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SYSTEMATIC REVIEW

Modified constraint induced movement therapy in children with obstetric brachial plexus palsy: a systematic review

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ABSTRACT

INTRODUCTION: Obstetric brachial plexus palsy (OBPP) is a flaccid paralysis occurring in the upper limb during birth. The OBPP includes mild lesions with complete spontaneous recovery and severe injuries with no regain of arm function. Among the most promising rehabilitation treatments aimed at improving upper extremity motor activities in individuals with neurological dysfunctions, there is the modified constraint-induced movement therapy (mCIMT). The aim of this systematic review is to assess and synthesize the critical aspects of the use of mCIMT in children with OBPP.

EVIDENCE ACQUISITION: This systematic review has been carried out according to the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analysis). A comprehensive search of the literature was conducted using PubMed, MEDLINE and Evidence Based Medicine Reviews, databases. We enclosed experimental and original articles, case reports and book chapters. Four articles were finally included.

EVIDENCE SYNTHESIS: One case report tested the feasibility of mCIMT to encourage use of the affected arm in a child with Erb-Duchenne palsy and documented the clinical changes observed. A case series had the purpose to determine if mCIMT in combination with botulinum toxin (BTX-A) improved arm function in 2 children with OBPP. A cohort study compared the use of mCIMT in 19 OBPP and 18 unilateral Cerebral Palsy. A prospective single-blind RCT described mCIMT *versus* conventional therapy in a group of 39 children with OBPP.

CONCLUSIONS: This systematic review on the use of mCIMT in children with OBPP shows that there is unanimous agreement that a program should last 2 weeks at least. However, there is no scientific evidence supporting a single common mCIMT protocol in the management of OBPP because of a considerable heterogeneity. Further high methodological studies regarding the application of mCIMT for OBPP and based on larger patients' sample should have the potential to optimize the appropriateness of care provided to infants with OBPP and, therefore, their quality of life.

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Key words: Motion therapy, continuous passive; Neonatal brachial plexus palsy; Child; Radiation induced brachial plexopathy.

Introduction

Obstetric brachial plexus palsy (OBPP) is a flaccid paralysis secondary to injury to the brachial plexus occurring in the upper limb during birth.[1, 2] The rate of OBPP is worldwide reported as 0.1 to 8.1 cases per 1000 live births.[3] OBPP is caused mainly by trauma resulting from traction on the shoulders during headfirst delivery, or by pressure on the raised arms during a breech (feet first) delivery.[4] Cranial nerve roots (C5-6-7) are most frequently involved in OBPP. In C5-C6 roots injuries, shoulder abductors, internal rotators and elbow flexors muscles are mostly affected, sometimes with a decreased forearm supination, along with intact hand functions. If the C7 root is damaged, then triceps and wrist extensors could also be affected.[5-8] The OBPP includes mild lesion with complete spontaneous recovery and severe injuries with no recovery of arm function.[9, 10] In incomplete recovery there are residual deficits with muscular imbalances. Different muscle strengths surrounding the joint can lead to development of soft tissue and muscle contractures and ultimately bone deformities.[11, 12] Functional impairments of the upper limb result in limitations of activities of daily living.[13, 14] Regardless of recovery, treatment should be initiated early to optimize outcomes (2-3 weeks after birth[15, 16]). The aims of rehabilitation treatment are: 1) to prevent contractures and joint deformities (tendons and bones) maintaining passive range of motion (RoM); 2) to promote muscular strengthening balancing agonists and antagonists around a joint; 3) to facilitate active movement; and 4) to improve performance in age-appropriate activities of daily living (ADL) (school, self-care) in accordance with the International Classification of Functioning (ICF).[17] Among the most promising rehabilitation treatments aimed at improving upper extremity motor activities in individuals with neurological dysfunctions, the constraint-induced movement therapy (CIMT) must be cited.[18, 19] The muscular deficits of OBPP lead to an under-use of the affected upper limb. This can cause a reorganization of the central nervous system (CNS) such as a cortical underdevelopment and lead to neglect the affected extremity. This under-use is called "learned non-use" or "developmental disregard."[20, 21] It is important to prevent apraxia and to promote activities that stimulate the use of the affected limb. Though OBPP a muscle function restoration is observed, children often continue not to use the affected arm. In order to improve performance in age-appropriate ADL and to promote functional improvement, CIMT can be used. This neurorehabilitation technique was designed to improve upper limb function in stroke patients.[22] The restricted use of the non-affected limb for 90% of waking hours by using a splint or sling is linked to intensive e repetitive training on task-related activities with the affected arm (for more than 3 hours a day for at least 14 consecutive days)[23] and leads to improvements in mobility and increased use of the affected limb in daily life[24] and helps to overcome the "learn no-use" of the impaired arm. In paediatric patients a modified CIMT (mCIMT) is preferred.[25] In order to increase feasibility, duration of restriction and intensity are reduced, while the constraint methods do not include casting. Despite the extensive literature focusing on the use of CIMT in stroke[26] and cerebral palsy (CP)[27] and recent studies on Multiple Sclerosis,[28, 29] very few studies address its use in peripheral neurological diseases. This work provides a structured and systematic overview of the literature on the use of mCIMT in children with OBPP.

Evidence acquisition

Search strategy

We followed the recommendations of the Preferred Reporting Items for Systematic reviews and Meta-analyses (PRISMA).[30] A comprehensive search of the literature was conducted using PubMed, MEDLINE and Evidence Based Medicine Reviews, databases. We consulted Scopus and Web of Sciences, but Scopus identified the same 4 articles found by PUBMED and we didn't find any article with Web of Sciences. Two authors (GD, VB) performed independently the selection of studies, then the decision for full-text articles eligible for quantitative analysis and any disagreement were resolved by discussing the issues that led to disaccord. Different combinations of the terms "perinatal brachial plexus injury," "infant brachial plexus," "obstetrical brachial plexus palsy" and "rehabilitation" and "physiotherapy" and "constraint therapy" were used. The terms indicated in the paper were combined each other using "AND" operator in MEDLINE. Additional records were identified through literature search.

Inclusion criteria

We included all experimental and original articles, case reports, and book chapters published until May 1, 2021. Only English written texts with availability of full text were considered for eligibility. We included only the studies in the childhood population (2-11 years).[31] A PRISMA flow diagram has been drafted (Figure 1).

Study analysis

Two reviewers (GD, VB) screened all titles and abstracts for eligibility. Studies were first reviewed using a list of predefined, pertinent issues concerning the characteristics of patients and treatments. Then full-text papers were reviewed using the inclusion criteria.

Evidence synthesis

The literature search yielded 502 citations. Additional 3 records were identified through literature search. After duplicate removal, 233 studies were included for further

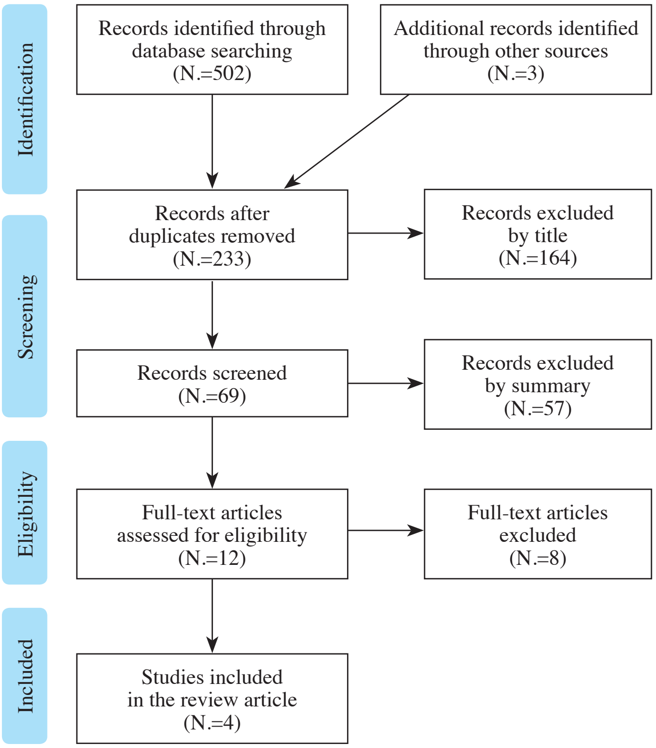

Figure 1.—PRISMA flowchart.

selection. Considering our specific inclusion criteria, and after title and abstracts screening, 4 articles were eligible for a full-text review. Two authors (GD, VB) extracted the following data for each study: study design, sample, number of patients, age, aims, outcome measures, follow-up, results, mCIMT duration, mCIMT mean of restraint, mCIMT setting, other treatment. The detailed information about the 4 articles which satisfy the inclusion criteria are available in Supplementary Digital Material 1 (Supplementary Table I) and Table I.[32-35] We deepened recorded data reliability using the Physiotherapy Evidence Database (PEDro) scale, a valid tool used to rate RCTs' quality and based on the Delphi list.[36] It comprehends 11 items evaluating a potential risk of bias of a trial: if the criterion is not met (or not reported), the item will get a score of 0 (Table II).[32-35] For a given trial, the sum of the scores can steer physicians about the quality of the study, but it does not give an exact measure of the validity of its conclusions. Moreover, PEDro scale might not provide an efficient method to compare studies of different research areas, since it is not possible to evaluate all its items for some areas of physiotherapy practice. In our review study, it has been possible to calculate a single PEDro score for the only RCT study included, with a high rate (9/11; Table

Table I.—*Summary of findings: mCIMT protocol and other associated treatments.*

Author	mCIMT: duration	mCIMT: mean of restraint	mCIMT: setting	Other treatment
Vaz *et al.*[32]	30'/die, 7 dd/week, 14 weeks	Jumper, closing the opening of the sleeve and tying into the child's back with an elastic band.	At home, a schedule of 3 tasks, each practiced for 10'/day (total time of 30') changed after a 2-weeks period (7 schedules in14 weeks)	-
Santamato *et al.*[33]	30'/die, 7dd/week, 8 weeks,	Jumpsuit with velcro-closure, arm was parallel to the chest under the jumpsuit.	Reaching, prehension and manipulation were trained.	BTX-A in biceps brachii 20U and pectoralis major 15U, followed by 10 dd of stretching.
Zelinski *et al.*[34]	54h (first 6 weeks: 2×4.5 h or 3×3 h)	Splint or sling (during the first 6 weeks)	Individual, intensive, repetitive, task-specific, and goal-oriented training for the affected arm to work on children's specific goals, 1 h/day	Bimanual training, group therapy, 18 h (2 weeks: 3×3h or 4 weeks: 2×2 h), during 8 to 10 weeks (either 2-3 times/week for a duration of 4.5 or 3 h accordingly);
Eren *et al.*[35]	1 h/day, 14 (consecutive) dd;	Custom-made static upper limb orthosis, 6h/day (2h on- 1h off- 2h on)	Study group was hospitalized 14 dd (group of 2 or 3 pts).	Control group: 1 h/day, 14 (consecutive) dd. All children continue with same exercise program at home.

Table II.—*Four studies designed to investigate the reliability of data obtained with the Physiotherapy Evidence Database (PEDro) scale developed to rate the quality of RCTs evaluating physical therapist interventions.*

	PEDRO Score											
References	1	2	3	4	5	6	7	8	9	10	11	TOT
Vaz *et al.*[32]	/	/	/	/	/	/	/	/	/	/	/	
Santamato *et al.*[33]	/	/	/	/	/	/	/	/	/	/	/	
Zelinski *et al.*[34]	/	/	/	/	/	/	/	/	/	/	/	
Eren *et al.*[35]	1	1	1	1	1	0	0	1	1	1	1	9

II).[32-35] In this sense, a direct reliability comparison between the included works has not been possible, both for their different study designs and because most PEDro items could not be examined. This heterogeneous scenario – even for the few studies included – reflects the lack of methodology and the scarcity of studies on CIMT topic, that makes it difficult a clear quality evaluation between them. Vaz *et al*[32] demonstrated how a CIMT-based rehabilitation program had strong potentials to promote functional gains for children with OBPP. They studied the application of CIMT in a 2-year-old child with Erb-Duchenne palsy of the right arm due to OBPP. Restriction was attained by dressing the child with a jumper, closing the opening of the left sleeve, and tying into the child's back with an elastic band. She had a 14-weeks daily home-based treatment with a daily program of 30-minutes sessions. Seven schedule(s) of 3 tasks were proposed, each one to be practiced for 10 minutes every day. Each schedule was used for a 2-weeks period during which tasks difficulty was increased progressively. Each task was chosen according to its suitability to the child's age and interests. Despite the initial low tolerance to treatment, the child soon adapted to training helped by encouragement and rewards given by the mother. Upper limb functional outcome was assessed with the Toddler Arm Use Test (TAUT) before, during and after treatment. Support for the understanding of the improvements in ADL was given by a form filled in by the child's mother. Results showed an increasing of movement quality, willingness and use of affected arm. TAUT scales scores changes began from the fifth assessment session (after 4 weeks of treatment). There was no follow-up assessment. Santamato *et al.*[33] suggested that a combined treatment with BTX-A and mCIMT could have an important role in the functional recovery in children with OBPP. They described the experience of two children with Erb-Duchenne palsy. They reported clinical improvement gained following combined treatment of BTX-A injections and a rehabilitation program based on mCIMT. The first child was a 6-year-old girl, who could reach objects with the affected arm but did not use it spontaneously. The second one was a 7-year-old girl with a major impairment of the upper limb; she was not able to use it at all. Before mCIMT, the children were treated with intramuscular injection of BTX-A, under ultrasound guide; they were administrated 20 UI into biceps brachii at two sites and 15 UI into pectoralis muscle at two sites, in order to inhibit co-contraction and to facilitate motor control of the affected arm. After BTX-A injections the children were enrolled in a daily rehabilitation program based on stretching of muscles injected for 10 days. Then the mCIMT protocol was initiated. The treatment protocol consisted in a 30-minute session once a day for 8 weeks. The healthy limb was restrained in a jumpsuit with velcro-closure in order to minimize the irritation to the children. The healthy arm was collocated parallel to the chest under the jumpsuit. Patients were evaluated before treatment, after treatment and at two-months follow-up. Outcome measures used were Medical Research Council (MRC) Scale for muscle strength, the Gilbert Shoulder (GS) Score for the shoulder movement, the Gilbert–Raimondi (GR) score for elbow function, the Raimondi Hand (RH) Score, the Nine-Hole Peg Test (NHPT) for dexterity and the Mallet Scale to value active articular range of motion of shoulder. Results showed an improvement of extension, abduction, and adduction of the affected limb, while no modification in MRC scores were found. Functional improvement persisted 6 months after the end of treatment and parents reported important improvements in the execution of daily activities and in bimanual tasks. Zielinski *et al.*[34] used a pretest / post-test design (cohort study) to compare the effects of the combination of mCIMT with bimanual training based on the "Pirate group intervention" in children with OBPP and in children with unilateral CP (uCP). The population was composed by 19 children with OBPP and 18 with uCP. The "Pirate group intervention" consists of a total of 72h: 54 h (6 weeks: 2×4.5 h or 6 weeks: 3×3 h) mCIMT and 18 h (2 weeks: 3×3h or 4 weeks: 2×2 h) goal directed and task specific bimanual training, all performed during 8 to 10 weeks. During the first 6 weeks, the unaffected upper limb was restrained using a splint or a sling while at the same time providing intensive structured training for the affected upper limb. Most of the treatment was provided in a group setting by experienced occupational therapists and physiotherapists. Besides the group therapy, an individual training was scheduled 1 h per day (included in the 72 h) to work on children's specific goals. During both treatments, intensive, repetitive, task-specific, and goal-oriented training strategies were used. The improvement was investigated by assessing spontaneous affected-upper-limb-use ("assisting hand assessment"), manual abilities ("ABILHAND-kids") and subjective performance and satisfaction of problematic bimanual activities ("Canadian Occupational Performance Measure") at three time points (pretreatment, post-treatment, follow-up). The assessments were administered and scored by a trained occupational therapist who was blinded for testing session. This data were analyzed using repeated-measures analysis. As a first step, t-tests were conducted to test for possible differences between groups at baseline (T1) for each outcome measure separately. Secondly, all outcome measures were analyzed separately using a repeated measures general linear model analysis with time point related to treatment onset (T1, T2, T3) as independent within-subject variable and group (OBPP *vs*. uCP) as between-subject factor. Children with OBPP showed significant positive treatment effects following mCIMT combined with bimanual training. These effects were comparable to those observed in the comparison group of children with uCP. In children with OBPP, spontaneous affected upper limb use seems to be more stable compared to the group of children with uCP. Eren *et al*.[35] observed the difference between the effect of mCIMT and conventional therapy in children with OBPP of upper and middle trunks. This single-blind randomized study included 39 patients, divided in two groups: 26 received conventional rehabilitation program (control group) and 13 children participated in a mCIMT program (study group). The patients had a mean age 4.7 years. The study group has been hospitalized; an intensive motor exercise program was applied to the affected limb 1 hour per day for 14 consecutive days. Their unaffected limbs were restricted for 6h/day with a custom-made static upper limb orthosis, the daily restriction time was divided into two 3 hours sessions with an hour interspace. The control group, instead, received standard conventional therapy to their affected extremity 1 hour a day for 14 consecutive days. After this time children's parents of both groups have been trained to continue with same exercise program at home. Upper limb active ROMs, Active Movement Scale, hand dynamometer, and Box and Blocks Test (BBT) were used as assessment scales to investigate the improvements in active range motion and functional use of affected limb. Observing the results, mCIMT seems to be an effective treatment method, especially as the study group exhibited greater benefits in shoulder internal rotation, elbow flexion, and forearm supination active ROMs as compared with the control group. Nonetheless, there are no statistically significant differences between the two groups.

Heterogeneity

This systematic review on the use of mCIMT in children with OBPP shows that there is unanimous agreement that mCIMT program should last 2 weeks at least as for CP. However, there is no scientific evidence supporting a single common mCIMT protocol in the management of OBPP because of the considerable heterogeneity: 1) information about inclusion or exclusion criteria (*i.e.,* age, type of lesion, previous surgical treatment) are often missing; 2) 2 of the 4 studies are case report without control group; 3) the control group is made of CP in one RCT; 4) the sample size of the 2 RTC is small (37 and 39) because of the low incidence of the pathology and because of ethical reasons (mCIMT is experimental for OBPP); 5) there are differences in mCIMT protocol: duration (49h in 14 weeks, 28h in 8 weeks, 54h in 6 weeks, 14h in 2 weeks), mean of restraint (jumper, jumpsuit, splint or sling, orthosis), setting (home, hospitalization, DH), associated treatments (BTX-A, individual therapy, bimanual therapy); 6) there is a large variation of outcome measures and very poor standardization; 7) there is no assessment of activity and participation; and 8) follow-up is missing or short (2, 3, 6 months). All these limits lead to difficulties with interpretation of the results. In particular, there is no clear guidance regarding age, type of lesion, follow-up.

Childhood: neural plasticity and motivation

In this review, child age ranges between 2 and 10 years. "Childhood," that means age between 2 and 11 years,[31] was an inclusion criterion of this review. The aim was evaluating the effects of mCIMT in a population that could be more compliant with the therapy and would have better brain reorganization and so more benefits because of the age. Younger children have great neural plasticity of CNS, but the stage of motor development influences the type of activity practiced during mCIMT and higher developmental level is related with better gains in CP.[37] Moreover, they have no awareness of their impairments and so have less motivation to improve their own motor function. Older children better understand the mCIMT concept and so pay more attention to the task and are more self-intentioned for success because of their desire for social inclusion; treatment intensity is more important than duration of restraint wear.[38] Neural plasticity is important to correct the learn-no-use and motivation is necessary for long training without complaint or fatigue,[39] for these reasons childhood is the better age to practice mCIMT in OBPP. However neural development for hand control continued until the second decade of life[40] and cortico-spinal organization was found through Transcranial Magnetic Stimulation in adults aged 10-30 years who suffered CP,[41] so mCIMT could be efficient also in adolescents with OBPP as it was already observed in CP.[42] On the other hand, mCIMT was used also in children with CP under 0,5 years old with good results,[27] for this reason we can't exclude this treatment in children with OBPP before 2 years.

Follow-up and partial lesions

The changes in the CNS after mCIMT are long-lived; Santamato *et al.*[33] found persisted improvements at 6 months after the end of treatment. That means that longer follow-up periods are needed, while they are often short (2-6 months in this review). It is important to study if the mCIMT effect is maintained over time and if and when could be necessary a reminding of practice for children with OBPP. The retention of gains over time varied widely in CP. In some study benefits persisted 6 months in a population of CP.[37]The same authors[43] proposed a weekly monitoring by phone the first month post-treatment to enhance the compliance to home exercises needed to maintain the mCIMT effect in CP. Other authors[44] found that a second treatment session given 12 months after the first session, permitted retention of skills acquired during the first intervention. For all these reasons the follow-up after mCIMT in OBPP should be longer at least 52 weeks as in CP.[27] Information about anamnesis and in particular type of lesion is missing in the studies included in this review. Different nerve injuries have different prognosis for recovery and some of them need reconstructive surgery. In this review children had often no previous surgery suggesting that they suffered partial lesions. Buesch *et al.*[24] chose as inclusion criteria the ability of a minimal grasping and of being able to lift the arm against gravity. mCIMT could be suggested mainly for partial lesions, independent of lesion level, because of the potential of this therapy in enhancing cortical reorganization. Stimulating information could be obtained by studies with long follow-up among patients with partial lesions, not undergone to reconstructive surgery but only to conservative therapy and in particular mCIMT. The aim of these studies could be to assess the functional improvement after mCIMT over time. In selected cases of a good motor recovery, the functional surgical interventions on sequelae[8] could be eventually avoided. mCIMT was also used after surgery with good results in Berggren's[45] case report. The child had a total lesion, he underwent to brachial plexus surgical reconstruction and started mCIMT after 3 months (this treatment was proposed again at 10, 14, 20 and 21 months of age). Functional recovery lasted untill 4-5 years after nerve surgery,[2] therefore could be interesting investigate how mCIMT enhances this motor improvement in long follow-up. In the end, mCIMT could be suggested as a conservative treatment in patients managed to surgery and as a supported therapy in the others. In both cases mCIMT could increase the cortical activation due to the increased peripheral feedback to the sensory-motor cortex as in CP.[46]

Limitations of the study

This review has some limitations. One limitation was represented by the selected inclusion criteria: in fact, we only included studies in English language and with patients non undergone to surgery. Another one was represented by the low level of evidence: we could calculate PEDro Score only for the two RCT. The consequence was a small number of studies with heterogeneous results and difficult conclusions.

Conclusions

This review underlies the need for consensus on the use of mCIMT in peripheral nerve injury in children. Further studies are necessary to evaluate the effectiveness of mCIMT in clinical practice. A multicenter (to have a wider sample) randomized clinical trial (with control group) with defined inclusion criteria (2-11 years, partial lesions, no previous surgery) and child functional treatment goals should be affirmed to confirm the effectiveness of this recent rehabilitation method. mCIMT could be associated with other complementary rehabilitative techniques such as electrical stimulation (ES) of agonists to enhance active motion (ES and mCIMT provided improvements in the study of Berggren *et al*.)[45] and BTX-A antagonists to reduce muscle imbalances and co-contractions (Santamato *et al.* found good results for elbow).[33] Functional integrations of upper limb in ADL should be evaluated with assessment of activity and participation. A long-term follow-up (6-12 months) should be affirmed. There is still heterogeneity in the mCIMT treatments for children with OBPP. Without standardization of all variables, it is difficult to identify the most useful mCIMT program for that specific OBPP cohort. Further high methodological studies regarding the application of mCIMT for peripheral nervous system injuries as OBPP and based on larger patients' sample should have the potential to increase the appropriateness of care provided to infants with OBPP and, therefore, their quality of life.

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