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SYSTEMATIC REVIEW

Constraint-induced movement therapy of upper limb of children with cerebral palsy in clinical practice: systematic review of the literature

Terapia de movimento induzido por restrição do membro superior de crianças com paralisia cerebral na prática clínica: uma revisão sistemática da literatura

Terapia de movimiento inducido por restricción para el miembro superior de niños con parálisis cerebral en práctica clínica: revisión sistemática de la literatura

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ABSTRACT | The purpose of the present study was to perform a systematic review of the literature to investigate how and with what modifications or adaptations constraint-induced movement therapy has been employed in clinical practice for therapeutic interventions in children with cerebral palsy. Searches were conducted of the CAPES (Brazilian fostering agency) periodical portal, Pubmed, Bireme, Science Direct, Scielo and PEDro databases for relevant articles published between January 2010 and May 2016. The articles retrieved were evaluated, scored and qualified by two blinded reviewers using the Physical therapy Evidence Database Scale. The searches led to the retrieval of 102 articles, 12 of which were included in the present systematic review. A table was created containing information on the study groups, inclusion criteria, intervention, intervention frequency, difficulties encountered, evaluations and outcomes. Considerable variety was found in the therapeutic intervention models. The findings of the present review demonstrate that constraint-induced movement therapy in pediatric clinical practice is not employed in its original form. Although the studies analyzed did not have a common methodology regarding the use of this type of therapy, the method has been adapted with considerable flexibility, providing promising, positive results regarding the therapeutic intervention of the paretic upper limb in children with cerebral palsy.

Keywords | Cerebral Palsy; Upper Extremity; Hemiplegia; Immobilization; Movement.

RESUMO | Este estudo se propôs a realizar uma revisão sistemática da literatura para investigar como e com que modificações ou adaptações a terapia de movimento induzido por restrição tem sido empregada na prática clínica para intervenções terapêuticas em crianças com paralisia cerebral. As pesquisas foram conduzidas do portal periódico da CAPES (Agência brasileira de amparo), e dos bancos de dados Pubmed, Bireme, Science Direct, Scielo e PEDro para artigos relevantes publicados entre janeiro de 2010 e maio de 2016. Os artigos obtidos foram avaliados, quantificados e qualificados por dois revisores anônimos usando a Base de Dados em Evidências em Fisioterapia. As pesquisas levaram para a recuperação de 102 artigos, 12 dos quais foram incluídos nesta revisão sistemática. Uma tabela foi criada contendo informações sobre os grupos de estudo, critérios de inclusão, intervenção, frequência de intervenção, dificuldades encontradas, avaliações e resultados. Foi encontrada uma variedade considerável nos modelos de intervenção terapêutica. Os resultados desta revisão demonstram que a terapia de movimento induzido por restrição na prática clínica pediátrica não é empregada na sua forma original. Embora os estudos analisados não tenham uma metodologia comum em relação ao uso deste tipo de terapia, o método foi adaptado com flexibilidade considerável, fornecendo resultados promissores e positivos sobre a intervenção terapêutica do parético membro superior em crianças com paralisia cerebral.

Descritores | Paralisia Cerebral; Extremidade Superior; Hemiplegia; Imobilização; Movimento.

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RESUMEN | El propósito del presente estudio fue realizar una revisión sistemática de la literatura para investigar cómo y con qué modificaciones o adaptaciones la terapia de movimiento inducido por restricción ha sido empleada en la práctica clínica para intervenciones terapéuticas en niños con parálisis cerebral. Se realizaron búsquedas en CAPES (Agencia brasileña de fomento) portal periodico, Pubmed, Bireme, Science Direct, Scielo y PEDro bases de datos para artículos relevantes publicados entre enero de 2010 y mayo de 2016. Los artículos recuperados fueron evaluados, puntuados y calificados por dos revisores ciegos utilizando la Escala de base de datos de Pruebas de Fisioterapia (Physical therapy Evidence Database Scale). Las búsquedas condujeron a la recuperación de 102 artículos, 12 de los cuales se incluyeron en la presente revisión sistemática. Se creó una tabla que contiene información sobre los grupos de estudio, criterios de inclusión, intervención, frecuencia de intervención, dificultades encontradas, evaluaciones y resultados. Se encontró una variedad considerable en los modelos de intervención terapéutica. Los resultados de la presente revisión muestran que la terapia de movimiento inducido por restricción en la práctica clínica pediátrica no se emplea en su forma original. Aunque los estudios analizados no tenían una metodología común respecto al uso de este tipo de terapia, el método se ha adaptado con una flexibilidad considerable, promoviendo resultados promisores y positivos con respecto a la intervención terapéutica del miembro parético superior en niños con parálisis cerebral.

Palabras clave | Parálisis Cerebral; Extremidad Superior; Hemiplejía; Inmovilización; Movimiento.

INTRODUCTION

Cerebral palsy (CP) is a group of movement and postural development disorders that causes limitations with regard to activities of daily living due to a non-progressive brain damage, occurring during fetal or infant development, resulting in chronic physical deficiencies and possible sensory deficits[1]. Motor impairment is the major characteristic of CP and is characterized by the type of motor disorder (spasticity, ataxia, dystonia and athetosis) as well as the predominance of the affected limbs (hemiparesis, paraparesis and tetraparesis)[2].

Hemiparesis is the most frequent manifestation of CP, affecting as many as 38% of cases in one population-based study[2], and can lead to disuse of the affected upper limb, with negative consequences for reaching, bimanual tasks and functionality, regarding activities performed in home, school and community settings[3].

In recent years, a large number of randomized clinical trials, investigating particularly CIMT and "modified CIMT" (mCIMT) have emerged[4]. CIMT began with preclinical research involving young male primates and was founded on overcoming "learned non-use"[5]. Some researchers suggest two possible mechanisms that can lead to functional improvements of the paretic upper limb through CIMT: overcoming "learned non-use", which is the learning of a patient not to use the paretic limb due to the difficulty encountered; and cortical reorganization, involving anatomic connections through neuronal sprouting, the enhancement of synaptic efficiency of existing connections (disinhibition) or the recruitment of a large number of neurons in the innervation of the affected limb, adjacent to those involved before the brain damage[6,7].

These strategies combine the principles of motor learning (practice, specificity feedback, etc.) and neuroplasticity (cerebral changes induced by the practice of repeated actions that enhance movement complexity, motivation and reward) in intensive blocks of training sessions[8]. The classic CIMT, described in previous studies[9,10], was initially developed for adults with hemiparesis after stroke. This involves restriction of the upper limb not affected by 90% of the waking hours for at least 2 weeks, while the upper limb is intensively trained for 3 hours or more per day[11]. During this approach, the paretic limb is used for numerous activities involving two aspects: the practice of repetitive tasks and training. In the first, the tasks are carried out continuously for 15 to 20 minutes to practice the movement incorporated into a functional task. In this approach, movement is practiced first, followed by performance of the functional task. Environments can be manipulated to vary the requirements of the task and induce specific movements, or to change the degree of difficulty. Tasks are planned so that frequent successes can be achieved. Training involves a meta-motor task performed in small steps with increasing degrees of difficulty, based on the patient's abilities[1].

Modifications to the classic protocol (mCIMT) were made to encourage children to perform. The mCIMT

protocols similarly involve restraint of the non-affected limb with variations in the type of restriction applied (e.g., glove, glove, sling) and are accompanied by a unimanual repetitive practice, differing in part from the classic CIMT in terms of the model of therapy (short-term intensity, long-term distribution model) and dose intervention[4]. The location, context and provider of training (house/camp, individual/group, therapist/parent) are also differentiated in relation to the classic CIMT[11]. Recently, hybrid models have been reported applying sequentially mCIMT followed by bimanual training, significantly altering the unimanual construction of the method[4,11].

CIMT is an analytical-behavioral technique designed to improve deficits resulting from different types of damage to the central nervous system, such as stroke, traumatic brain injury, spinal cord injury, multiple sclerosis, CP and other disorders. The deficits are mainly of a motor nature, but also include verbal aspects (aphasia) and phantom limb pain following an amputation[12].

The study by DeLuca et al.[13] was the first to test the effectiveness of CIMT in children through a randomized controlled crossover study. The treatment protocol was originally developed and evaluated for a 15-month-old child, with virtually no voluntary use of upper limbs and a contemptuous almost complete development by his compromised upper limb.

Learned non-use also occurs in individuals with hemiparetic CP, who do not employ the affected arm for diverse tasks. Thus, CIMT is a therapeutic resource that enables the use of the paretic upper limb in unimanual tasks. However, a major concern in relation to the administration of CIMT to children with hemiparetic CP regards the impact on the child's self-esteem. Unlike stroke survivors, who are often very motivated to recover lost function, children with CP may have never used the paretic limb during functional activities and are therefore obligated to concentrate on their deficiencies. Moreover, the high rate of early failures during the execution of such tasks can be the cause of considerable frustration. Another point of concern with classic CIMT for pediatric patients is related to the use of the constraint during the rest of the 90% of the day, forcing children to continue exclusively using their compromised limb. This demand can be the source of additional frustration, resulting in concerns on the part of the family regarding the potential risk of falls due to the constraint of the unaffected limb. Thus, the procedures involved in CIMT for adults may not be altogether appropriate for children[1].

Recent systematic reviews of literature and meta-analysis[11,14,15] have addressed the effectiveness of the use of CIMT in children with CP, reporting results such as improvements in the manual capacity of the affected limb. The aim of the present study was to perform a systematic review of the literature to investigate how and with which modifications or adaptations CIMT has been used in the therapeutic process of children with hemiparetic CP, without merit on the evaluation of the results obtained in the clinical trials

METHODOLOGY

Searches were conducted from the CAPES (Brazilian fostering agency) periodical portal, Pubmed, Bireme, Science Direct, Scielo and PEDro databases for relevant articles published between January 2010 and May 2016, using the following keywords in English, Spanish and Portuguese. The search for the articles was done using the terminology registered in the Descriptors in Health Sciences (DECS) and Medical Subject Headings of the U.S. National Library of Medicine (Mesh). They were: *cerebral palsy, upper extremity, hemiplegia, immobilization, movement.* All the synonyms of these descriptors were considered for the search.

The following were the inclusion criteria: 1) type of study – controlled clinical trial; 2) intervention – constraint-induced movement therapy for the upper limb; 3) experimental group – children with cerebral palsy; 4) publication between 2010 and 2016; and 5) score of 5 or more points on the Physical therapy Evidence Database Scale (PEDro). Titles and abstracts were analyzed in the first stage of the selection process. Pre-selected articles were then submitted to full-text analysis for the determination of inclusion to the systematic review based on the eligibility criteria.

Pre-selected articles were evaluated for methodological quality using the 11-item PEDro scale. All items (except Item 1, which is not scored) received a score of either 1 or 0 depending respectively on the presence or absence of the criterion in question. Thus, the final score ranges from 0 to 10 points. The purpose of this scale is to offer a numeric representation of the methodological quality of randomized and controlled clinical trials, placing emphasis on internal validity (whether the results

provide sufficient information) as well as clinical and statistical relevance, in a way that the interpretation of the findings is clear and other researchers can reproduce the study. The classification of the analyzed studies based on the PEDro scale was performed by two evaluators, independently and blind to the objective of the present study, so that if a controversy occurred to the score obtained in the study, a third evaluator would be selected to answer the question of the score. The articles selected by inclusion criterion through the PEDro scale would have to have a score greater than or equal to 6 (table 2).

The PEDro scale was created based on the Delphi list of criteria for the quality evaluation of randomized clinical trials to be included in systematic reviews. This list was developed from the consensus of a panel of experts in 1998, but was considered insufficient regarding statistical parameters. The creation and validation of an adequate measure for the evaluation of methodological quality stemmed from the need to catalog clinical trials in the Physical therapy Evidence Database (PEDro). The purpose of the PEDro scale is to assist researchers in the rapid identification of which known or suspected (i.e., randomized controlled study or controlled clinical trial) randomized clinical trials indexed in the PEDro databank are internally valid (Items 2 to 9) and have sufficient statistical information for the adequate interpretation of the results (Items 10 and 11). An additional criterion (Item 1), which is related to external validity (generalizability or applicability of the trial), was maintained so that the content of the Delphi list would be complete, but this criterion is not used to calculate the methodological quality score. However, the PEDro scale should not be used as a validity measure of conclusion from a study or to compare the quality of clinical trials conducted in different fields of therapy, because it is not possible to meet all scale items in some areas of physical therapy. Moreover, studies with significant treatment effects and high PEDro scores do not necessarily provide evidence of a clinically useful treatment[16].

All articles that met the inclusion criteria and received a score of 6 or more points on the PEDro scale were included in the present systematic review. Table 2 offers a summary of the studies and relevant characteristics. The "groups" column contains information on sample size. The inclusion criteria are listed to allow a comparison of patient characteristics and the results. Type and frequency of the intervention employed are essential for understanding how CIMT is performed in clinical practice. The "evaluation" column lists the measures employed in the different studies for the assessment of the findings reliability. Finally, the "difficulties encountered" column lists problems involved in managing CIMT to children, which is analyzed in depth in the study by Gordon et al.[1]. Table 3 lists the main outcomes of the clinical trials analyzed in the present systematic review.

RESULTS

One hundred two articles were retrieved from the initial searches of the databases. Following the analyses of the titles, abstracts and full texts as well as the scoring of methodological quality using the PEDro scale (score of 6 or more points), 12 articles met the eligibility criteria and were selected for the present systematic review. Figure 1 displays the flowchart of the article selection process.

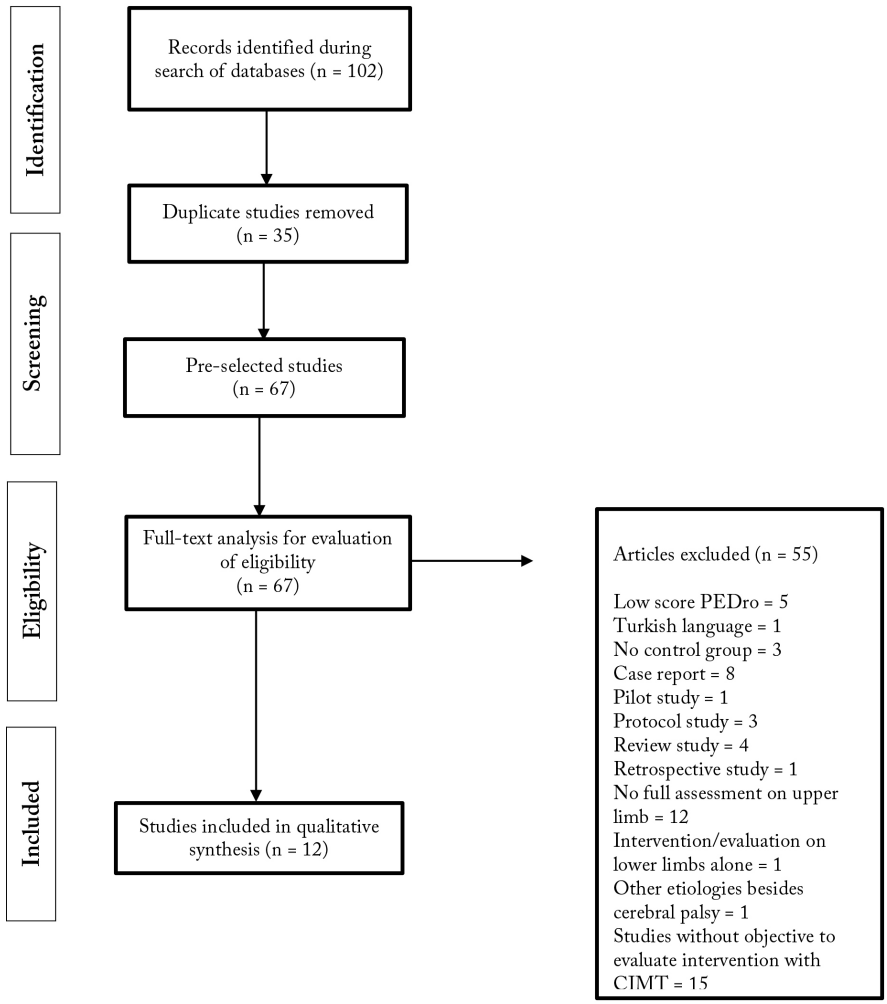

Figure 1 – Overview of selection process

Table 1 – Methodological quality score of each study (PEDro scale)

	Reference	Item											Score
		Eligibility	1- Randomized allocation	2- Allocation concealment	3- Similar prognosis	4- Blinding of participants	5- Blinding of therapists	6- Blinding of examiners	7- Outcome measures	8- Intention to treat	9- Inter-group comparisons	10- Variability and precision	
1	Aarts PB. et al[17]	1	1	0	1	0	0	1	1	0	1	1	6/10
2	Aarts PB. et al[18]	1	1	0	1	0	0	1	1	0	1	1	6/10
3	Brandão MB. et al.[19]	1	1	1	1	0	0	0	1	0	1	1	6/10
4	tBrandão MB. et al.[20]	1	1	1	1	0	0	1	1	1	1	1	8/10
5	Chen HC.et al.[21]	1	1	1	1	0	0	1	1	0	1	1	7/10
6	Chen CL.et al.[22]	1	1	0	1	0	0	1	1	0	1	1	6/10
7	Choudhary A. et al.[23]	1	1	1	1	0	0	1	1	1	1	1	8/10
8	Hsin YJ. et al.[24]	1	1	1	1	0	0	1	1	0	1	1	7/10
9	Sakzewski L et al.[25]	1	1	1	1	0	0	1	1	1	1	1	8/10
10	Sakzewski L et al.[26]	1	1	1	1	0	0	1	0	0	1	1	6/10
11	Case-Smith J. et al.[27]	1	1	0	1	0	0	1	1	0	1	1	6/10
12	Wallen M. et al.[28]	1	1	0	1	0	0	1	1	1	1	1	7/10

Table 2 – Characteristics of studies included in present systematic review

Reference	Groups	Inclusion criteria	Intervention	Intervention frequency	Evaluations	Difficulties encountered
Aarts PB et al.17	n = 52 (2 dropouts) CIMT-BIT = 28 Control = 22	2.5 to 8 years CP with unilateral, bilateral or severely asymmetrical impairment MACS I, II or III	Both groups provided with games and functional activities CIMT-BIT: Unimanual activities with affected limb in first 6 weeks with unaffected limb constrained in sling; goal-oriented bimanual activities in last 2 weeks Control: Conventional therapy involving goal-oriented activities with affected limb; training performed at home and school by parents and teachers	CIMT-BIT: 8 weeks x 3 sessions/week x 3 hr = 72 hr (at rehabilitation center) Control: 8 weeks x 2 sessions/week x 1 hour = 12 hr (at rehabilitation center); 8 weeks x 7.5 hr/week = 60 hr (at home)	Primary outcomes: Assisting Hand Assessment (AHA) ABILHAND-KIDS Secondary outcomes: Melbourne Assessment of Unilateral Upper Limb Function (MUUL) Canadian Occupational Performance Measure (COPM) Goal Attainment Scaling (GAS)	Two children withdrawn from control group due to family circumstances after randomization, impeding true intention-to-treat analysis
Aarts PB et al.18	n = 50 CIMT-BIT = 28 Control = 22	2.5 to 8 years CP with unilateral, bilateral or severely asymmetrical impairment MACS I, II or III	Both groups provided with games and functional activities CIMT-BIT: Unimanual activities with affected limb in first 6 weeks with unaffected limb constrained in sling; goal-oriented bimanual activities in last 2 weeks Control: Conventional therapy involving goal-oriented activities with affected limb; training performed at home and school by parents and teachers	CIMT-BIT: 8 weeks x 3 sessions/week x 3 hr = 72 hr (at rehabilitation center) Control: 8 weeks x 2 sessions/week x 1 hour = 12 hr (at rehabilitation center); 8 weeks x 7.5 hr/week = 60 hr (at home)	Determine Developmental Disregard module of Video Observations Aarts and Aarts, (VOAA-DDD) Active and passive range of motion of wrist and elbow (goniometer)	Two children withdrawn from control group due to family circumstances after randomization, impeding true intention-to-treat analysis

Table 2 – Continuation

Reference	Groups	Inclusion criteria	Intervention	Intervention frequency	Evaluations	Difficulties encountered
Brandão MB et al.19	n = 16 CIMT = 8 HABIT = 8	3 to 10 years Hemiparesis with difference of at least 50% between limbs on timed motor tasks of Jebsen-Taylor Hand Function Test Wrist extension capacity at least 20°; fingers with 10° of complete flexion Normal cognitive skills	Both groups provided with games, fine and gross motor activities (individual and group activities) CIMT: Unimanual activities involving affected limb with unaffected limb constrained in sling, complemented with unimanual or bimanual practice of activities of daily living and games at home HABIT: Bimanual activities in accordance with appropriate age, complemented with unimanual or bimanual practice of activities of daily living and games at home	CIMT: 15 days x 6 hr./day = 90 hr. (rehabilitation center); 15 days x 1 hr./day = 15 hr. (at home) HABIT: 15 days x 6 hr./day = 90 hr (rehabilitation center); 15 days x 1 hr/day = 15 hr (at home)	Pediatric Evaluation of Disability Inventory (PEDI) Canadian Occupational Performance Measure (COPM)	Not possible to administer COPM directly to children since some participants were too young to understand the content of the questionnaire and provide a reliable result.
Brandão MB et al.20	n = 16 (1 dropout) Intervention = 8 Control = 7	4 to 8 years Spastic hemiparetic CP Understand verbal commands Execute proposed activities	Intervention: Unimanual fine motor tasks involving affected limb in first 2 weeks with unaffected limb constrained in sling during therapy and at home (total: 10 h); routine daily bimanual activities during last week Control: Conventional therapy with functional activities, bimanual activities and sensory stimulation	Intervention: 2 weeks x 5 sessions/week x 3 hr = 30 hrs; 1 week x 3 sessions/day x 45 min = 11 hr 15 min Control: 3 weeks x 1 session/week x 45 min = 2 hr 15 min	Jebsen–Taylor Hand Function Test (JTHF) Pediatric Evaluation of Disability Inventory (PEDI)	One child in control group interrupted study due to family problems.
Chen HC et al.21	n = 48 (3 dropouts) Home CIT = 23 Traditional rehabilitation (TR) = 22	6 to 12 years Spastic unilateral CP Considerable non-use of affected limb Wrist and MCP joints ≥ 10º Absence of excessive muscle tone in affected limb	Both groups received individualized at-home intervention with functional activities Home-Based CIT: Unimanual activities involving affected limb with unaffected limb constrained by elastic band and mitt; encouraged by parents to perform daily functional activities with affected limb TR: Guided unimanual and bimanual activities; encouraged by parents to perform daily functional unilateral and bilateral activities	Home-Based CIT: 4 weeks x 2 sessions/week x 3.5 to 4 hr = 32 hr TR: 4 weeks x 2 sessions/week x 3.5 to 4 hr = 32 hr	Primary outcomes Bruininks-Oseretsky Test of Motor Proficiency (BOTMP) Peabody Developmental Motor Scales, Second Edition (PDMS-2) Secondary outcomes Functional Independence Measure for children (WeeFIM) Kinematic and clinical evaluations	One child in TR group unable to complete follow-up due to family schedule and lack of transportation to post-intervention evaluation One child in each group excluded due to insufficient motor skills to conclude kinematic evaluation of reaching task

continues...

Table 2 – Continuation

Reference	Groups	Inclusion criteria	Intervention	Intervention frequency	Evaluations	Difficulties encountered
Chen CL et al.22	n = 48 (1 dropout) CIMT = 24 Traditional rehabilitation (TR) = 23	6 to 12 years Unilateral spastic CP Considerable non-use of affected limb (score on PMAL "how often" scale less than 2.5) Wrist and MCP joints ≥ 10º Absence of excessive muscle tone in affected limb (≤ 2 on Ashworth scale)	Both groups received individualized intervention with functional activities CIMT: Unimanual activities involving affected limb with unaffected limb constrained by elastic band and mitt; encouraged by parents to perform daily functional activities with affected limb TR: Guided unimanual and bimanual activities; encouraged by parents to perform daily functional unilateral and bilateral activities	CIMT: 4 weeks x 2 sessions/ week x 3.5 to 4 hr = 32 hr TR: 4 weeks x 2 sessions/ week x 3.5 to 4 hr = 32 hr	Peabody Developmental Motor Scales, Second Edition (PDMS-2) Pediatric Motor Activity Log (PMAL) Kinematic and clinical evaluations	One child in TR group unable to complete follow-up due to family schedule and lack of transportation to post-intervention evaluation
Choudhary A et al.23	n = 31 (1 dropout) CIMT = 15 Control = 15	3 to 8 years Hemiparetic CP with minimum difference between upper limbs of 10 points on QUEST Understand simple commands Sit without support See objects at distance of 1 m	CIMT: Unimanual reaching activities involving paretic limb with unaffected limb wrapped in triangular bandage Control: Conventional therapy with stretching, strengthening, bimanual activities and practice of activities of daily living	CIMT: 10 days distributed over 4 weeks x 2 h/day = 20 hr (at rehabilitation center) Control: 4 weeks x 20 min/ day = 10 hr (at home)	Primary outcomes Quality of Upper Extremity Skills Test (QUEST) Secondary outcomes QUEST score Nine-hole pegboard	One patient in CIMT group received 5 supervised intervention sessions, but did not return for scheduled visits afterward.
Hsin YJ et al.24	n = 22 CIMT = 11 Control = 11	6 to 8 years Spastic unilateral CP Considerable non-use of affected limb (score on PMAL "how often" scale less than 2.5) Wrist and MCP joints ≥ 10º Absence of excessive muscle tone in affected limb (≤ 2 on Ashworth scale)	Both groups received individualized intervention with functional activities at home CIMT: Unimanual activities involving affected limb with unaffected limb constrained by elastic bandage and mitt; encouraged by parents to perform daily functional activities with affected limb Control: Guided unimanual and bimanual activities; encouraged by parents to perform daily unimanual and bimanual functional activities	CIMT: 4 weeks x 2 sessions/ week x 3.5 to 4 hr = 32 hr Control: 4 weeks x 2 sessions/week x 3.5 to 4 hr = 32 hr	Primary outcome Subtest 8 – Bruininks-Oseretsky Test of Motor Proficiency (BOTMP) Secondary outcomes Pediatric Motor Activity Log (PMAL) Cerebral Palsy-Specific Quality of Life (CPQOL)	No difficulties described

continues...

Table 2 – Continuation

Reference	Groups	Inclusion criteria	Intervention	Intervention frequency	Evaluations	Difficulties encountered
Sakzewski L et al.25	n = 64 (3 dropouts) CIMT = 31 BIT = 30	5 to 16 years Congenital hemipareiss Understand commands Muscle tone of affected limb grade 1 to 3 on Ashworth scale	Both groups provided with fine and gross motor activities, functional reach activities and balance activities in setting with circus theme CIMT: Unaffected limb constrained by mitt during unilateral activities BIT: Guided bimanual activities	6 hr/day x 10 days = 60 hr (daily camping)	Primary outcomes Melbourne Assessment of Unilateral Upper Limb Function (MUUL) Assisting Hand Assessment (AHA) Canadian Occupational Performance Measure (COPM)	Three children did not complete intervention program.
Sakzewski L et al.26	n= 53 (9 dropouts) Hybrid-CIMT = 25 Standard Care = 19	5 to 16 years Unilateral CP Understand commands Muscle tone of affected limb grade 1 to 3 on Ashworth scale	Both groups provided with fine and gross motor activities, functional reach activities and balance activities in setting with circus theme Hybrid-CIMT: Unaffected limb constrained by mitt during unilateral activities; bimanual activities performed in second week Standard Care: Bimanual activities; at-home training with parents	Hybrid-CIMT: 6 hr/day x 10 days = 60 hr (daily camping) Standard Care: 1.5 hr/day x 6 days = 9 hr (daily camping) 12 weeks x 6 sessions/week x 30 min = 36 hr (at home)	Primary outcomes MUUL AHA Secondary outcomes COPM JTTHF Box and Block Test Children's Hand-use Experience Questionnaire (CHEQ)	Six children withdrew from Standard Care group and 3 withdrew from Hybrid-CIMT One child had seizure due to fever during intervention program.
Case-Smith J et al.27	n = 18 3-hr = 9 6-hr = 9	3 to 6 years Unilateral CP	Both groups submitted to intensive intervention in natural environment – functional activities, activities of daily living, reaching and sensory perception First 18 days – Unilateral activities involving affected limb with unaffected limb constrained by cast Last 3 days – bimanual activities	3-hr: 4 weeks x 21 days x 3 hr = 63 hr 6-hr: 4 weeks x 21 days x 6 hr = 126 hr (performed in three different clinical settings)	Assisting Hand Assessment (AHA) Quality of Upper Extremity Skills Test (QUEST) Pediatric Motor Activity Log (PMAL)	One child in 3-hr group and two in 6-hr group did not undergo six-month follow-up evaluation due to scheduling difficulties.
Wallen M et al.28	n = 50 CIMT = 25 Intensive occupational therapy (IOT) = 25	1.5 to 8 years Spastic hemiparetic CP 10º wrist and finger extension of affected limb Functional passive range of motion of affected limb Cooperation	Both groups provided with functional and play activities CIMT: Unilateral activities involving affected limb with unaffected limb constrained by mitt IOT: Bimanual activities complemented with at-home program supervised by parents	8 weeks x 7 sessions/week x 2 hr = 112 hr	Primary outcomes Canadian Occupational Performance Measure (COPM) Secondary outcomes Goal Attainment Scaling(GAS) Assisting Hand Assessment (AHA) Pediatric Motor Activity Log (PMAL) Modified Tardieu Scale (MTS) Ashworth	No difficulties described

Table 3 – Outcomes of studies

Reference	Outcomes
Aarts PB et al.[17]	Improvements on AHA and ABILHAND-KIDS in both groups, with slight diminishment at follow-up; Improvements on Melbourne, COPM and GAS in both groups, with increased improvement at follow-up
Aarts PB et al.[18]	"Capacity" and "performance" scores on VOAA-DDD increased, whereas "development" score remained stable in *CIMT-BT* group; No improvement in scores of *Control group* after intervention, but improvement in "performance" at follow-up; No significant improvements in active or passive range of motion in either group
Brandão MB et al.[19] Brandão MB et al.[20]	Improvements in "self-care", "independence" (PEDI), "performance" and "satisfaction" (COPM) in both groups No significant improvement on JTHF test in either group; Significant improvements in functional abilities and independence (PEDI) in both groups at post-intervention and follow-up evaluations
Chen HC et al.[21]	Improvements on "grasping" subscale (PDMS-2), subtest 8 (BOTMP), "self-care" subscale (WeeFIM), kinematic analyses of reach and grasping in both groups at post-intervention and both follow-up (3 and 6 months) evaluations
Chen CL et al.[22]	*CIMT* group demonstrated significant improvement on "grasping" subscale (PDMS-2), quality/quantity of hand use (PMAL), reaction time, normalized movement time and peak velocity in comparison to *TR* group.
Choudhary A et al.[23]	*CIMT* group demonstrated significant improvement in QUEST score and time required to complete nine-hole pegboard test in comparison to *Control*, with difference persisting at both follow-up evaluations (4 and 8 weeks).
Hsin YJ et al.[24]	Improvements on BOTMP subtest 8 in both groups at post-intervention and 3-month follow-up evaluations; Improvement on PMAL in both groups, with *CIMT* group demonstrating greater quality/quantity of hand use than *Control* group, persisting at 3-month follow up
Sakzewski L et al.[25]	Older children, those with left-side hemiparesis and those with poorer manual function benefitted more from therapy. Better effect on MUUL in *CIMT* group than *BIT* group; More changes in AHA in *BIT* group than *CIMT* group
Sakzewski L et al.[26]	Significant improvements in "satisfaction", "performance" (COPM) and dexterity (BBT and JTTHF) in both groups; Significant gains in AHA in Standard Care group at 26-week follow-up evaluation
Case-Smith J et al.[27]	Significant improvements in AHA, PMAL and movement dissociation (QUEST) in both groups
Wallen M et al.[28]	Significant improvements in post-intervention "satisfaction" and "performance" (COPM) in both groups

DISCUSSION

Classic CIMT was originally developed for adults with neurological disorders and consequent motor impairment, and involves the constraint of the unaffected upper limb with a sling, mitt or other type of device for 90% of the day for 14 consecutive days. The patient engages in six hours of intensive training of the affected upper limb for 10 of the 14 days using a set of activities involving repetitive actions and formation therapy. Morris et al.[29] highlight the importance of constraining the unaffected limb for 90% of the time during the intervention for the reorganization of the motor cortex and the long-term increase in the use of the affected limb. A substantial number of studies published in recent years demonstrate that CIMT leads to considerable neuroplastic cortical reorganization and to improved function of the upper limb in both the short and long terms. In a pioneering study, Liepert et al.[30] employed transcranial magnetic stimulation to demonstrate an increase in the area of cortical representation of the affected limb following CIMT as well as improved limb use, as demonstrated by the Motor Activity Log.

In all studies analyzed in the present systematic review, games and functional activities were used during CIMT, but methodological quality, sample size, treatment modality, training intensity and evaluation tools differed among the studies. CIMT was not employed in its classic form and was modified with respect to the constraint method, duration of constraint (days or weeks), type and duration of therapy, intervention setting (home, school or clinic) and intervention provider (therapist, parent or teacher). The first significant variant was the method employed to constrain the unaffected limb, for which a range of techniques was used, such as a mitt[21,22,24-26,28], sling[17-20], cast[27] and splint[23]. Secondly, the treatment programs varied the intensity, ranging from 4 weeks of intervention distributed in 10 days, 2 hours a day, totaling 20 hours of intervention[23] for 4 weeks, distributed in 21 days, 6 hours per session, totaling 126 hours of intervention[27]. The fact that the frequency, intensity and duration varied among the trials analyzed in the present review limits the development of guidelines regarding these aspects in interventions involving CIMT for children with CP.

In two clinical trials conducted by Aarts et al.[17,18], the treatment group submitted to CIMT received more sessions per week and more hours per session than the control group, but the individuals in the control group complemented their training at home to match the total number of hours to which the treatment group was submitted. Choudhary et al.[23] conducted interventions on ten days distributed over a four-week period, in which the treatment group received two hours per day at a rehabilitation center, and the control group

received 20 minutes a day at home. The clinical trials of Sakzewski L et al.[25] also diverged in intensity in both groups (treatment and control).

The use of containment at home after treatment sessions was not used in any clinical trial. In some studies, children were encouraged to use the affected limb in functional and avd's activities at home under parental supervision, with no need for restraint of the affected limb[21,22,24] or were submitted to complementary therapy with unimanual and bimanual exercises through games at home[19]. Chen et al.[21] employed home-based CIMT, which consisted of the same principles as modified CIMT, but the therapist conducted the training in the child's home. A hybrid CIMT was used by Sakzewski et al.[26], which was composed of the combination of modified CIMT and bimanual training involving high intensity duration with the aim of improving unimanual and bimanual capacity.

All authors of the selected studies specified the children's age and degree of impairment at the time of treatment, which were chosen based on the expected benefits of treatment. For the functional classification of individuals eligible for inclusion in the study, the Manual Abilities Classification System (MACS) was used in two studies[17,18], which was developed to categorize, respectively, the mobility and manual function of children with CP[31,32]. Other studies included in this review used the results of the Quality of Upper Extremity Skills Test (QUEST), Pediatric Motor Activity Log (PMAL) and Jebsen-Taylor Hand Function Test (JTHF) as part of the inclusion criteria[19,22-24]. It is recognized that the PMAL evaluation scale is an evaluation tool of little reliability and insufficient validity[33]. Minimum functional capacities of the affected limb were also used in the majority of studies, which required minimum wrist extension and finger flexion of 10º. The classification of muscle tone at the time of treatment was determined in some studies, using grades 1 and 2 of the modified Ashworth Scale as part of the inclusion criteria. Cognitive capacity, cooperation and comprehension of the commands were employed as inclusion criteria in the majority of studies, which are essential to conducting studies of this nature and obtaining the expected benefits. According to Moura[34], adequate treatment planning is fundamental and requires ample knowledge of all upper limb disorders. A clinical evaluation combined with quantitative upper limb measures can provide necessary information for the detection of clinically significant changes in upper limb function, following an intervention.

All studies selected presented valid and reliable results using one or more types of primary and secondary evaluations. The PMAL, QUEST, Canadian Occupational Performance Measure (COPM) and Assisting Hand Assessment (AHA) were the most used outcome measures. In two clinical trials, Aarts et al.[17,18] used the COPM, AHA, ABILHAND-KIDS, Melbourne Assessment of Unilateral Upper Limb Function (MUUL) and Goal Attainment Scaling (GAS) as well as the Determine Developmental Disregard module of the Video Observations Aarts and Aarts module (VOAA-DDD), which was created by the authors themselves. The Bruininks-Oseretsky Test of Motor Proficiency (BOTMP) was used in two studies[21,24], the Peabody Developmental Motor Scales – Second Edition (PDMS-2) was used in two studies[21,22] and the Pediatric Evaluation of Disability Inventory (PEDI) was used by Brandão et al.[19].

Other outcome measures were employed in the remaining studies. The Functional Independence Measure for Children (WeeFIM), together with a kinematic evaluation, was used in the study by Chen et al.[21] for the evaluation of performance on activities of daily living and functional independence. Hsin et al.[24] employed the Cerebral Palsy-Specific Quality of Life (CPQOL) assessment tool as a secondary outcome measure[35]. Along with other measures, Sakzewski et al.[26] used the Box and Block Test and Children's Hand-Use Experience Questionnaire (CHEQ) as secondary outcome measures. Along with previously described measures, Wallen et al.[28] used the Modified Tardieu Scale (MTS) and Modified Ashworth Scale as secondary outcome measures for the evaluation of spasticity of the elbow flexors as well as the wrist pronators and extenders.

All studies included in the present systematic review reported significant improvements in some outcome measure, demonstrating the positive effects of the proposed treatment during both the post-intervention and follow-up evaluations. Despite the small sample sizes, all studies offered satisfactory consistency regarding the outcome measures.

The majority of studies reported difficulties with the use of CIMT for children with CP, but the reason for the found difficulties does not have the correlation of something with a restraint of a non-affected limb

or there is a process of irritability during a therapy. In 9 of the 12 clinical trials[17-20,22,23,25-27], difficulties and dropouts occurred due to family problems, scheduling problems, changes of address and a lack of transportation. In the study by Sakzewski et al.[26], nine of the participants dropped out of the study groups and a seizure occurred in one child during treatment; however, the authors did not describe the dropouts in detail. In the study by Chen et al.[21], dropouts occurred due to family problems and two children were excluded from the study during treatment due to a lack of sufficient motor skills to perform the kinematic evaluation of the reaching task proposed as an outcome measure. Brandão et al.[19] found that it was impossible to administer the COPM directly to the children due to their young age and difficulty of understanding the questionnaire content, which was therefore answered by parents/caregivers.

Based on the studies selected for the present review, CIMT requires modifications for children with CP and the children's response to a given intervention needs to be evaluated using a biopsychosocial approach, which can directly or indirectly exert an influence on the results. Information regarding the types of intervention, modifications and dose-response relationship as well as the effects on structural and functional changes in children with CP is fundamental to the development of guidelines for the reliable, reproducible practice of CIMT.

CONCLUSION

The present systematic review of the literature findings demonstrate that, despite the lack of a common methodology among studies regarding the use of constraint-induced movement therapy for children with cerebral palsy, this form of intervention has been adapted with considerable flexibility, providing promising, positive results of the therapeutic intervention of the paretic upper limb.

This systematic review is not intended to synthesize and evaluate the results obtained with the use of the CIMT in clinical trials, but only to demonstrate its use and/or possible modifications/adaptations in clinical practice. Because of this limitation in our study, a summary of outcome measures is required, as well as synthesis of data on the studies reviewed in a future version.

DISCLOSURE

The authors declare no conflicts of interest in relation to this study. The authors alone are responsible for the content and writing of the paper. No commercial party having a direct financial interest in the results of the research supporting this article has or will confer a benefit upon the authors or upon any organization with which the authors are associated. This systematic review was conducted in compliance with the norms of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).

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