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Effect of botulinum toxin-A phonophoresis on spasticity in children with hemiplegia

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ABSTRACT

Background: Spasticity is one of the most challenging problems in the management of cerebral palsy. Various trials, treatment modalities, therapeutic approaches, and exercises have been used to treat or modulate spasticity. Phonophoresis uses therapeutic ultrasound to enhance the percutaneous absorption of medication.

Objectives: To determine the effect of botulinum toxin-A phonophoresis on calf muscle spasticity and ankle range of motion in children with hemiplegia.

Materials and methods: This study was conducted on thirty children with hemiplegic cerebral palsy. Their age ranged from 5 to 10 years, their grade of ankle plantar flexors spasticity ranged from 2 to 3 according to Modified Ashworth Scale and they were able to walk alone with some limitations, classified as level II according to Gross Motor Function Classification System (GMFCS). They were randomly classified into two groups: the study group, which received botulinum toxin-A phonophoresis in addition to traditional physiotherapy program, and the control group, which received placebo ultrasonic therapy and the same traditional physiotherapy program. The Neuro-EMG-Micro (Neurosoft) was used as surface electromyography device to measure H/M ratio of calf muscles. The EasyAngle digital goniometer was used to measure ankle dorsiflexion range of motion. The SoLo Therasonic 455 ultrasonic device was used to apply botulinum toxin-A phonophoresis.

Results: Comparison within the study group revealed a significant decrease in post-treatment H/M ratio of gastrocnemius (GC) and soleus muscles compared to pre-treatment values. Additionally, there was a significant increase in post-treatment passive and active dorsiflexion range of motion (DF ROM) of ankle joint. Furthermore, there was a significant difference between the study and control groups in post-treatment H/M ratio of GC and soleus muscles, as well as in post-treatment passive and active DF ROM of ankle joint.

Conclusion: Botulinum toxin-A phonophoresis significantly decreases spasticity of calf muscle and improves ankle ROM in children with hemiplegic cerebral palsy, especially when combined with traditional physical therapy.

Introduction

Calf muscle spasticity is a common feature in children with hemiplegic cerebral palsy that can lead to equinus deformity, gait abnormalities, and functional limitations. It results from hyperexcitability of the stretch reflex. Persistent spasticity interferes with motor development, balance, and mobility, and

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often necessitates physical therapy, orthoses, or pharmacological interventions.[1-3]

The H-reflex to M-wave (H/M) ratio is widely used to assess spinal excitability in calf muscles. Normal H/M ratio ranges from 0.5 to 0.7 in healthy individuals. It is measured by electrical stimulation of the posterior tibial nerve in the popliteal fossa and recording commonly from the soleus and can also be recorded from gastrocnemius (GC) muscle. The maximal amplitude of the H-reflex is often obtained with low intensity and with the gradual increase of intensity, the M response increases its amplitude while the H-reflex amplitude is decreasing. An increased H/M ratio indicates enhanced alpha motor neuron excitability, commonly seen in spasticity.[4-6]

Botulinum toxin type-A (BoNT-A) reduces spasticity by inhibition of acetylcholine release at the neuromuscular junction. It cleaves synaptosomal associated protein of 25 kilodaltons (SNAP-25), a protein essential for synaptic vesicle fusion, thereby preventing muscle fiber depolarization and action potential. This leads to temporary chemodenervation, muscle relaxation, and reduced reflex hyperexcitability. Its effect typically lasts 3-6 months, providing a therapeutic window for physiotherapy and functional training in patients with spasticity.[7,8]

During the past 25 years, BoNT-A injection has become the most widely used medical intervention in children with cerebral palsy for spasticity management. Intramuscular injection of BoNT-A causes a decrease in muscle activity, usually reported as a reduction in spasticity. Injection of the GC muscle in children with hemiplegia usually increases the ankle dorsiflexion ROM.[9] Intramuscular BoNT-A injection is an effective option in spasticity treatment. However, it is limited by its cost and local discomfort.[10] Botulinum toxin-A injection is considered a complex medical intervention that may require general anesthesia for children and radiological guidance for drug delivery and requires highly skilled medical team members including a neurosurgeon, anesthesiologist, nurse and possibly a radiologist. Phonophoresis is a noninvasive method of administering molecules through the skin via ultrasonic waves that increase the transdermal absorption of drugs. Drugs such as BoNT-A can be delivered transdermally via phonophoresis or iontophoresis.[10-12] Phonophoresis can be used for delivery of BoNT-A with no adverse effects. It is safer than injection, relatively inexpensive and easy to apply.[10]

Treatment of spasticity in children with cerebral palsy by BoNT-A phonophoresis may provide a new physical therapy technique and may open a new field for physiotherapists in the treatment of cerebral palsy, which will result in improvement of physical therapy services.

Materials and methods

Study design

It was a single-blind randomized controlled study design. A preliminary power analysis was conducted for the soleus H/M ratio as the primary outcome. Using a pilot study of 10 participants (5 per group), the effect size was 1.92. Two-tailed analysis with α=0.05 and actual power (1-β)=96.8% determined a required sample size of 9 per group, which was increased by 66% to 15 per group to account for expected dropouts. Sample size calculation was performed using G*Power software (3.1.9.2).

Participants

Thirty children (17 boys and 13 girls) with hemiplegic cerebral palsy participated in this study; they were recruited from the outpatient clinic of the Faculty of Physical Therapy, Cairo University. The age range of the selected children was from 5 to 10 years old. Their ankle plantar flexors spasticity grade ranged from 2 to 3 according to Modified Ashworth Scale and they were able to walk alone with some limitations, classified as level II according to Gross Motor Function Classification System (GMFCS). They were able to follow instructions and understand commands. Children who had bone deformities in the lower leg, ankle or foot, fixed contracture of ankle plantar flexors, any metal implant in the lower leg near the area of treatment application were excluded from the study. Children who had received botulinum toxin injection or undergone surgery in gastro-soleus muscle within the 12 months prior to taking part in the study were also excluded.

Randomization

The thirty eligible children in this study were randomly classified into two equal groups through simple lottery method. Allocation concealment was ensured by sealed, opaque envelops prepared by independent person not involved in recruitment or assessment (Figure 1).

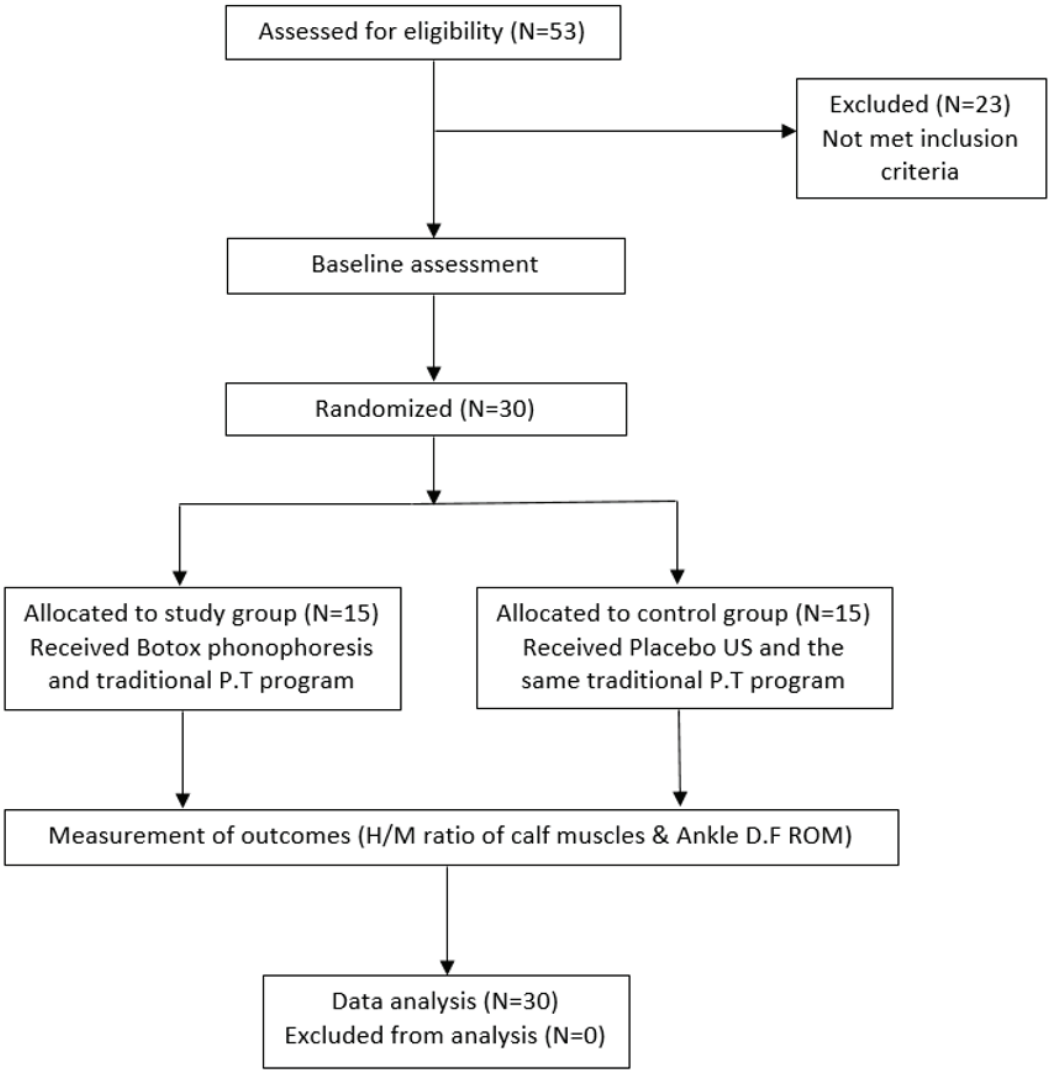

Figure 1. *Flowchart of the study.*

Study group (group A)

Botulinum toxin-A phonophoresis was applied to subjects of this group in addition to a designed traditional physical therapy program.

Control group (group B)

Subjects in this group received placebo ultrasonic therapy in addition to the same traditional physical therapy program as the study group.

Measurement of ankle dorsiflexion ROM

EasyAngle (EA) digital goniometer (Meloq AB, Stockholm, Sweden) was used to measure ankle dorsiflexion ROM (Figure 2). It is a device powered by a rechargeable battery. It has inertial measurement unit technology, with a three-axis accelerometer and a three-axis gyroscope to detect and determine its motion and position in space. It is a recent instrument for measuring joint ROM.[13] EasyAngle is supported by clinical evidence with many EA studies completed and more underway, it conforms to the highest clinical standards. With EA, the process of taking these measurements is fast, consistent, and reliable. The EA digital goniometer is a powerful tool in the hands of a physical therapist or other movement professional.[14] It is valid, reliable, easy, and fast for measuring ROM.[15]

Figure 2. *EasyAngle (EA) digital goniometer.*

The dorsi-flexion range of motion (DF ROM) was measured passively and actively before starting and at the end of treatment procedures. The child assumed supine lying position on a plinth with extended knee and full ankle plantar flexion. As shown in Figure 3, the goniometer was positioned and fixed by strap on the lateral aspect of the foot with the black line of goniometer's ruler on the lateral aspect of fifth metatarsal bone. To measure the passive DF ROM, the therapist clicked on the power button to turn on the device, then clicked on the main button to set the device to zero. The therapist clicked again on the main button taking the ankle joint toward dorsiflexion by grasping the child's foot by one hand while fixing the leg by the other hand then he clicked for the third time on the main button to record the angle once the available DF ROM was reached, defined as the first point of firm resistance perceived without eliciting pain or allowing compensatory movements. The measurement was repeated three times, and the mean value was recorded. The same procedure was applied for measurement of active DF ROM by giving instructions to the child to actively dorsiflex the ankle.

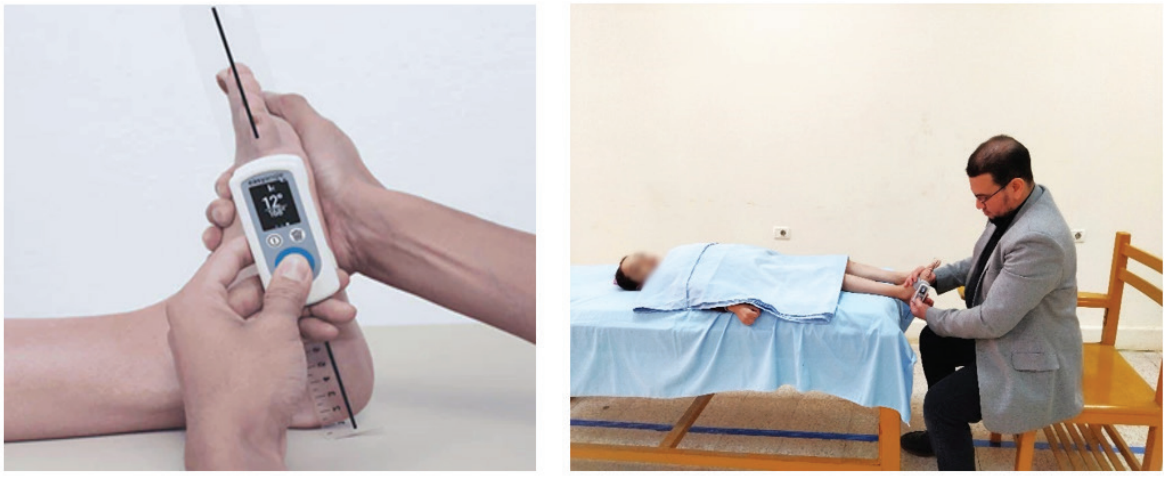

Figure 3. *ROM measurement.*

Surface electromyography

For measuring the H/M ratio, an electromyography device (Neurosoft, Ivanovo, Russia) was used for recording of myoelectric signals from calf muscles of the affected limb. The device consists of computer processing unit, screen, printer, keyboard and other components including amplifier, bipolar stimulating electrode, recording and ground electrodes and dedicated keyboard as shown in Figure 4. Surface electromyography (sEMG) is valid and reliable tool to assess the electrical activity of the muscles. It has been used in research and clinical applications for the non-invasive analysis of the myoelectric activity of the calf muscle.[16] Calf muscle electromyography was also done before starting and at the end of treatment procedures.

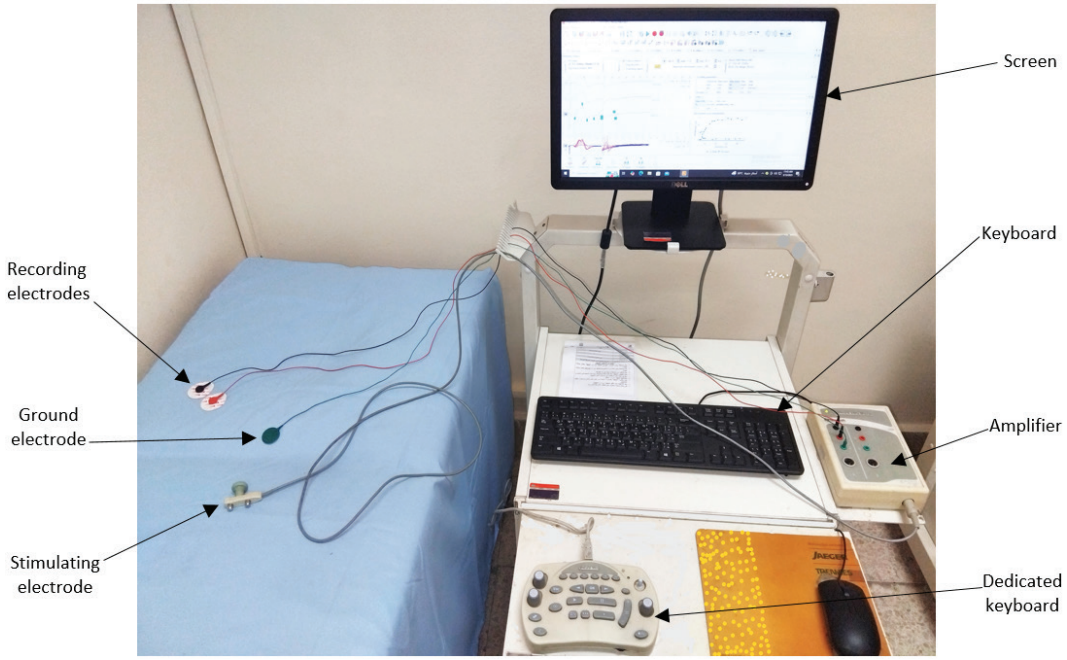

Figure 4. *Surface electromyography system.*

Before starting the electromyography procedure, all children refrained from strenuous activities and caffeine intake and stopped taking any anti-spastic drugs at least 12 hours before EMG evaluation. All procedures were applied with the patient lying in prone position and the foot outside the plinth, well positioned and relaxed for easy access to the calf muscle. The surface area of the calf muscle was cleaned with cotton wool and alcohol to reduce skin resistance.

For measuring the H/M ratio of soleus muscle as shown in Figure 5, the active recording electrode (negative, black electrode) was placed on the soleus muscle just below the contour of the gastrocnemius (GC) muscle, while the reference electrode (positive, red electrode) was placed on the heel. The ground electrode was placed midway between the negative and positive electrodes.[17,18]

For measuring the H/M ratio of GC muscle, the recording electrodes were placed on the bulkiest area of the medial head of GC muscle, and the ground electrode was placed distally on the heel (Figure 5). The stimulating electrode was used to stimulate the posterior tibial nerve at the back of knee. The stimulus duration was 1 msec. to stimulate sensory nerve fibers (Ia). It was stimulated manually at rate of once every ten seconds to reduce post-activation depression effects. The intensity of the current was gradually increased and the H-reflex and M-wave were observed on the screen. After recording, a clean towel was used to wipe the recording area.[17,18]

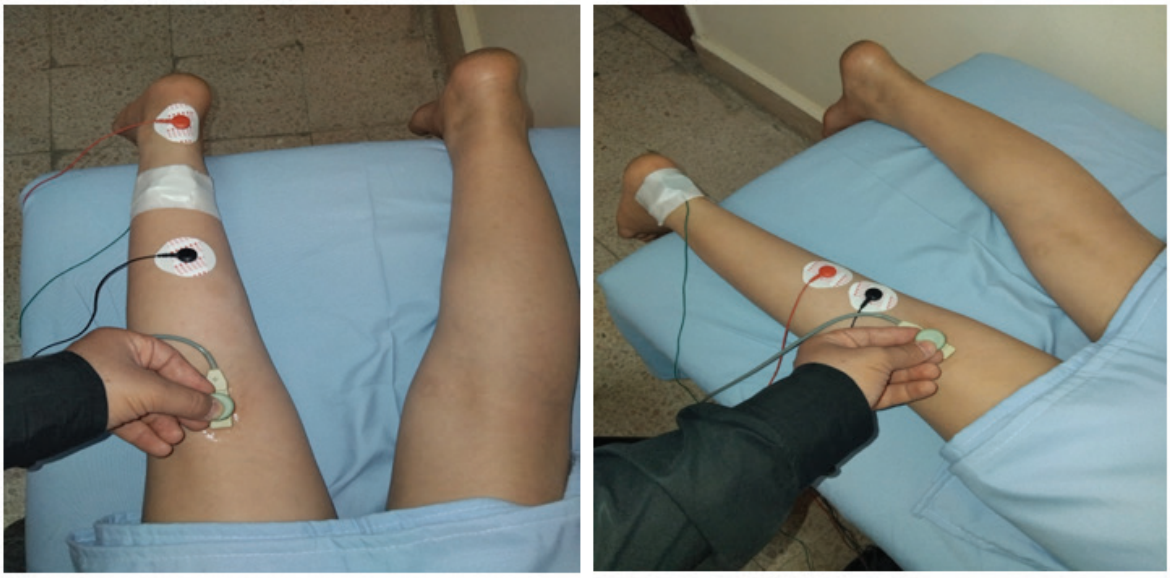

Figure 5. *Electrodes placement during EMG of soleus and GC muscles.*

The electromyography signals were checked on an amplitude-time display of the recordings on the screen to exclude artifacts, such as direct current artifact, motion artifact or electric noise before calculation of electromyography variables. The H_{max} to M_{max} ratio was computed via the system software by dividing the H_{max} amplitude by M_{max} amplitude.[18] The report of each muscle measurement was then printed and saved in the system software.

Intervention

Botulinum toxin-A phonophoresis session

The SoLo Therasonic 455 device (EMS Physio Ltd, Oxfordshire, England) was used for application of BoNT-A (Figure 6). It offers a broad range of uses with state-of-the-art technology in a unique design. It has the availability to use 1MHz or 3MHz frequency from the same treatment head.

Vials of BoNT-A (Dysport® 500 U/vial, Ipsen Ltd, UK) were used to prepare a mixture with carbopol gel. Each vial was dissolved in 5 ml of sterile saline solution (0.9% NaCl) and each 1 ml of the solution was gently mixed with 50 grams of carbopol gel in a sterile, capped small container. A separate labeled container was assigned for each child in the study group. All containers were stored in the refrigerator between 2 °C and 8 °C and the total amount was used for phonophoresis sessions.[10] The dosage of 100 units per child was determined based on the recommended intramuscular injection dosage (3 to 6 units/kg),[19] although the actual amount absorbed transdermally via phonophoresis remains undetermined. This dosage was selected empirically as no standardized transdermal recommendations currently exist for BoNT-A phonophoresis.

Each child in the study group received 10 phonophoresis sessions over 5 consecutive days (two sessions per day). This schedule was adopted in consideration of the stability of reconstituted BoNT-A, which does not exceed 5 days when stored in the refrigerator at 2 °C to 8 °C. A minimum interval of two hours was maintained between the two daily sessions to allow for optimal transdermal absorption and to minimize potential saturation of local tissue receptors. The ultrasonic device was applied in continuous mode, with a frequency of 1MHz, an intensity of 1W/cm^2 and a duration of 10 minutes per session.[10] Each child in the control group received 10 placebo ultrasonic sessions with the same schedule and session time.

All phonophoresis sessions as shown in Figure 6 were applied while the child was in prone position with the feet outside the plinth. The patient's skin was carefully inspected for the barriers of transcutaneous absorption of drugs such as poor circulation and skin dehydration to ensure the maximum effectiveness of phonophoresis. The surface area of the calf muscle was cleaned with cotton wool and alcohol, then an appropriate amount of gel was applied on the calf muscle and the parameters were set. The ultrasonic head was moved slowly in a circular motion over the calf muscle bulk, while maintaining a safe distance from the epiphyseal plate of growing bone. After the end of session, tissues were used to wipe the area and the skin was inspected for any signs of irritation.

Figure 6. *Phonophoresis session and SoLo Therasonic 455 device.*

Traditional physical therapy program

All participants in this study received the same traditional physiotherapy program for one month (12 sessions/month, 3 sessions/week, and 1 hr/session) after the end of all phonophresis and placebo ultrasonic therapy sessions. The program consisted of functional strengthening exercises, isolated strengthening exercises for ankle dorsi-flexors, stretching exercises for calf muscles, balance exercises and gait training. In addition, participants were instructed to wear night ankle-foot orthosis with adjustable straps and knee immobilizer at least 8 hours daily to apply positional prolonged stretching of the calf muscles.

Statistical analysis

Data were analyzed using SPSS Version 26.0. For normality test of data, Shapiro-Wilk test was performed. Unpaired t-test was used for comparison of age, pre-treatment active and passive ankle DF ROM, pre-treatment H/M ratio of GC and soleus muscle, post-treatment active and passive ankle DF ROM and post-treatment H/M ratio of GC and soleus muscle between both groups. Paired t-test was used for comparison of pre and post-treatment H/M ratio of soleus muscle within both groups and for comparison of ankle active DF ROM within group A and ankle passive DF ROM within group B. Wilcoxon signed rank test was conducted for comparison of pre and post-treatment H/M ratio of GC muscle within both groups and for comparison of ankle passive DF ROM within group A and ankle active DF ROM within group B. Chi-squared test was performed for comparison of sex and hemiplegic side distribution between the two groups. Mann-Whitney test was used for comparison of spasticity grade distribution between both groups. Descriptive statistics such as arithmetic mean and standard deviation were also performed. The level of significance for all statistical tests was set at $p<0.05$.

Results

Subject characteristics

As shown in Table (1) there was no significant difference between both groups in age ($p>0.05$). In addition, there was no significant difference in the distribution of sex, hemiplegic side, and spasticity grades between both groups ($p>0.05$).

Table 1. Basic characteristics of participants.

	Group A (N=15)	Group B (N=15)	*p* value
Age (years) mean±SD	8.20±1.70	8.07±1.91	0.841
Gender [N (%)]			
Girls	7 (46.7%)	6 (40%)	0.713
Boys	8 (53.3%)	9 (60%)	
Hemiplegic side [N (%)]			
Right	10 (66.7%)	9 (60%)	0.705
Left	5 (33.3%)	6 (40%)	
Spasticity grades [N (%)]			
MAS, Grade II	11 (73.3%)	10 (66.7%)	0.695
MAS, Grade III	4 (26.7%)	5 (33.3%)	

Note: *MAS: modified Ashworth scale*

Effect of treatment on H/M ratio and ROM

Comparison within group A

Comparison within group A revealed a significant decrease in post-treatment H/M ratio of GC muscle (p=0.001) and a significant decrease in post-treatment H/M ratio of soleus muscle (p<0.001) when compared with those of pre-treatment. In addition, there was a significant increase in post-treatment passive dorsiflexion ROM of ankle joint (p=0.001) and a significant increase in post-treatment active dorsiflexion ROM of ankle joint (p<0.001) when compared with those of pre-treatment. (Table 2).

Table 2. Comparison of pre- and post-treatment H/M ratio and ROM within group A.

Variable	Group A				
	Pre-treatment (Mean±SD)	**Post-treatment** (Mean±SD)	**MD**	**% of change**	***p* value**
GC H/M ratio, (%)	60.56±21.33	28.78±12.60	31.78	52.48%	0.001
Soleus H/M ratio, (%)	36.33±9.94	16.39±7.66	19.59	54.91%	<0.001
Passive DF ROM, (degrees)	56.53±5.85	64.47±4.21	-7.93	14.03%	0.001
Active DF ROM, (degrees)	21.53±6.93	37.80±7.05	-16.23	75.38%	<0.001

Note: *GC: gastrocnemius muscle, DF: dorsiflexion, ROM: Range of motion, MD: mean difference, H/M: Hoffman reflex/ Motor wave.*

Comparison within group B

Comparison within group B revealed a non-significant decrease in post-treatment H/M ratio of GC muscle (p=0.069) and a significant decrease in post-treatment H/M ratio of soleus muscle (p=0.009) when compared with those of pre-treatment. In addition, there was a significant increase in post-treatment passive dorsiflexion ROM of ankle joint (p<0.001) and a significant increase in post-treatment active dorsiflexion ROM of ankle joint (p=0.001) when compared with those of pre-treatment (Table 3).

Table 3. Comparison of pre- and post-treatment H/M ratio and ROM within group B.

Variable	Group B				
	Pre-treatment (Mean±SD)	**Post-treatment** (Mean±SD)	**MD**	**% of change**	***p* value**
GC H/M ratio, (%)	57.27±13.43	55.61±15.34	1.65	2.88%	0.069
Soleus H/M ratio, (%)	37.43±10.00	35.33±11.05	2.09	5.58%	0.009
Passive DF ROM, (degrees)	55.53±4.85	57.73±4.88	-2.20	3.96%	<0.001
Active DF ROM, (degrees)	21.07±6.83	23.60±7.31	-2.53	12.01%	0.001

Note: *GC: gastrocnemius muscle, DF: dorsiflexion, ROM: range of motion, MD: mean difference, H/M: Hoffman reflex/ Motor wave.*

Comparison between groups

Pre-treatment comparison

Comparison between groups revealed a non-significant difference in both pre-treatment H/M ratio of GC muscle (p=0.617) and pre-treatment H/M ratio of soleus muscle (p=0.766). In addition, there was a non-significant difference in both pre-treatment passive dorsiflexion ROM of ankle joint (p=0.615) and pre-treatment active dorsiflexion ROM of ankle joint (p=0.854). (Table 4).

Table 4. Comparison of pre-treatment H/M ratio and ROM between groups.

Variable	**Group A** (Mean±SD)	**Group B** (Mean±SD)	**MD**	***p* value**
GC H/M ratio, (%)	60.56±21.33	57.27±13.43	3.29	0.617
Soleus H/M ratio, (%)	36.33±9.94	37.43±10.00	-1.09	0.766
Passive DF ROM, (degrees)	56.53±5.85	55.53±4.85	1.00	0.615
Active DF ROM, (degrees)	21.53±6.93	21.07±6.83	0.47	0.854

Note: *GC: gastrocnemius muscle, DF: dorsiflexion, ROM: range of motion, MD: mean difference, H/M: Hoffman reflex/Motor wave.*

Post-treatment comparison

Comparison between groups revealed a significant difference in post-treatment H/M ratio of GC muscle (p<0.001) and in post-treatment H/M ratio of soleus muscle (p<0.001). In addition, there was a significant difference in post-treatment passive dorsiflexion ROM of ankle joint (p<0.001) and in post-treatment active dorsiflexion ROM of ankle joint (p<0.001) (Table 5).

Table 5. Comparison of post-treatment H/M ratio and ROM between groups

Variable	Group A (Mean±SD)	Group B (Mean±SD)	MD	*p* value
GC H/M ratio, (%)	28.78±12.60	55.61±15.34	-26.83	<0.001
Soleus H/M ratio, (%)	16.39±7.66	35.33±11.05	-18.95	<0.001
Passive DF ROM, (degrees)	64.47±4.21	57.73±4.88	6.73	<0.001
Active DF ROM, (degrees)	37.80±7.05	23.60±7.31	14.20	<0.001

Note: *GC: gastrocnemius muscle, DF: dorsiflexion, ROM: range of motion, MD: mean difference, H/M: Hoffman reflex/Motor wave.*

Discussion

This randomized controlled study investigated the efficacy of BoNT-A delivered via phonophoresis on calf muscle spasticity and ankle ROM in children with hemiplegic CP. Thirty children were divided equally into a study group, which received BoNT-A phonophoresis plus traditional physiotherapy program and a control group, which received placebo ultrasound with the same physiotherapy program. Outcomes included the H/M ratio of the soleus and gastrocnemius muscles (measured via Neurosoft EMG) and active and passive ankle dorsiflexion ROM (assessed by an EasyAngle goniometer). The study group demonstrated significant decreases in H/M ratio for both gastrocnemius and soleus muscles, along with substantial increases in active and passive dorsiflexion ROM. The control group also showed significant but smaller improvements in H/M ratio (significant only for soleus) and smaller significant ROM gains, likely arising from the physical therapy alone. Between-group comparison clearly favored the study group significantly on all primary measures, indicating a superior effect attributable to BoNT-A phonophoresis.

Potential mechanisms of BoNT-A phonophoresis

To date, BoNT-A injections are widely recognized as an effective intervention for management of spasticity in children with CP. These injections reduce muscle hyperactivity by blocking acetylcholine release at neuromuscular junctions, leading to decreased spasticity, improved ROM, and enhanced function, though often transient and requiring adjunctive interventions such as casting or orthosis to maintain benefits. In this context, several systematic reviews confirmed the role of BoNT-A as a focal spasticity management tool when combined with comprehensive rehabilitation.[9,20,21]

The present outcomes of our study, marked reductions in H/M ratio and meaningful gains in ROM are congruent with injection-based findings, suggesting that BoNT-A delivered via phonophoresis may induce neuromodulatory effects comparable to those observed following injection without implying confirmed intramuscular delivery, potentially offering a non-invasive alternative and achieving greater improvements than physiotherapy alone.

Phonophoresis employs ultrasound waves to enhance transdermal delivery of pharmacological agents. Mechanisms include thermal effects, cavitation leading to increased skin permeability, and acoustic streaming that facilitates molecular transport.[22] Despite the relatively large molecular size of BoNT-A, the significant outcomes in spasticity and ROM indicate that effective skin penetration may have occurred. In comparison to intramuscular injections, phonophoresis could offer a safer and more user-friendly option, especially for children by avoiding needle-associated discomfort, infection risk, and possible muscle damage as a non-invasive approach; however, it should not be considered equivalent to intramuscular injection in terms of pharmacokinetics or tissue distribution.

Role of traditional physical therapy

Both study and control groups received the identical physiotherapy program, including stretching, night splints, balance and gait training, functional strengthening, and dorsiflexors strengthening. While these interventions alone led to small improvements in the control group, the combined BoNT-A phonophoresis significantly enhanced outcomes. This multiplicative effect mirrors injection-based protocols where BoNT-A is most effective when paired with appropriate rehabilitative strategies.[9,21]

Phonophoresis in Spasticity: Other Agents

Although BoNT-A phonophoresis is considered a recent method in spasticity management, other pharmacologic agents delivered via phonophoresis have been studied. During our literature review, we did not find any previous studies that used BoNT-A phonophoresis in the treatment of spasticity. Most similar previous studies used other medications like lidocaine, baclofen, hydrocortisone acetate, and non-

steroidal anti-inflammatory drugs including ibuprofen, piroxicam, diclofenac sodium, and ketoprofen.[23-25]

A previous study was conducted to identify the effect of baclofen phonophoresis on spasticity in children with diplegia. It showed that baclofen delivered via phonophoresis to gastrocnemius combined with traditional physical therapy had no significant effect on decreasing spasticity but led to significant improvement in standing ability mainly because of the physical therapy program as these findings were also presented in the control group that received only physiotherapy program.[25]

Another study in children with spastic diplegic CP applied phonophoresis (using unspecified agent) combined with physical therapy and compared outcomes against traditional therapy alone. The experimental group showed significant improvements in spasticity and ankle ROM.[26] This aligns with the current findings and supports the utility of phonophoresis in CP.

Botulinum toxin phonophoresis and iontophoresis in hyperhidrosis management

Although BoNT-A is typically administered via intradermal injection for hyperhidrosis, recent explorations have examined non-invasive transdermal delivery methods, including phonophoresis and iontophoresis, to avoid the discomfort and side effects associated with needle-based therapy.

There are previous studies that used phonophoresis or iontophoresis to deliver botulinum toxin A into tissues to evaluate its effect on the treatment of palmar and axillary hyperhidrosis.[10,27]

In one of these studies, BoNT-A phonophoresis was conducted to identify its effect on palmar hyperhidrosis by using ultrasonic with continuous mode, 1MHz frequency for 10 minutes. Also in this study, BoNT-A was successfully delivered via iontophoresis by using galvanic micro current to identify it effect on palmar hyperhidrosis. Both methods revealed a significant reduction in sweating with no adverse effect over a 16-week period with higher patient acceptance due to the painless procedure.[10]

In a related investigation to compare between BoNT-A injection and iontophoresis, researchers explored BoNT-A iontophoresis for axillary hyperhidrosis, applying alternating electrical current for 30 minutes with an electrode was soaked in BoNT-A solution and fixed over the axillary region. While the sample size was small, results indicated a measurable decrease in sweat production sustained over several weeks. This study indicates that BoNT-A iontophoresis may represent a promising alternative to injections, especially for patient's intolerant to needle-based therapies or seeking a less invasive option.[27]

These findings support the feasibility of BoNT-A transdermal delivery in targeting peripheral autonomic dysfunction and provide an important conceptual precedent for its application in neuromuscular conditions like spasticity.

Collectively, the previous studies that used phonophoresis with other pharmacological agents in spasticity treatment and those that were applied for hyperhidrosis reinforce that BoNT-A delivered transdermally via ultrasound can yield clinically meaningful outcomes in spasticity management without direct evidence of muscle penetration.

Safety and practical implications

Although traditional BoNT-A injection is effective in decreasing muscle spasticity, it is invasive and carries risks of pain, muscle atrophy, systemic spread, and infection, especially concerning in pediatric populations.[9,21] Phonophoresis potentially avoids these drawbacks while delivering comparable efficacy. However, as a novel modality for delivering BoNT-A, its safety profile, long-term effects, optimal dosing, and ultrasound parameters remain to be established. Future work should include imaging and histological studies to assess potential muscle morphology changes, systemic absorption, and functional integrity over time.

Limitations

Although participants were blinded to group allocation, blinding of the outcome assessor was not possible because of the practical constraints inherent to rehabilitation-based interventions. However, the primary outcome measures (H/M ratio and ankle dorsiflexion ROM) were objective and instrument-based, which minimizes the potential risk of assessor-related detection bias and strengthens the validity of the findings. As no standardized dosage guidelines exist for BoNT-A phonophoresis, the selected dose was pragmatically based on commonly used clinical injection doses, aiming to ensure safety rather than to establish dose equivalence.

The present study did not confirm the intramuscular delivery of BoNT-A; therefore, further studies are required to investigate the pharmacokinetics and tissue distribution of BoNT-A delivered via phonophoresis.

Conclusion

Botulinum toxin-A phonophoresis significantly decreases spasticity of calf muscle and improves ankle ROM in children with hemiplegic cerebral palsy who had ankle plantar flexors spasticity grade ranged from 2 to 3 according to Modified Ashworth Scale, especially when combined with traditional physical therapy.

Ethical approval

The Research Ethics Committee, Faculty of Physical Therapy, Cairo University approved this study under approval number (P.T.REC/012/005088) and each participant's caregiver signed an informed consent form prior to take part in the study.

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Conflict of interest

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CRediT authorship contribution statement

Ahmed F Attia: conceptualization, methodology, investigation, data curation, formal analysis, visualization, writing: original draft; **Amira M El-Tohamy:** main supervisor, project administration, writing: review and edit; **Gehan H El-Meniawy:** supervision, writing: review and edit; **Walaa ElNaggar:** supervision, writing: review and edit.

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