are present as mean±standard deviation or number (%); BI=Barthel Index scale, BMI=Body mass index, CUR=chronic urinary retention, PV-VRU=post voiding residual urine volume, Q_{max}=maximum urinary flow rate, TBI=traumatic brain injury.

The results of the present study are inconsistent with the previous studies.^[30–31,41]

Results of present study showed that patients who received NMES did not show promising effectiveness either in primary outcome measurement of PV-VRU, nor in the secondary outcome measurements of voided volume, Q_{max}, and BI scale. In addition, both groups had similar safety profile. The results of the present study indicated that NMES may not benefit for patients with CUR following TBI.

The present study had several drawbacks. First, the ethnicity of all included patients is Chinese Han. Therefore, it might affect its findings generalization to the other ethnicities in China. Second, the treatment dose of the present study may be insufficient. All patients in the present study received NMES or sham NMES once weekly for 8 weeks, with a total of 8 sessions, which may be insufficient to show the promising effectiveness of NMES. Third, although all patients with CUR caused by TBI, there may still other different reasons can result in the CUR. Fourth, the effectiveness of interventions in this study is the results of NMES or sham NEMS combined with indwelling urinary catheter, but not the NMES or sham NEMS alone. Thus, further studies should avoid the above drawbacks.

5. Conclusion

The findings of the present study showed that NMES may not benefit for patients with CUR following TBI after 8-week treatment.

Table 2**Comparison of primary outcome (change from baseline).**

Primary outcome	8-week treatment			P	4-week follow-up			P
	Treatment group (n=43)	Control group (n=43)	Difference		Treatment group (n=43)	Control group (n=43)	Difference	
PV-VRU	-16.9 (-25.8, -7.5)	-10.5 (-18.7, -6.1)	-6.5 (-10.3, -3.1)	0.66	-17.8 (-23.4 -9.9)	-10.1 (-16.5, -5.0)	-7.8 (-13.5, -3.4)	0.42

Data are present as mean (range); PV-VRU=post voiding residual urine volume.

Table 3**Comparison of secondary outcomes (change from baseline).**

Secondary outcomes	8-week treatment			P	4-week follow-up			P
	Treatment group (n=43)	Control group (n=43)	Difference		Treatment group (n=43)	Control group (n=43)	Difference	
Voided volume	27.8 (18.4, 41.3)	16.6 (9.7, 25.5)	12.2 (7.5, 16.9)	0.59	25.9 (16.3, 36.2)	15.1 (8.8, 22.2)	10.7 (6.4, 15.8)	0.71
Q _{max}	4.1 (2.1, 6.9)	2.6 (1.2, 4.0)	1.6 (0.8, 2.5)	0.53	4.4 (2.3, 7.6)	2.0 (1.1, 3.8)	2.3 (1.4, 3.2)	0.24
BI	3.2 (1.4, 4.5)	1.9 (1.1, 3.0)	1.2 (0.5, 2.0)	0.67	3.0 (1.2, 4.8)	1.9 (0.9, 3.2)	1.0 (0.4, 18)	0.75

Data are present as mean (range); BI=Barthel Index scale, Q_{max}=maximum urinary flow rate.

Author contributions

Conceptualization: Yong-bing Zhang, Yan-na Cheng.

Data curation: Yong-bing Zhang, Yan-na Cheng.

Formal analysis: Yong-bing Zhang.

Investigation: Yan-na Cheng.

Methodology: Yong-bing Zhang.

Project administration: Yan-na Cheng.

Resources: Yong-bing Zhang.

Software: Yong-bing Zhang.

Supervision: Yan-na Cheng.

Validation: Yong-bing Zhang, Yan-na Cheng.

Visualization: Yong-bing Zhang, Yan-na Cheng.

Writing – original draft: Yong-bing Zhang, Yan-na Cheng.

Writing – review & editing: Yong-bing Zhang, Yan-na Cheng.

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