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Original Article

Effects of a 12-hour neuromuscular electrical stimulation treatment program on the recovery of upper extremity function in sub-acute stroke patients: a randomized controlled pilot trial

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Abstract. [Purpose] This study investigated the effects of a 12-hour neuromuscular electrical stimulation program in the evening hours on upper extremity function in sub-acute stroke patients. [Subjects and Methods] Forty-five subjects were randomized to one of three groups: 12-hour neuromuscular electrical stimulation group (n=15), which received 12 hours of neuromuscular electrical stimulation and conventional rehabilitation for the affected upper extremity; neuromuscular electrical stimulation group (n=15), which received 30 min of neuromuscular electrical stimulation and conventional rehabilitation; and control group (n=15), which received conventional rehabilitation only. The Fugl-Meyer assessment, Action Research Arm Test, and modified Ashworth scale were used to evaluate the effects before and after intervention, and 4 weeks later. [Results] The improvement in the distal (wrist-hand) components of the Fugl-Meyer assessment and Action Research Arm Test in the 12-hour neuromuscular electrical stimulation group was more significant than that in the neuromuscular electrical stimulation group. No significant difference was found between the two groups in the proximal component (shoulder-elbow) of the Fugl-Meyer assessment. [Conclusion] The 12-hour neuromuscular electrical stimulation group achieved better improvement in upper extremity motor function, especially in the wrist-hand function. This alternative therapeutic approach is easily applicable and can be used in stroke patients during rest or sleep.
Key words: Neuromuscular electrical stimulation, Upper extremity function, Stroke

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INTRODUCTION

Upper extremity (UE) hemiparesis is a frequently encountered post-stroke impairment[1)]; most of the UE functional recovery is thought to occur within the initial 6 months after the stroke, and the extent of recovery is very limited[2)]. UE disability has a great impact on the activities of daily living and imparts a heavy burden on survivors' families and society[3)].

Neuromuscular electrical stimulation (NMES) has long been used in post-stroke rehabilitation[4)]. Many studies have reported the effects of NMES in the prevention of muscle atrophy, decrease of spasticity, increase of muscle strength, and facilitation of functional movement recovery[4–7)]. However, performing NMES in daily practice is challenging because of the differences in the stimulation characteristics: technique, frequency, intensity, and duration[8)]. The best choice for rehabilitation of the paretic upper extremity is still unclear. Past studies have shown that totally a minimum of 10 hours of NMES in combination with regular rehabilitation may improve the recovery of arm function in stroke patients during the acute stage[9)]. The implication was that the cumulative effect of treatment time might be a key player in NMES therapy. However, in standard clinical settings, increasing the stimulation time beyond 1 hour during the day is not practically feasible[9)].

Treatment involving 12 hours of NMES (12h-NMES) maybe a new alternative therapeutic approach in which the treatment is assigned in the evening when subjects wear a portable device while remaining at rest or during sleep. The intensity of the electrical current is adjusted to produce a small contraction of the target muscle without inducing obvious limb/joint movement, with the subject in a comfortable state and undistracted by the stimulation[10)].

A randomized, controlled, observer-blinded pilot trial was conducted to compare the improvement in motor control and muscle tone in sub-acute stroke patients who participated in a 12h-NMES, NMES, or conventional rehabilitation program.

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Table 1. Inclusion and exclusion criteria

Inclusion criteria	Age, 18–80 years
	Time from stroke onset≥4 weeks
	First stroke and unilateral involvement
	Medically and neurologically stable condition
	No visual or auditory defects
Exclusion criteria	Recurrent or progressive stroke
	Pre-existing arm impairment such as rheumatoid arthritis
	Cardiac pacemaker or other implanted stimulator
	History of seizures within 2 years
	History of fatal cardiac arrhythmias
	Refusal to sign the consent form

The purpose of this trial was to evaluate the effects of long-duration (12 hours in the evening), low-intensity NMES on upper extremity function in stroke patients.

SUBJECTS AND METHODS

A total of 132 patients who had developed hemiplegia as a result of stroke were recruited from the Second Hospital of Shandong University from July 2012 to May 2014. The inclusion and exclusion criteria are listed in Table 1. Eighty-seven patients who did not fulfill the inclusion criteria were excluded. The remaining 45 patients were enrolled and randomized to one of three groups, (1) 12h-NMES group, (2) NMES group, or (3) control group, via a computer-generated blocked randomization sequence. Approval was received from the ethics committees of the study site, and written informed consent was obtained from each participant in accordance with the ethical standards of the Declaration of Helsinki.

Eligible subjects, regardless of their group assignment, underwent standard inpatient rehabilitation that included physical therapy, occupational therapy, activities of daily living training, mobility training, and speech therapy. Additionally, the patients in the12h-NMES and NMES groups received electric stimulation treatment for a 12-h or 30-min session/day, respectively, 6 days/week, for 4 weeks. A portable surface neuromuscular stimulator (Chattanooga-2773AS) was used to deliver the NMES. Rectangular-wave pulsed currents (300 μs pulse width; 40 Hz; 1 s on/off ramp) were applied to the affected upper extremities of the subjects in both NMES groups. The amplitude of the current in the NMES group was adjusted to obtain the maximum range of wrist and finger extension without discomfort, and in the 12h-NMES group, the intensity was adjusted to produce a small muscle contraction without obvious limb/joint movement, with the patient in a comfortable state and undistracted by the stimulation. The surface electrodes(5×5 cm; square) were applied over the motor points near the middle of the supraspinatus, the biceps brachii and the deltoid muscle on the paretic side, as well as over the wrist extensors. The NMES treatment was applied for 12 hours in the evening in the 12h-NMES group and for 30 min during the day in the NMES group.

Outcome measures included the upper extremity component of the Fugl-Meyer assessment (FMA-UE), the Action Research Arm Test (ARAT), and the modified Ashworth scale (MAS). The FMA-UE scores were divided into proximal (FMA-p, shoulder-elbow score, 0–42) and distal components (FMA-d, wrist-hand score, 0–24). The ARAT consists of 19 items divided into four subscales (grasp, grip, pinch, and gross movement) with a maximum score of 57 points. The muscle tone of the biceps brachii and wrist flexors was assessed by the MAS, which uses a 6-point scale to assess the mean resistance to passive movement of the elbow and wrist. The three measures were assessed at baseline, after four weeks of treatment, and at the four-week follow-up by the physical therapists, who were blinded to the group assignment. A flow chart of the study is shown in Fig. 1.

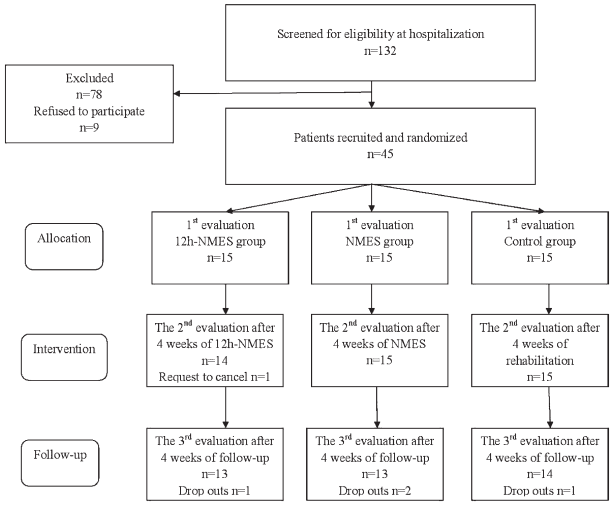

Fig. 1. Flow-chart of the randomization procedure
NMES: neuromuscular electrical stimulation

All statistical analyses were performed with SPSS version 15.0 (IBM Corp., Armonk, NY, USA). Using one-way ANOVA and χ^2 test, we compared the patients' baseline characteristics. The post-intervention and follow-up improvements in the groups were compared using an independent-samples t-test. One-way ANOVA was used to compare outcome measurements in each group, and p values<0.05 were considered statistically significant.

Table 2. Baseline characteristics of patients included in the study (n=45)[a]

	12h-NMES group n=15	NMES group n=15	Control group n=15	p value
Age (years)	61.5±14.8	64.6±7.5	61.5±12.6	0.72[b]
Gender (male)	11 (15)	12 (15)	7 (15)	0.12[c]
Time since onset of stroke (weeks)	12.6±6.1	12.8±5.1	14.4±4.9	0.61[b]
Affected side (left)	9 (15)	5 (15)	6 (15)	0.31[c]
Type of stroke				
Infarction	13 (15)	12 (15)	12 (15)	0.86[c]
hemorrhage	2 (15)	4 (15)	3 (15)	0.89[c]
FMA	17.1±4.59	17.5±4.56	17.1±4.5	0.96[b]
ARAT	16.1±5.58	16.9±2.71	17.3±2.8	0.52[b]
MAS (elbow)	1.4±0.91	1.5±0.92	1.5±0.92	0. 90[b]
MAS (wrist)	1.4±0.83	1.7±0.89	1.5±0.92	0.59[b]

NMES: Neuromuscular electrical stimulation; FMA: Fugl-Meyer assessment; ARAT: Action Research Arm Test; MAS: Modified Ashworth scale
[a] Values are mean ± SD or number (percentage)
[b] One-way-ANOVA test
[c] χ^2 test

RESULTS

Forty subjects completed the treatment and follow-up process. No adverse treatment effects, such as burns, skin allergic responses, increased muscle tone, or obvious muscle fatigue were noted. The patients in this study showed good adherence; only one patient in the12h-NMES group denied treatment due to affected sleep quality. Four patients were lost to follow-up because of transportation difficulties and inconvenience. No significant differences were found in the baseline characteristics of the groups (Table 2).

Significant improvements in the FMA-d were found in the 12h-NMES group compared with the NMES group at week 4 and at follow-up (T=2.89, p=0.007; T=3.01, p=0.003, respectively), and improvements were also found in the control group (T=4.59, p=0.000; T=2.18, p=0.04, respectively). Significant improvements in the FMA-p were obtained in the 12h-NMES group compared with the control group at week 4 and at follow-up (T=2.78, p=0.01; T=4.55, p=0.000, respectively), but no significant improvement was found in the NMES group between week 4 and the follow-up (T=1.18, p=0.25; T=0.63, p=0.54, respectively). There was no difference between the two NMES groups (T=1.41, p=0.17; T=1.20, p=0.43, respectively). Both NMES groups showed significant improvements on the ARAT at week 4 and at follow-up. Furthermore, the difference on the ARAT between the two NMES groups was significant (Table 3).

No significant difference was found on the MAS for the elbow and wrist flexors among the three groups at week 4 and at follow-up. There was no evidence of exacerbation or alleviation of spasticity among the subjects, who showed mild to moderate elbow and wrist spasticity (MAS 1–2) (Table 3).

Table 3. Changes in clinical assessments among the three groups

	12h-NMES group	NMES group	Control group
FMA-p			
Baseline	12.1±3.01	12.1±2.85	11.8±2.96
Week 4	24.3±3.71**¶	22.1±4.65**	20.1±4.29**
Week 8	24.8±3.33**§	23.7±4.55**	22.7±3.50**
FMA-d			
Baseline	5.07±1.94	5.40±1.72	5.33±1.76
Week 4	13.7±3.25**§	10.7±2.38**	9.0±2.24**
Week 8	18.8±3.07**¶	15.4±3.53**	14.29±2.90**
ARAT			
Baseline	16.1±3.575	16.9±2.71	17.3±2.85
Week 4	26.6±3.28**§	22.8±3.14**	21.6±2.47**
Week 8	30.8±2.14**§	26.9±2.85**	24.6±2.98**
MAS elbow			
Baseline	1.40±0.91	1.53±0.92	1.53±0.92
Week 4	1.50±0.52	1.67±0.49	1.80±0.68
Week 8	1.67±0.65	1.69±0.48	1.71±0.47
MAS wrist			
Baseline	1.40±0.83	1.73±0.88	1.53±0.91
Week 4	1.36±0.63	1.67±0.49	1.53±0.52
Week 8	1.33±0.49	1.66±0.49	1.57±0.51

NMES: Neuromuscular electrical stimulation; FMA: Fugl-Meyer assessment; FMA-d: Fugl-Meyer assessment distal component (wrist-hand); FMA-p: Fugl-Meyer assessment proximal component (shoulder-elbow); ARAT: Action Research Arm Test; MAS: Modified Ashworth scale
Comparison within group with independent-samples t-test: *p<0.05, **p<0.001
Comparison among groups with one-way ANOVA: ¶p<0.05, §p<0.001

DISCUSSION

The present study evaluated the effectiveness of rehabilitation using 12h-NMES in the evening hours in sub-acute stroke patients. Compared with the NMES group, the 12h-NMES group experienced the following effects: (1) better improvement of motor function in the affected UE, especially in the wrist-hand function; and (2) limited improvement in spasticity. Our findings support the effectiveness of the 12h-NMES therapy, which maybe an alternative therapeutic approach for patients at rest or during sleep.

A 12h-NMES program can facilitate motor function recovery in the affected UE after stroke, especially in the distal UE. At present, brain plasticity is the most widely accepted functional theory of recovery after stroke. The adult animal brain has been proven to demonstrate plasticity, including nerve sprouting and synaptic activation, under repetitive stimulation[11]. The mechanism underlying 12h-NMES-driven changes in motor function remains unclear but is thought to be the activation of brain plasticity through electrical enhancement of the afferent input[12]. Dose-dependent use is known to induce reorganization of the damaged motor cortex[13]. The 12h-NMES treatment and constraint-induced movement therapy are supposed to induce dose-dependent plasticity[14]. The 12h-NMES treatment allowed patients to receive stimulation for 12hours in the evening, with sustained electrical afferent input and without affected sleep quality. The 12h-NMES treatment had the advantage of long-duration stimulation over the NMES treatment, which maintained stimulation for only 30 min per day. In this study, the 12h-NMES group showed significant improvements on the FMA and the ARAT and achieved greater improvement on the FMA-d than the FMA-p. Several factors may account for the relatively small changes in FMA-p. Generally, most sub-acute and chronic stroke patients have better proximal UE motor function than distal, mainly due to more effective training of the proximal UE than the distal UE in the early stages of stroke recovery, and the FMA-p scores tend to change more easily in acute than sub-acute or chronic stroke patients. As mentioned above, in the present study, most of the subjects were sub-acute stroke patients. Therefore, the small significant improvements in FMA-p are not surprising. Additionally, the low intensity of the electrical current and limited stimulus field (with a large variation between the muscle volumes in the proximal and distal parts of the UE) dedicated to the proximal portion of the UE muscles possibly limited the magnitude of improvement. The significant difference on the ARAT between the two NMES groups also indicated that the 12h-NMES group improved more in the distal UE because most of the items (16/19) on the ARAT assessment are related to distal function (finger tasks). In line with our results, a recent study also observed that additional NMES applications during treatment could bring about more improvement in distal motor functions and found difference in the muscle activities between the wrist and the elbow; improved distal muscle coordination led to better motor functional recovery[15].To verify and extend these findings, future investigations of this study's treatment method should focus on determining the type of stimulation that might be most effective, the optimum dose, and the optimum application time after stroke.

The 12h-NMES treatment showed limited effects on spasticity. The MAS is important for assessing the degree of spasticity that develops as a result of upper motor neuron lesions. However, the results of the NMES studies performed to evaluate spasticity are controversial. Although some studies have shown that NMES relieved spasticity[16, 17], others have suggested that NMES had a limited effect on spasticity[4, 15, 18]. These differences may be due to sample size, intervention time, treatment therapy, and outcome measures. In this present study, there was no evidence of exacerbation or alleviation of spasticity among the subjects who showed mild to moderate spasticity in their elbow and wrist muscles during the treatment and follow-up sessions.

This study demonstrated that four weeks of 12h-NMES can improve motor control of the paretic UE in sub-acute stroke patients. The stimulation protocol (long-duration, low-intensity) seemed to provide greater improvement in the distal UE than in the proximal UE. The positive effects observed in this study suggest that further development of this long-duration, low-intensity NMES is warranted. An important advantage of the 12h-NMES treatment is that it is not restricted by time, equipment, or space. Furthermore, the device used is easily portable due to its size, and after receiving instructions, patients are easily able to apply the device themselves or with the help of family members.

Our study had several limitations. One limitation was the sample size, which was small because the study was designed to perform an initial assessment of the 12h-NMES treatment program. Other weaknesses included the mixture of stroke types and levels of impairment at the sub-acute stages of stroke. Further studies using a similar stimulation treatment program with a larger sample size are needed to verify the effectiveness of the 12h-NMES and gain further insight into the mechanism of the intervention.

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REFERENCES

1) Boyaci A, Topuz O, Alkan H, et al.: Comparison of the effectiveness of active and passive neuromuscular electrical stimulation of hemiplegic upper extremities: a randomized, controlled trial. Int J Rehabil Res, 2013, 36: 315–322. [Medline] [CrossRef]
2) Duncan PW, Lai SM, Keighley J: Defining post-stroke recovery: implications for design and interpretation of drug trials. Neuropharmacology, 2000, 39: 835–841. [Medline] [CrossRef]
3) Aoyagi Y, Tsubahara A: Therapeutic orthosis and electrical stimulation for upper extremity hemiplegia after stroke: a review of effectiveness based on evidence. Top Stroke Rehabil, 2004, 11: 9–15. [Medline] [CrossRef]
4) Malhotra S, Rosewilliam S, Hermens H, et al.: A randomized controlled trial of surface neuromuscular electrical stimulation applied early after acute stroke: effects on wrist pain, spasticity and contractures. Clin Rehabil, 2013, 27: 579–590. [Medline] [CrossRef]
5) Kim JH, Lee LK, Lee JU, et al.: A pilot study on the effect of functional electrical stimulation of stroke patients in a sitting position on balance and activities of daily living. J Phys Ther Sci, 2013, 25: 1097–1101. [Medline] [CrossRef]

6) Kim MY, Kim JH, Lee JU, et al.: The effects of functional electrical stimulation on balance of stroke patients in the standing posture. J Phys Ther Sci, 2012, 24: 77–81. [CrossRef]
7) Levine M, McElroy K, Stakich V, et al.: Comparing conventional physical therapy rehabilitation with neuromuscular electrical stimulation after TKA. Orthopedics, 2013, 36: e319–e324. [Medline] [CrossRef]
8) de Kroon JR, Ijzerman MJ, Chae J, et al.: Relation between stimulation characteristics and clinical outcome in studies using electrical stimulation to improve motor control of the upper extremity in stroke. J Rehabil Med, 2005, 37: 65–74. [Medline] [CrossRef]
9) Hsu SS, Hu MH, Wang YH, et al.: Dose-response relation between neuromuscular electrical stimulation and upper-extremity function in patients with stroke. Stroke, 2010, 41: 821–824. [Medline] [CrossRef]
10) Shimodozono M, Noma T, Matsumoto S, et al.: Repetitive facilitative exercise under continuous electrical stimulation for severe arm impairment after sub-acute stroke: a randomized controlled pilot study. Brain Inj, 2014, 28: 203–210. [Medline] [CrossRef]
11) Peurala SH, Pitkänen K, Sivenius J, et al.: Cutaneous electrical stimulation may enhance sensorimotor recovery in chronic stroke. Clin Rehabil, 2002, 16: 709–716. [Medline] [CrossRef]
12) Schuhfried O, Crevenna R, Fialka-Moser V, et al.: Non-invasive neuromuscular electrical stimulation in patients with central nervous system lesions: an educational review. J Rehabil Med, 2012, 44: 99–105. [Medline] [CrossRef]
13) Nudo RJ, Milliken GW: Reorganization of movement representations in primary motor cortex following focal ischemic infarcts in adult squirrel monkeys. J Neurophysiol, 1996, 75: 2144–2149. [Medline]
14) Wolf SL, Winstein CJ, Miller JP, et al.: Retention of upper limb function in stroke survivors who have received constraint-induced movement therapy: the EXCITE randomised trial. Lancet Neurol, 2008, 7: 33–40. [Medline] [CrossRef]
15) Hu XL, Tong RK, Ho NS, et al.: Wrist rehabilitation assisted by an electromyography-driven neuromuscular electrical stimulation robot after stroke. Neurorehabil Neural Repair, 2014. [Medline] [CrossRef]
16) Lin Z, Yan T: Long-term effectiveness of neuromuscular electrical stimulation for promoting motor recovery of the upper extremity after stroke. J Rehabil Med, 2011, 43: 506–510. [Medline] [CrossRef]
17) Sahin N, Ugurlu H, Albayrak I: The efficacy of electrical stimulation in reducing the post-stroke spasticity: a randomized controlled study. Disabil Rehabil, 2012, 34: 151–156. [Medline] [CrossRef]
18) Noma T, Matsumoto S, Shimodozono M, et al.: Novel neuromuscular electrical stimulation system for the upper limbs in chronic stroke patients: a feasibility study. Am J Phys Med Rehabil, 2014, 93: 503–510. [Medline] [CrossRef]