Neuromuscular Electrical Stimulation of Upper Limbs in Patients With Cerebral Palsy

A Systematic Review and Meta-analysis of Randomized Controlled Trials

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Objective: The aim of the study is to assess the effects of neuromuscular electrical stimulation on the upper limbs of patients with cerebral palsy. Design: We searched PubMed, Cochrane, Embase, and Scopus databases for randomized controlled trials examining the effects of neuromuscular electrical stimulation on the upper limbs of children with cerebral palsy. **Results:** Eight randomized controlled trials (N = 294) were included in the meta-analysis. Compared with traditional physical therapy, sensorimotor training and task-oriented training, constraint-induced movement therapy, dynamic bracing, and conventional robot-assisted therapy, neuromuscular electrical stimulation in combination with these therapies resulted in significantly greater functional scale scores (standardized mean difference = 0.80; 95% confidence interval = 0.54 to 1.06), muscle strength of upper limbs (standardized mean difference = 0.57; 95% confidence interval = 0.25 to 0.88), and spasticity of upper limbs (relative risk = 2.53; 95% confidence interval = 1.46 to 4.39; standardized mean difference = -0.18; 95% confidence interval = -0.29 to -0.06) but did not improve the wrist range of motion (standardized mean difference = 0.43; 95% confidence interval = -0.04 to 0.91). In addition, the effect of neuromuscular electrical stimulation on functional scale scores remained after 3-mo follow-up (standardized mean difference = 0.68; 95% confidence interval = 0.16 to 1.2).

Conclusions: Neuromuscular electrical stimulation effectively improved hand function, muscle strength, and spasticity in patients with cerebral palsy.

Key Words: Cerebral Palsy, Neuromuscular Electrical Stimulation, Upper limbs, Meta-analysis

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C erebral palsy (CP) is a group of permanent but nonprogressive disorders affecting the development of movement and posture; CP can also affect sensation, perception, cognition, communication, and behavior.^{1–3} The estimated prevalence of CP worldwide ranges from 0.74 to 3.6 per 1000 live births, and its prevalence in Taiwan varies from 1.3 to 4.1 per 1000 live

What Is Known

 Neuromuscular electrical stimulation, a modality of producing muscle contraction by depolarizing local motor nerves to improve muscle strength and reduce spasticity, has been commonly used in clinical settings. Previous studies have proven neuromuscular electrical stimulation to be an effective adjuvant therapy in the enhancement of lower limb function in children with cerebral palsy.

What Is New

Neuromuscular electrical stimulation significantly improved hand function, muscle strength, and spasticity of upper limbs in patients with cerebral palsy. Therefore, we recommend neuromuscular electrical stimulation as the treatment of choice in upper limbs for children with cerebral palsy.

births.^{1,4,5} Hemiplegia, in which spastic paresis is unilateral, accounts for 21%–40% of all cases of CP, whereas tetraplegia, involving mainly upper limb paresis, accounts for 20%–43%.^{1,6} Upper limb impairment occurs in 50%–70% of children with CP.⁷

Approaches to rehabilitating the upper limbs in hemiplegic or tetraplegic CP include constraint-induced movement therapy, hand-arm intensive bimanual training, neurodevelopmental treatment, intramuscular injections of botulinum toxin A, and augmenting occupational therapy.⁸ Neuromuscular electrical stimulation (NMES) is a common modality wherein electrical impulses propagate orthodromically along the motor axons toward a muscle to induce muscle contractions. Such impulses can also propagate antidromically along the motor axons toward the central nervous system, thereby inducing short- and long-term neurophysiological effects on the spinal reflex circuits, the corticospinal tract, and cortical networks and affecting neuroplasticity.⁹ Neuromuscular electrical stimulation is divided

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into three types: sensory electrical stimulation, cyclic electrical stimulation, and electromyography (EMG)-triggered electrical stimulation. Neuromuscular electrical stimulation has been widely used in poststroke rehabilitation to improve motor recovery of the arm.¹⁰ Neuromuscular electrical stimulation has also been used as an adjuvant therapy to improve limb function in children with CP.¹¹

A meta-analysis and systemic review reported the efficacy of NMES in improving gross motor function in children with spastic CP, particularly in terms of the sitting and standing dimensions of the Gross Motor Function Measure scale as well as gait velocity and stride length.^{12,13} However, the study reported the use of NMES for only the lower limbs. In this meta-analysis, the aim is to verify the effectiveness of NMES for the upper limbs of children with spastic CP.

METHODS

Study Protocol

This review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses checklist is presented in detail in Supplementary Appendix 1 (Supplemental Digital Content 1, http://links.lww.com/PHM/ B702). The study protocol was prospectively registered with the International Prospective Register of Systematic Reviews (registration number CRD42021245913).

Eligibility Criteria

We included randomized controlled trials (RCTs) that investigated the outcome of using NMES for the upper limbs of children with CP. The following PICO criteria were used to identify eligible RCTs:

P: Participants had CP.

I: Any type of NMES, including sensory, cyclic, or EMG-triggered NMES, was used as the intervention.

C: The results of NMES were compared with those of placebo or NMES as a cointervention with the baseline therapy.

O: Outcomes for the upper limbs were reported.

Randomized controlled trials that investigated the outcomes for only the lower limbs were excluded. Eligibility was not restricted by language or type of journal.

Information Sources and Search Strategy

Relevant articles were identified by searching the PubMed, Cochrane Library, Scopus, and Embase electronic databases. More articles were obtained by manually searching the references in relevant articles. The literature was searched from the date of database inception until October 7, 2021. The following combinations of key words related to the disease and interventions were used: (cerebral palsy or CP or cerebral palsy [MeSH]) AND ([electrical and stimulation] or [electric and stimulation] or electrostimulation or ES or FES or NMES). The search terms were adapted for each electronic database, although Scopus does not include a search function equivalent to MeSH.

Study Selection

Two independent reviewers (C-HO and C-CS) identified relevant studies, and disagreements regarding the PICO criteria were resolved through consensus with a senior reviewer (H-CC).

Other considerations, such as the misclassification of study type, were considered after articles were deemed to have PICO eligibility; for example, RCTs comparing NMES only with other therapies were excluded.

Risk-of-Bias Assessment

Two reviewers (C-HO and C-CS) independently assessed the risk of bias of individual studies by using the Physiotherapy Evidence Database scale.¹⁴ Any discrepancy in the domain scores between the two reviewers was resolved through discussion with a third reviewer (T-JK). We examined whether the discrepancy was related to incomplete or vague reporting; if not, we considered the possibility of misunderstanding or confusion regarding the definitions of the scoring domains.

The Physiotherapy Evidence Database scale consists of 11 items, one of which (regarding eligibility criteria) is related to external validity and is often not included in calculations. The other 10 items are random allocation, concealed allocation, similarity at baseline, subject blinding, therapist blinding, assessor blinding, less than 15% dropout, intention-to-treat analysis, between-group statistical comparison, and point and variability measures. A score less than 4 is considered "poor," scores of 4–5 are considered "fair," scores of 6–8 are considered "good," and scores of 9–10 are considered "excellent."¹⁵

Data Extraction and Outcome Measurement

The two authors independently extracted data from each included study. The following parameters were extracted from each RCT: patient numbers, age, CP type and follow-up duration. The type (sensory, cyclic, EMG triggered), location, intensity, and the duration of NMES were assessed. The outcomes evaluated in the study were functional status, strength, spasticity, and range of motion (ROM) of the upper limbs. The primary outcome for each study was defined as functional status. Follow-up outcomes after completion of the intervention were also assessed. Only outcomes documented in two or more RCTs were included in the metaanalysis. Discrepancies were identified and resolved through discussion with the third author. Unclear or missing data were addressed by contacting the study authors via email.

Data Synthesis and Analysis

Statistical analysis was performed using RevMan, which was provided by the Cochrane Collaboration (version 5.4, Cochrane Collaboration, London, United Kingdom). Relevant continuous data with different scales were converted to the same scale by using standardized mean differences (SMDs) with 95% confidence intervals (CIs). We analyzed pooled data by using the random effects model because of the various study methods used in each RCT. For spasticity, we used improvement or no improvement in Zancolli classification as a dichotomous variable. Meanwhile, modified Ashworth scale (MAS) was presented as a continuous variable. Statistical heterogeneity was assessed using the l^2 test, and heterogeneity was considered significant when the result of the I^2 test exceeded 50%. In the case of high heterogeneity, a sensitivity analysis was performed to confirm the effect. All results were considered statistically significant when a P value was 0.05 or less.

RESULTS

Study Selection

The database search yielded a total of 4199 studies; 752 studies were excluded because they were duplicates, 3291 were excluded because they were irrelevant, and 127 were excluded because NMES was not used for the upper limbs. Among the remaining 29 articles, three were excluded because the full text was not available, one was excluded because of incompleteness, and 17 were excluded because they were not RCTs. Finally, eight studies met the inclusion criteria, two of which appeared to have the same study population; therefore, one was considered a duplicate and was excluded. Figure 1 presents a detailed flowchart of the selection process.

Study Characteristics

The eight included studies were published between 2006 and 2021. Two of the studies were conducted in the same cohort.^{16,17} A total of 294 patients (148 patients in NMES groups and 146 in control groups) with a diagnosis of hemiplegic or spastic CP were included. Four studies used cyclic NMES^{16–19}; the pulse intensity ranged from 10 to 100 mA, the pulse duration ranged from 200 to 300 μ s, the pulse frequency ranged from 30 to 60 Hz, and the intervention duration ranged from 20 mins 5 times/wk to 0.5 to 1 hr/d every day. Three studies used sensory NMES^{20–22}; the pulse intensity ranged from 2 to 100 mA, pulse duration from 200 to 300 μ s, pulse frequency from 30 to 100 Hz, and intervention duration from 0.5 to 1 hr/d 3 times per week. However, one study did not report the type of NMES used in detail.²³ The baseline treatments for the intervention and control

groups were as follows: traditional physical therapy^{20,22}; sensorimotor training and task-oriented training (SM-TOT)²¹; conventional rehabilitation consisting of neurophysiologic exercises using a Bobath approach, active-passive ROM, and stretching exercises¹⁸; constraint-induced movement therapy^{16,17}; dynamic bracing¹⁹; and conventional physical therapy and occupational therapy combined with robot-assisted therapy.²³ Supplementary Table 1 (Supplemental Digital Content 2, http://links.lww.com/ PHM/B703)²⁴ summarizes the characteristics of the eight RCTs.

Risk of Bias Across Studies

The overall quality ranged from 5 to 9; five studies were classified as having "good" quality,^{16–19,22} one was classified as having "excellent" quality,²¹ and two were classified as having "fair" quality.^{20,23} All the studies adhered to random allocation, more than 85% follow-up for at least one key outcome, intention-to-treat analysis, between-group statistical comparison for at least one key outcome, and point and variability measures for at least one key outcome. Allocation concealment was noted only in the study by Ozer et al.¹⁹ Three studies did not have similar conditions at baseline.^{19,20,23} In particular, the patient, therapist, and assessor were not blinded, except in the study by Satheeskumar et al.,²¹ which was a placebo-controlled study. Table 1 presents the results of the risk-of-bias assessment.

Synthesis of Results

Functional Status

The primary functional outcomes of the RCTs were based on one of the following assessments: the upper limb functional test,¹⁷ ABILHAND-Kids questionnaire scores,¹⁸ Melbourne

Records identified through database searching (n= 4199) Pubmed (n = 263) Embase (n= 1540) dentification Cochrane (n= 433) Scopus (n= 1963) Records after duplicates removed (n = 752)Screening Records screened (n = 3447) Records excluded Non-relevant (n= 3291) Full-text articles assessed Full-text articles excluded, for eligibility (n = 156) Eligibility with reasons (n= 148) ES for lower extremities (n= 93) ES for dysphagia (n= 5) ES for others (n= 29) No full-text (n= 3) Studies included in Only protocal (n= 1) No comparison (n= 15) qualitative synthesis (n = 8) Systemic review (n= 2) Included Studies included in quantitative synthesis (meta-analysis) (n = 7)

FIGURE 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses flowchart of selection process.

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	1	2	3	4	5	6	7	8	9	10	Overall (Points)	Quality ^a
Alhusaini et al. ²⁰ (2019)	V						V	V	V	V	5	Fair
Satheeskumar et al. ²¹ (2018)	V		V	V	V	V	V	V	V	V	9	Excellent
Yıldızgören et al. ¹⁸ (2014)	V		V				V	V	V	V	6	Good
Xu et al. ¹⁶ (2015)	V		V			V	V	V	V	V	7	Good
Xu et al. ¹⁷ (2012)	V		V			V	V	V	V	V	7	Good
Ozer et al. ¹⁹ (2006)	V	V				V	V	V	V	V	7	Good
Azzam ²² (2012)	V		V				V	V	V	V	6	Good
Sporea et al. ²³ (2021)	V					V	V	V		V	5	Fair

TABLE 1. Summa	ry of methodological o	quality based on the Physio	otherapy Evidence Database classification scale
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1 = random allocation, 2 = concealed allocation, 3 = similarity at the baseline, 4 = subject blinding, 5 = therapist blinding, 6 = assessor blinding, 7 = more than 85% follow-up for at least one key outcome, 8 = intention-to-treat analysis, 9 = between-group statistical comparison for at least one key outcome, 10 = point and variability measures for at least one key outcome.

^{*a*} Methodological quality: excellent, 9–10 points; good, 6–8 points; fair, 4–5 points; poor, \leq 4 points.

Assessment scores,¹⁹ Jebsen-Taylor hand function test,²⁰ Grasp-QUEST (unimanual function) test,²¹ or Action Research Arm Test.²³

The meta-analysis revealed that the NMES group exhibited significantly higher levels of improvement in functional status than the control group (SMD = 1.00; 95% CI = 0.47 to 1.53; n = 264; $I^2 = 71\%$). Because of the high degree of heterogeneity, a sensitivity analysis was performed by excluding data from the study by Ozer et al.,¹⁹ which was significant outlier. The results indicated that this finding was reliable (SMD = 0.8;

A

95% CI = 0.54 to 1.06; n = 248; $l^2 = 0\%$). Figures 2A and B displays a forest plot of functional status.

Functional Status After 3-Mos of Follow-up

Two of the studies involved a 3-mo follow-up for functional status^{17,19} (Xu et al.¹⁷ for the upper limb functional test and Ozer et al.¹⁹ for the Melbourne Assessment), with 31 participants in the ES groups and 30 in the control groups. The meta-analysis revealed that the NMES group exhibited significantly higher

•		NMES		(Control			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% C	I IV, Random, 95% CI
Alhusaini 2019 [20]	-67.95	23.75	15	-80.66	23.39	14	17.5%	0.52 [-0.22, 1.27] +
Ozer 2006 [19]	70	3	8	49	4	8	4.0%	5.62 [3.17, 8.06	1
Satheeskumar 2018 [21]	25.85	7.78	30	21.24	6.58	30	21.1%	0.63 [0.11, 1.15	1 -
Sporea 2021 [23]	5.93	4.6815	45	2.33	2.7053	45	22.5%	0.93 [0.50, 1.37	1 +
Xu 2012 [17]	4.9	2.9	23	3	2.1	22	19.7%	0.73 [0.13, 1.34] -
Yıldızgören 2014 [18]	13.5	2.5	12	8.8	4.4	12	15.2%	1.27 [0.38, 2.16	1 -
Total (95% CI)			133			131	100.0%	1.00 [0.47, 1.53	1
Heterogeneity: Tau ² = 0.	.28; Chi ² =	: 17.13, d	f = 5 (F	9 = 0.004	4); I ² = 7	1%			-4 -2 0 2 4
Test for overall effect: Z	= 3.67 (P	= 0.0002)						-4 -2 U 2 4 Favours [Control] Favours [NMES]
									ravours (control) ravours (nines)
3									
J		NMES		C	ontrol		1	Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% C	IV, Random, 95% CI
Alhusaini 2019 [20]	-67.95	23.75	15	-80.66	23.39	14	12.3%	0.52 [-0.22, 1.27] +-
Satheeskumar 2018 [21]	25.85	7.78	30	21.24	6.58	30	25.1%	0.63 [0.11, 1.15]] +
Sporea 2021 [23]	5.93	4.6815	45	2.33	2.7053	45	35.6%	0.93 [0.50, 1.37) +
Xu 2012 [17]	4.9	2.9	23	3	2.1	22	18.5%	0.73 [0.13, 1.34]
Yıldızgören 2014 [18]	13.5	2.5	12	8.8	4.4	12	8.5%	1.27 [0.38, 2.16	j
Total (95% CI)			125			123	100.0%	0.80 [0.54, 1.06]	. ♦
Heterogeneity: Tau ² = 0.	.00; Chi ² =	2.40, df	= 4 (P :	= 0.66);	l ² = 0%				-4 -2 0 2 4
Test for overall effect: Z	= 6.02 (P	< 0.0000	1)						-4 -2 0 2 4 Favours [Control] Favours [NMES]
									Favours (Control) Favours (IMMES)
0									
<i>.</i>	NN			Contro			Ctd M	an Difference	Std. Mean Difference
Study or Subgroup		SD Tota				Weiah		andom, 95% CI	IV, Random, 95% Cl
Ozer 2006 [19]				8 6	8	27.79		29 [-0.70, 1.28]	
Xu 2012 [17]	10.3 5			.6 3.4	22	72.39		.82 [0.21, 1.43]	
VU 2012 [1/]	10.5	0.2 Z	5 0	.0 3.4	22	12.37	0 U	.02 [0.21, 1.43]	•
Total (95% CI)		3	1		30	100.09	6 0	.68 [0.16, 1.20]	•
Heterogeneity: Tau ² =	= 0.00: Cł	$i^2 = 0.8$	1. df =	1 (P =	0.37): I ⁱ	² = 0%		_	
Test for overall effect:				- •/		•,••			
rest for overall effect.	L - L.J.	- u - u	· • /						Favours [Control] Favours [NMES]

FIGURE 2. A, Forest plot of the functional status of the upper limbs in the neuromuscular electrical stimulation and placebo groups immediately after treatment. B, Sensitivity test of forest plots for functional status of upper limbs in the neuromuscular electrical stimulation and placebo groups immediately after treatment. C, Forest plot of functional status of upper limbs in the neuromuscular electrical stimulation and placebo groups 3 mos after treatment.

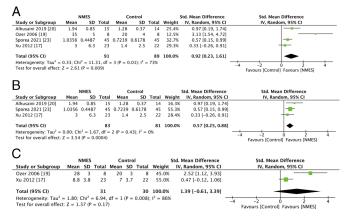


FIGURE 3. A, Forest plot of muscle strength of upper limbs in the neuromuscular electrical stimulation and placebo groups immediately after treatment. B, Sensitivity test of forest plot of muscle strength of upper limbs in the neuromuscular electrical stimulation and placebo groups immediately after treatment. C, Forest plot of muscle strength of upper limbs in the NMES and placebo groups 3 mos after treatment.

levels of improvement in functional status after 3 mos than the control group (SMD = 0.68; 95% CI = 0.16 to 1.20; n = 61; $I^2 = 0\%$). Figure 2C presents a forest plot of the functional status after 3-mo follow-up.

Muscle Strength

Four studies investigated muscle strength, 17,19,20,23 with 91 patients in the ES groups and 89 in the control groups. The meta-analysis revealed a significantly larger improvement in muscle strength in the NMES group than in the control group (SMD = 0.92; 95% CI = 0.23 to 1.61; n = 180; $I^2 = 73\%$). However, because of the high degree of heterogeneity, a sensitivity analysis was performed by excluding outlier data from the study by Ozer et al.¹⁹ The results indicated that this finding was reliable (SMD = 0.57; 95% CI = 0.25 to 0.88; n = 164; $I^2 = 0\%$). Figures 3A and B presents forest plots for muscle strength.

Muscle Strength After 3-Mo Follow-up

Two studies reported a 3-mo follow-up data for muscle strength,^{17,19} with 31 participants in the NMES groups and 30 in the control groups. The meta-analysis revealed that the NMES group did not exhibit a significant improvement in muscle strength after 3 mos compared with the control group (SMD = 1.39; 95% CI = -0.61 to 3.39; n = 61; $I^2 = 86\%$). Figure 3C displays a forest plot of muscle strength after 3-mo follow-up.

Range of Motion

Three studies investigated wrist ROM,^{17,18,23} with 80 patients in the NMES groups and 79 in the control groups. The meta-analysis did not reveal a significant improvement in wrist ROM in the NMES group compared with the control group (SMD = 0.43; 95% CI = -0.04 to 0.91; n = 159; $l^2 = 47\%$). Figure 4 presents a forest plot of wrist ROM.

Spasticity

Two studies assessed spasticity on the basis of the Zancolli classification, with 20 patients in the NMES groups and 20 in the control groups.^{18,19} The meta-analysis indicated that the NMES group exhibited significantly higher levels of improvement in the Zancolli classification than did the control group (risk ratio = 2.53; 95% CI = 1.46 to 4.39, n = 40; $l^2 = 0\%$). Figure 5A presents a forest plot of improvement of the Zancolli classification. Two studies assessed spasticity using the MAS, with 38 patients in the NMES group and 37 in the control group.^{17,22} The meta-analysis revealed significantly higher improvement in MAS in the NMES group than in the control group (SMD = -0.19; 95% CI = -0.06 to -0.29; n = 75; $l^2 = 0\%$). Figure 5B presents a forest plot of the modified Ashworth scale.

DISCUSSION

Neuromuscular electrical stimulation is commonly used in daily clinical practice to generate muscle contractions and produce functional movements of limbs. The results of our study indicate that in patients with CP, NMES significantly improved functional scale scores, the muscle strength of upper limbs, and the spasticity of the upper limbs. However, we did not observe significant improvements in wrist ROM or long-term effects on the muscle strength of the upper limbs. Most participants had spastic CP; furthermore, no studies specifically included patients with dyskinetic or hypotonic CP, for whom the effectiveness of NMES remains unclear.

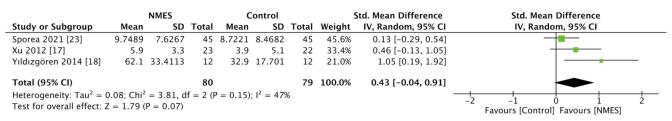


FIGURE 4. Forest plot of wrist ROM in the neuromuscular electrical stimulation and placebo groups immediately after treatment.

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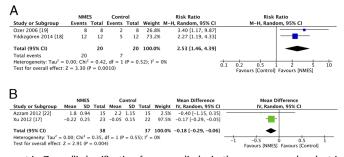


FIGURE 5. A, Forest plot of improvement in Zancolli classification for upper limbs in the neuromuscular electrical stimulation and placebo groups immediately after treatment. B, Forest plot for the modified Ashworth scale of the upper limbs in the neuromuscular electrical stimulation and placebo groups immediately after treatment.

To the best of our knowledge, this is the first meta-analysis of the effect of NMES on the upper limbs of the patients with CP. Wright et al.²⁵ stated that NMES may increase function and muscle strength in the upper limbs of children with CP, and additional benefits, such as improvements in upper limb proprioception, simultaneous bilateral manual coordination, and the performance of grasping and releasing tasks, may result from the combination of NMES with volitional movement.

Neuromuscular electrical stimulation of the lower limbs is more common than that of the upper limbs in children with CP. Improvements in hamstring spasticity, lower limb function,²⁶ and quadriceps-hamstring cocontraction²⁷ have been reported after extended quadriceps stimulation. In addition, significant improvements in spatiotemporal gait parameters and hip adductor tone were observed after stimulation of the bilateral gluteus medius.²⁸ Cauraugh et al.²⁹ demonstrated that NMES produced improvements with medium effect sizes in gait outcomes, including reductions in walking impairment and activity limitations, in children with CP. A systematic review by Salazar et al.¹² revealed low-quality evidence indicating that NMES may be used as an adjuvant therapy to improve the sitting and standing dimensions of the Gross Motor Function Measure in children with spastic CP.

Neuromuscular electrical stimulation positively affects the functional status of the upper limbs. When the study by Ozer et al.¹⁹ was excluded from the sensitivity test because of its high heterogeneity caused by its small number of participants, our results remained the same. The exact mechanism of the effects on functional status is not fully understood. These effects could be partially due to the peripheral effects of muscle training and strengthening, improved flexibility and ROM of the affected limbs, and reduced spasticity.9 In addition, we discovered that patients continued to exhibit improvements in upper limb functional status after 3-mo follow-up. However, the evidence for the duration of the effects may be insufficient because of the small number of RCTs included in the present meta-analysis. These results are consistent with those of Demesi-Drljan et al. (2011),³⁰ who reported an increase in Ouality of Upper Extremity Skill Test scores and wrist extension ROM after stimulation that remained consistent at the 1and 3-mo follow-ups. Wright and Granat³¹ (2000) reported that improvements in hand function test scores remained consistent over 6 wks of follow-up. Whether long-lasting effects can be achieved is unclear and requires further investigation.

Regarding the effects of NMES on wrist ROM, Atwater et al.³² reported that EMG-triggered electrical muscle stimulation

improved upper limb ROM and function. Wright and Granat³¹ (2000) reported improvements in active wrist extension ROM after cyclical ES that remained throughout follow-up. The pilot study by Postans et al.³³ (2010) documented an increase in passive elbow extension for two of six participants treated for elbow contractures with no accompanying change in upper limb function and an improvement in wrist ROM for one of six patients treated for wrist contractures. Acikbas et al.³⁴ (2020) reported that the ROMs for the shoulders and wrists of 15 children with CP significantly improved after NMES treatment to the wrist extensor muscles. These findings suggest that NMES effectively increases joint ROM when combined with other treatment regimens. However, we did not observe a significant improvement in wrist ROM in children with CP treated with NMES, which may be explained by the small sample size. Therefore, further studies are needed to prove the positive effect of NMES in wrist ROM.

The Zancolli classification and MAS are used to assess wrist and finger spasticity in patients with CP. The possible mechanism of electrical stimulation for the reduction of spasticity involves reductions in stretch reflex excitability in individuals with neurological deficits.^{35,36} Carmick³⁷ (1997) reported improvements in hand function and a reduction of spasticity after treatment with NMES and a static dorsal wrist splint in a patient with spastic hemiplegia. The study by Scheker et al.³⁸ (1999) revealed that the combination of NMES and dynamic orthotic traction considerably reduced upper limb spasticity in young patients with CP. Furthermore, Mäenpää et al.³⁹ (2004) reported that the improvements in the Zancolli classification for all 12 patients in their study were maintained for 3 mos, indicating that the effects of NMES may be substantial.

Significant improvements were observed in muscle strength after NMES was applied to upper limbs. A sensitivity test was performed in this meta-analysis, in which the study by Ozer et al.¹⁹ was excluded because of its high heterogeneity due to its small sample size, and the meta-analysis results remained the same. However, our meta-analysis did not confirm long-term improvements in upper limb muscle strength. This finding is supported by several studies. Kamper et al.⁴⁰ conducted a pilot study in which seven of the eight participants experienced significant improvements in wrist extension ROM and extensor strength. Daichman et al.²⁶ revealed that quadriceps strength increased substantially and hamstring spasticity decreased after NMES treatment was administered every other day for 6 wks. However, several studies have vielded different results. For example, Kerr et al.⁴¹ observed no statistically significant difference in the strength or function of the lower limbs between the NMES and placebo groups. No consensus has been reached regarding whether NMES can improve the muscle strength of patients with CP. The total number of participants enrolled in our meta-analysis was too small to determine the effects of NMES on muscle strength. Additional studies with larger sample sizes and homogeneous patient groups are required to assess the long-term effects of NMES on muscle strength.

Compared with the common therapeutic interventions used for baseline therapy,^{16–20,22,23} SM-TOT²¹ was rarely applied. The SM-TOT consisted of two sections. The first 30 mins of specific sensory-motor training focus on tactile discrimination function, for improving somatosensory processing.^{42,43} In the remaining 30 mins, the participants received task-oriented training to improve unilateral and bilateral upper limb function. When combined with other intervention strategies, including constraint-induced movement therapy and bimanual training, SM-TOT was effective in improving hand function and self-care skills.⁴⁴

All RCTs included in our study used an identical baseline therapy in both the intervention and placebo groups. Because the extent of improvement attributable to the baseline therapy is limited and the therapeutic effect of NMES was significant despite such therapy, the efficacy of NMES may be even more pronounced in the absence of such baseline therapy.

The studies included in this meta-analysis were assessed for their risk of bias by using the Physiotherapy Evidence Database scale. Most studies did not describe allocation concealment clearly, potentially resulting in allocation bias. In addition, most studies did not use patient or therapist blinding, which might be attributable to the nature of NMES, in which blinding the assessor is possible but blinding the patient and the therapist is difficult. The placebo-controlled study conducted by Satheeskumar et al.²¹ was double blinded. The placebo-sensory NMES was designed as not delivering current but the continuous beeping sound was given, and the patients were told that they would not feel the stimulation. Placebo-control should be considered when designing future RCTs. However, applying such a design to other types of NMES may be difficult.

Our systematic review has several limitations. First, only eight RCTs were included in this study, two of which involved the same group of patients; the total number of participants was small. Additional RCTs are required to prove the effectiveness of NMES for the upper limbs of children with spastic CP. Second, the studies included for review were heterogeneous in terms of the NMES type, intensity, frequency, duration, and treatment protocol. In addition, the baseline therapies were different in each trial. Third, because of the nature of NMES, patients in most studies were not blinded to the method of treatment, potentially introducing bias to the analysis results.

CONCLUSIONS

This is the first meta-analysis to assess the effect of NEMS on upper limb function in children with CP. Combining NEMS with conventional neurodevelopmental treatment improved upper limb motor function (especially on the functional scale), muscle strength, and spasticity, but it did not significantly improve wrist ROM or increase muscle strength in the long term. Additional clinical studies are required to determine the most effective type, location, intensity, duration, and frequency of NMES for patients with CP. Future RCTs of patients with CP should be double blinded.

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