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Management of Muscle Spasticity in Children with Cerebral Palsy by Means of Extracorporeal Shockwave Therapy: A Systematic Review of the Literature

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ABSTRACT

The purpose of this systematic review was to investigate the effectiveness of extracorporeal shockwave therapy for the management of muscle spasticity in children with cerebral palsy. An electronic database search was performed to identify studies relevant to the research question. Assessment of the quality of evidence in all relevant studies was performed with the help of the Oxford Center for Evidence-based Medicine guide. Four studies met our inclusion criteria for review: one was a low-quality randomized controlled clinical trial, two were individual case-control studies and one was a case series study. Reduction in muscle stiffness and improvement in joint range of motion were the outcomes in all of the selected studies that used extracorporeal shockwave therapy. However, considering the limited evidence provided by these studies, further research is needed to support the use of extracorporeal shockwave therapy in the management of muscle spasticity in children with cerebral palsy.

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Introduction

Cerebral palsy (CP) includes a group of neurological disorders resulting from damage to the developing brain before, during, or immediately after birth.¹ With a reported prevalence of 2–3 per 1000 live births,² CP is the most common motor disability of childhood. Motor impairment in children with CP manifests as spasticity, poor muscle control, weakness, and poor balance. Spasticity, which is characterized by a velocity-dependent increase in muscle tone and exaggerated tendon jerks, results from hyperexcitability of the stretch reflex and is one component of the upper motor neuron syndrome.³ Spastic CP comprises almost 75% of all cases of CP.⁴ In spastic CP the muscles often develop contractures, leading to restricted range of motion (ROM) of the joints. Contractures most commonly affect the ankle plantar flexors and lead to the characteristic equinus foot deformity, which contributes to the abnormal gait and posture seen in some spastic CP patients. Recently, researchers have identified changes in the intrinsic properties of muscles in spastic CP patients; these include changes in sarcomere length, fiber type, extracellular matrix concentration, fiber bundle stiffness, and the stem cell population.⁵ Such structural alterations to skeletal muscle result in an increase in passive stiffness. Thus, muscle stiffness in CP has both active and passive components. The active component is mainly related to spasticity, whereas the passive component depends on the viscoelastic properties of muscles.^{6,7} Clinically, active muscle stiffness is the resistance of muscles during the contracted state, whereas passive muscle stiffness is the resistance exhibited by myofibrils when they are relaxed.

Measuring muscle stiffness in children with CP is difficult. Ordinal scales, such as the Ashworth scale (AS) and the modified Ashworth scale (MAS), are easy to apply but are unreliable and do not measure the passive component of muscle stiffness.^{8,9} Recent advances in ultrasound (US) elastography techniques, however, have made direct quantification of muscle stiffness possible. There are several US elastography methods currently available, the two most commonly used ones being transient elastography (TE) and shear wave elastography (SWE).¹⁰

Prevention of muscle contractures is a major challenge in spastic CP. The best way of increasing and maintaining muscle-tendon elasticity and preventing contractures is joint mobilization and muscle stretching – best carried out under the guidance of a physical therapist.¹¹ As is the case for all neuromuscular disorders, the sooner physical therapy is introduced, the better the outcome.^{12–14} For the purpose of preventing muscle contractures, other therapies can be added to physical therapy, including oral medications, splinting and casting, chemodenervation with botulinum toxin or phenol, selective dorsal rhizotomy, intrathecal baclofen, and orthopedic surgery.¹⁵ A recently introduced modality is extracorporeal shockwave therapy (ESWT).

ESWT was originally developed to disintegrate urinary stones.¹⁶ Since then, it has found other applications in the medical field and is now also used to treat musculoskeletal disorders. More than a decade ago, ESWT had emerged as the first-line treatment for proximal plantar fasciitis of the heel, lateral epicondylitis of the elbow, calcific tendinitis of the shoulder and nonunion of long bone fracture.^{17–20} Recently, ESWT has been used to treat patellar and Achilles tendinopathies, and avascular necrosis of the femoral

head.^{21–23} Research is underway on the use of ESWT in osteoarthritis and osteoporosis.^{24,25} Although ESWT is widely used in medicine, the mechanism of action remains unclear; all that is known is that the shock waves trigger changes at the molecular, cellular and tissue levels to produce the therapeutic effect.^{26,27}

ESWT can be administered using focused or defocused extracorporeal shock waves. Focused shock waves penetrate accurately into deep tissues and are useful for treating bone and tendon disorders. Defocused shock waves exert their effect at the body surface and are used for treatment of muscle and skin disorders.²⁸ It should be noted that there is another type of therapy that uses radial pressure waves; however, radial pressure waves differ greatly from extracorporeal shock waves in their mode of generation, mechanism of action and clinical indications (The International Society for Medical Shockwave Treatment – ISMST – Consensus Statement on ESWT Indications and Contraindications 2016).

ESWT has been found to be effective for managing muscle spasticity both in children with CP and in post-stroke patients.^{29–42} ESWT has several advantages over traditional methods used for management of spasticity: it has no adverse effects, it has high patient acceptance, it can be repeated without loss of efficacy, and it is affordable.^{29–42} However, due to the lack of high-quality evidence, the ISMST Consensus Statement on ESWT Terms and Definitions (2017) still considers spasticity as an exceptional indication for ESWT. A systematic review and a meta-analysis of the benefit of ESWT in post-stroke spasticity have been published,^{39,43} but there has so far been no review of the efficacy of ESWT in children with CP.

This systematic review was performed to assess the evidence regarding the effectiveness of ESWT for the management of muscle spasticity in children with CP.

Material and Methods

The PICOS method was used to formulate the clinical query. This systematic review followed the Preferred Reporting Reviews and Meta-Analysis (PRISMA) reporting guidelines for systematic review or a meta-analysis of intervention trials.⁴⁴

Study Eligibility Criteria and Report Eligibility Criteria

Studies were eligible for inclusion in this systematic review if 1) they were in the English language; 2) they had been published at any time before 15 March 2019; 3) they enrolled patients aged <18 years with muscle spasticity of the lower limbs because of CP; 4) ESWT was applied to at least a proportion of the patients; and 5) appropriate data were provided for the evaluation of the results, e.g., MAS score, Tardieu scale score, joint passive range of motion (pROM) and muscle US elastography results.

Studies were excluded from this review if non-extracorporeal shock waves (e.g., radial waves) were used for treatment or if ESWT was used in combination with other treatments such as botulinum toxin type-A injections. The use of concurrent physical therapy was not a disqualification as it is nearly always used in the management of muscle spasticity.

Letters, comments, editorials and practice guidelines were excluded.

Search Strategy

To identify relevant studies, two investigators independently searched the PubMed, Embase, Web of Science and the Cochrane Library databases using the following search terms: ‘cerebral palsy or CP’, ‘spasticity or hypertonia’ and ‘extracorporeal shockwave therapy or shock waves or ESWT’. The last search was performed on 15 March 2019.

Study Selection

The two investigators first scanned the study titles and abstracts and discarded obviously ineligible articles. The full texts of the remaining studies were then reviewed to check that all inclusion criteria were met. Disagreements between reviewers were resolved by consensus.

Data Collection Process

Data were extracted from the included studies using a data extraction form. Data were extracted by one investigator and crosschecked by the other. The following data were recorded: general information concerning the study (title and year of publication), participants (number and mean age), CP subtypes, adverse effects, study quality score, ESWT schedule, follow-up duration, tested muscles, evaluation tools, and results. Disagreements between the two investigators were resolved by discussion and, if necessary, by consultation with a third investigator.

Methodological Quality and Level of Evidence Assessment Process

Methodological quality and level of evidence were assessed independently by two of the investigators. Methodological quality was assessed using the Cochrane Risk of Bias Assessment Tool for randomized controlled studies (RCTs), the Newcastle–Ottawa Quality Assessment Scale for cohort studies, and the adapted Newcastle–Ottawa Quality Assessment Scale for case series.^{45–47} The level of evidence was assessed using the Oxford Center for Evidence-Based Medicine (OCEBM) – Levels of Evidence guide.⁴⁸ Publication bias was not assessed because of the very small sample sizes of all selected studies.

Results

A total of 68 potentially relevant studies were initially identified. After duplicates were excluded, 24 studies remained. Of these, 17 were excluded after review of the study titles and abstracts. After a reading of the full texts of the remaining seven studies, three were excluded because they did not meet all the inclusion criteria. Eventually, four studies remained that satisfied all the eligibility criteria. The PRISMA flow diagram in [Figure 1](#) shows the study selection process. [Table 1](#) lists the details of the studies selected for this systematic review.

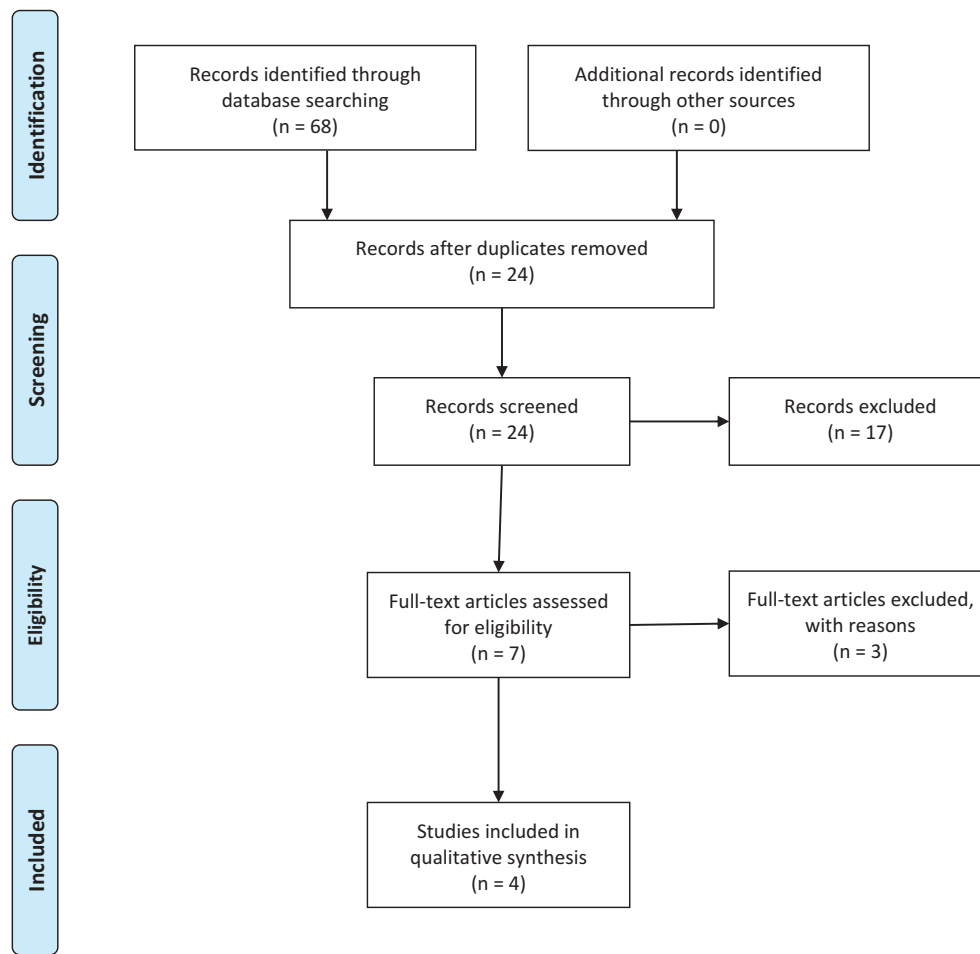


Figure 1. Flow diagram of study selection.

Amelio et al.²⁹ were the first to report the efficacy of ESWT for managing muscle spasticity in children with CP. In the study, 12 children with spastic equinus foot underwent a sham ESWT session followed, 6 weeks later, by one active focused ESWT session. No physiotherapy was administered after ESWT. This single active ESWT to the gastrocnemius and soleus muscles produced a significant reduction in muscle tone and consequent partial correction of ankle and foot posture. The difference from muscle tone after sham treatment remained statistically significant for up to 4 weeks. No side effects were reported. The Newcastle–Ottawa Quality Assessment Scale score for this case–control study was 6/9, indicating a fairly robust methodology.

In 2014, El-Shamy et al.³¹ investigated the effects of ESWT on muscle spasticity and gait pattern in children with hemiplegic CP. Fifteen children were randomly assigned to receive focused ESWT along with a conventional physical therapy exercise program (1 h/day, 3 days/week, 12 weeks). Both the gastrocnemius and the soleus muscles were treated. A control group of another 15 patients received only physical therapy. At 3 months (immediately after the last ESWT session) both groups showed reduction in the MAS score of the treated muscles; however, the reduction was statistically significant only for the group that received ESWT. The reduction of spasticity had a positive effect on patient functionality; three-

dimensional gait analysis showed significant improvement in the mean values of gait parameters (stride length, cadence, speed, cycle time, stance phase and swing phase percentages) in treated children compared to controls. It must be noted, however, that according to the Cochrane Risk of Bias Assessment Tool, this study was classified as a poor-quality RCT with a high risk of bias.

In a 2015 case–control study, Park et al.³² investigated the therapeutic effect of ESWT on gastrocnemius muscle spasticity in children with CP. Six children (group 1) underwent one focused ESWT session and two sham ESWT sessions, while another six children (group 2) underwent three focused ESWT sessions. In addition, all children received rehabilitation treatment, which included twice-weekly sessions of stretching and strengthening exercises, functional electrical stimulation, and progressive gait training. The MAS score of the gastrocnemius muscle and the pROM of the ankle joint (with the knee in extension) were used to evaluate if there was clinically relevant reduction in muscle spasticity. Furthermore, for objectively quantifying muscle stiffness, the median red pixel intensity (RPI) of the color histogram of the medial gastrocnemius was measured using real-time sonoelastography (RTS). Follow-up examinations were performed immediately after the first and third ESWT sessions and at 4 weeks after the third ESWT session. After the first ESWT session, mean ankle pROM was

Table 1. Details of studies selected for the systematic review.

Author/ published year	Number of patients (n) (F/M)	Average age of patients (years)	CP subtype (n):		Level of evidence (Oxford Center EBM)	Energy (mJ/mm ²)	Sessions (n) Interval SWs (n) Treated muscles	Follow-up times	Tested muscles	Evaluation instruments	Results
			Hemiplegia/ Diplegia/ Tetraplegia	Adverse effects							
Amelio et al. (2010)	12 (6M/6F)	8	12/0/0	No	3b	0.030 mJ/mm ²	1 session 1500 SWs per muscle per session Gastrocnemius and soleus muscles	Immediately after ESWT 1,4 and 12 weeks after ESWT	Ankle plantar flexors muscles	MAS pedobarography	MAS increment of plantar surface area
El Shamy et al. (2014)	30 (18M/12F)	7	30/0/0	Not mentioned	2b	0.030 mJ/mm ²	12 sessions once per week 1500 SWs per muscle per session gastrocnemius and soleus muscles	Immediately after ESWT	Ankle plantar flexors muscles	MAS Gait analysis	MAS improvement of gait analysis parameters
Park et al. (2015)	12 (7M/5F)	7	4/8/0	No	3b	0.030 mJ/mm ²	3 sessions once per week 1500 SWs per muscle per session gastrocnemius muscle	Immediately after ESWT 4 weeks after ESWT	Ankle plantar flexors muscles	MAS pROM elastosonography	MAS pRoM stiffness (US)
Corrado et al. (2019)	21 (15M/6F)	9.5	21/0/0	No	4	0.25 mJ/mm ² (defocused)	5 sessions once per week 500 SWs per muscle per session soleus muscle	Immediately after ESWT 1, 3, and 6 months after ESWT	Ankle plantar flexors muscles	MAS SW elastography	MAS stiffness (US)

F = female; M = male; CP = cerebral palsy; EBM = evidence-based medicine; SWs = shock waves; ESWT = extracorporeal shockwave therapy.
 MAS = modified Ashworth scale; pRoM = passive range of motion; US = ultrasound.

significantly increased in group 2, while the mean gastrocnemius MAS score and median gastrocnemius RPI were significantly decreased in both groups. Immediately after the third ESWT and at 4 weeks after the third ESWT, clinical and RTS parameters were significantly different from pretreatment recordings in group 2 only. In addition, immediately after the third ESWT and at 4 weeks after the third ESWT, mean ankle pROM, mean gastrocnemius MAS score and median gastrocnemius RPI showed significantly better improvement in group 2 than in group 1. No side effects were reported. Thus, the study demonstrated that three sessions of ESWT could produce significant and lasting decrease in ankle plantar-flexor muscle spasticity in children with CP. The study also showed that the therapeutic effect of ESWT is dependent on the number of treatment sessions: three ESWT sessions were more effective in reducing muscle stiffness than one ESWT session. On the Newcastle–Ottawa Quality Assessment Scale this case–control study scored 7/9 points, indicating a robust methodology.

Corrado et al.³⁴ used MAS score and SWE to evaluate the efficacy of ESWT for decreasing soleus spasticity in children with CP. SWE is an US elastography method that uses acoustic radiation force impulse to objectively measure muscle stiffness. A total of 21 children with spastic CP underwent ESWT. All children also received physiotherapy concurrently with ESWT; the physiotherapy consisted of positioning, stretching exercises, massages, proprioceptive neuromuscular facilitation, and sensory integration therapy. The effects were evaluated at 1, 3 and 6 months after therapy. Linear mixed effects modeling showed significant reduction in soleus stiffness, as measured both by MAS score and SWE. The lowest level of muscle stiffness was attained in the 9th week after completion of treatment, but the effect disappeared by the 24th week. The model also predicted that the effects of ESWT would be highest at the 13th week after treatment. Furthermore, repeated-measures correlation analysis showed positive correlation between the MAS score and the SWE parameters. No adverse effects were reported in the study. On the Newcastle–Ottawa Quality Assessment Scale (adapted for case series), the study scored 6/6 points, indicating a highly robust methodology.

The level of evidence of studies included in this review ranged from 2b to 4 on the OCEBM scale. One study was a low-quality RCT with level of evidence of 2b.³¹ Two studies were nonrandomized case–control studies with level of evidence of 3b.^{29,32} One study was a case series with level of evidence of 4.³⁴ According to the OCEBM grades of recommendation, three of the studies were categorized as grade B and one as grade C.

Discussion

In children with CP, muscle spasticity can affect posture and gait, significantly impairing transfers from one surface to another and adversely impacting the performance of daily living activities. Muscle contractures occur as a result of both muscle hypertonia and structural changes in muscle and tendon. Prevention of muscle contractures is a key therapeutic target in the management of children with CP. However, there is still no standardized approach. Current

treatment strategy depends on the degree of functional impairment caused by the spasticity and the muscles involved.

ESWT is one of the several therapies available for management of spasticity. The exact mechanism of action of ESWT on spastic muscles has not yet been clarified, but various possibilities have been suggested, including production of NO, degeneration of acetylcholine receptors at the neuromuscular junction, enhancement of neurotrophin-3 expression (which promotes impulses to peripheral nerves and neurororganisation), and the release of endogenous angiogenic factors (which improve tissue microcirculation).^{49–52}

We conducted this systematic review to evaluate the evidence for the effectiveness of ESWT in the management of muscle spasticity in children with CP. All the studies reviewed were consistent in showing that shock waves could reduce muscle spasticity. The studies by Amelio et al.², El-Shamy et al.³¹ and Park et al.³² largely agreed on the optimal ESWT schedule, energy level (0.030 mJ/mm²), number of shock waves to be delivered per session (1500), and the target muscles (gastrocnemius and soleus). The ESWT parameter with the highest variability between the three above-mentioned studies was the number of sessions: one, three and twelve, respectively. The dose–response relationship was analyzed only in the study by Park et al.,³² which concluded that three ESWT sessions were more effective than one session for reducing muscle stiffness.

Corrado et al.³⁴ recommended a somewhat different ESWT protocol, with application of a higher energy level to the muscle but fewer shock waves per session. The rationale was the difference between focused and defocused shock waves; with the latter, a larger area can be treated with each shock wave, and therefore a higher energy level is necessary to maintain the same energy flux density per treated unit area. The authors justified their administration of comparatively fewer shock waves by arguing that the soleus muscle is smaller than the gastrocnemius. They also analyzed the intensity and duration of action of ESWT on spastic muscle. They found that the effect of ESWT on the MAS score was most evident in the 13th week post-treatment, after which the beneficial effect progressively declined up until the 24th week.

All the selected studies used the MAS score for evaluation of changes in muscle spasticity. However, the timing of the evaluation differed between the studies: from immediately after treatment to up to 12 weeks after ESWT. Some of the studies used instrumental evaluation tools such as pedobarography, gait analysis, and elastosonography. In the study by El-Shamy et al.,³¹ the use of gait analysis allowed the authors to also report improvement in the functioning of CP patients post-ESWT. In the studies by Park et al.³² and Corrado et al.,³⁴ the use of elastosonography allowed a more objective assessment of the effects of ESWT on spastic muscles than is achieved with the MAS score.

None of the selected studies could definitively identify the mechanisms by which shock waves achieved spasticity reduction in children with CP. However, in light of the most recent findings, we assume that ESWT mainly acts through two different pathways: 1) by temporarily reducing the hyperexcitability of the stretch reflexes and 2) by modifying the intrinsic stiffness of spastic muscles. The first effect is probably achieved

via different mechanisms such as enhanced production of NO, interference with the segmental reflex arc, and a direct effect on Golgi tendon organs. The possibility of shock waves producing changes in the intrinsic mechanical properties of muscle is supported by the evidence that ESWT stimulates healing and regeneration of injured skeletal muscle.⁵³ It is reasonable to assume that reduction in hyperexcitability of the stretch reflexes is the basis for the short-term effect of ESWT, while the changes in intrinsic muscle properties are the basis for the long-term effect of ESWT on muscle spasticity.

This review has some limitations. First, the number of included studies and the number of patients in each study were very small. Second, the quality of the selected studies was relatively poor; the best evidence was from a low-quality RCT with OCEBM recommendation grade B. Nevertheless, this systematic review highlights several key points that require more research. The exact mechanism of action of ESWT needs to be elucidated, especially the ability of shock waves to modify the rheological properties of spastic muscles. The optimal therapeutic schedule and parameters of ESWT for treatment of spasticity also needs to be established. For this last purpose, future studies should verify whether the effects of shock waves on spastic muscle will change either with different frequencies of therapy (e.g. less or more than weekly sessions) or with energy level other than 0.030 mJ/mm². In addition, it will be useful to know if the benefits of ESWT could be increased by using it in combination with other treatments for muscle spasticity, e.g., orthoses, drugs or botulinum toxin injections.³³

In conclusion, ESWT appears to be a safe, noninvasive and effective modality for managing muscle spasticity and improving motor function of children with CP. Repeatability, good acceptance by children, and reasonable cost are major advantages of ESWT. However, the results regarding the effectiveness of ESWT should be interpreted carefully because of the low quality of the studies included in this review. Further high-quality studies, especially large RCTs, are necessary to confirm the efficacy of ESWT in CP and to clarify its mechanism of action.

Declaration of interest

We have no conflicts of interest to disclose.

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