Effectiveness of median nerve neural mobilization versus oral ibuprofen treatment in subjects who suffer from cervicobrachial pain: a randomized clinical trial

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Abstract

Introduction: Oral ibuprofen (OI) and median nerve neural mobilization (MNNM) are first line treatments for patients who suffer cervicobrachial pain (CP). OI may produce side effects which are not tolerated by all subjects who suffer CP, whereas MNNM has no known side effects. Therefore, the aim of this study was to assess the effectiveness of both treatments (OI vs. MNNM) in CP.
Material and methods: This investigation was a blinded parallel randomized clinical trial (NCT02593721). Sixty-two participants diagnosed with CP were recruited and randomly assigned to 2 groups (n = 31), which received MNNM or 1200 mg/day OI treatment for 6 weeks. The numeric rating scale for pain intensity was the primary outcome. The cervical rotation range of motion (CROM) and the upper limb function were the secondary outcomes.
Results: The results showed that OI treatment (η^2 = 0.612–0.755) was clearly superior to MNNM (η^2 = 0.816–0.821) in all assessments ($p < 0.05$) except for the CROM device results, which were equivalent to those of the MNNM group ($p > 0.05$). Three subjects were discharged because of OI side effects.
Conclusions: Oral ibuprofen may be superior to MNNM for pain reduction and upper limb function increase of subjects with CP. Nevertheless, both treatments were effective. Median nerve neural mobilization may be considered an effective non-pharmaceutical treatment option in subjects with CP. Regarding OI adverse effects, our findings challenge the role of pharmacologic versus manual therapy as possible treatments that may improve pain intensity and upper limb functionality in subjects with CP.

Key words: non-steroidal anti-inflammatory agents, musculoskeletal manipulations, rehabilitation, upper extremity.

Introduction

Cervicobrachialgia, also known as cervicobrachial pain (CP), is a high incidence and high prevalent well-described disabling medical condition

that affects 83 per every 100,000 people in the course of their lives [1–3]. It is described in the scientific literature as the presence of pain in the neck that radiates to or is associated with the arm [4, 5], and has a gold standard diagnosis through correlative pathological findings in a magnetic resonance imaging (MRI) [6–8]. Other helpful tools in the proper diagnosis of CP may be the presence of positive outcomes in the Spurling, upper limb and distraction orthopedic tests, as well as altered results in nerve conduction assessment [9–11]. The classical pattern of pain symptoms related to this condition are caused by the existence of musculoskeletal damage and neuropathic irradiation of pain due to underlying neural tissue injuries of the cervicobrachial anatomical region [12–14]. There is current evidence of pathologic nerve trunk mechano-sensibility alterations, central sensitizing and visco-elastic distortion of the cervicobrachial neural tissue during the onset of CP symptoms; this constitutes a key point in the proper treatment selection for CP and its adequate implementation [12–17].

Traditionally, first line treatment of CP involves the use of non-steroidal anti-inflammatory drugs (NSAIDs) and physical therapy techniques such as neural tissue mobilization of the median nerve. The principal NSAIDs prescribed worldwide to treat pain and CP include oral ibuprofen (OI) [18–25]. Both median nerve neural mobilization (MNNM) and OI relieve CP, but through different mechanisms and with a different onset of side effects. MNNM is a specific physical therapy technique for the treatment of CP described by Butler, Butler and Coppieters, and Elvey-Hall [14, 26–31] that achieves pain relief through mechanical stimulation of the median nerve and the brachial plexus. The proper mechanical stimulation of the nerve and its surrounding neural tissue induces a wide variety of physiologic responses that may reduce cervicobrachial pain including the activation of descending nervous system pain modulation mechanisms, although the entire set of underlying reasons for this pain reduction is not completely understood. The effects caused by the neural tissue mobilization that produce pain relief include intraneural edema reduction, changes in the intraneural nerve pressure, dispersion of pro-inflammatory substances and an increase in nerve mobility [31–33].

OI is a nonsteroidal anti-inflammatory drug used worldwide to control pain, fever and inflammation [34, 35]. Oral intake of ibuprofen, like most NSAIDs, produces a hypoalgesic effect due to biochemical inhibition of the COX enzymes, which convert arachidonic acid to prostaglandin H2 (PGH2). PGH2 is converted by other enzymes to several types of prostaglandins and thromboxanes (which are mediators of pain and inflammation) [36–38]. Side effects derived from the oral intake of ibuprofen are related to its systemic action and can be severe in some patients. This issue suggests that OI and other NSAIDs with similar mechanisms of action may not be suitable to be administered in all types of patients suffering from CP, whereas MNNM has little to no known side effects when applied properly. This reveals a point of interest in determining comparative effectiveness between these two first line therapeutic options of CP [18, 35, 37, 38].

Currently, there is a lack of single blinded randomized controlled clinical trials (RCT) regarding the comparison between MNNM and OI in CP, which by itself is an additional stand-alone problem for the practicing clinician who desires high quality evidence on the level of effectiveness of MNNM when compared to common over-the-counter pharmaceutical treatment for CP [36, 39–47]. Therefore, the purpose of the present study was to compare the effectiveness for pain intensity, range of movement and functionality between MNNM and OI in treating patients who suffer from CP.

Material and methods

Study design

This investigation was an interventional phase 2/phase 3 parallel (2 arm) single blind (outcome assessor) randomized clinical trial with an endpoint classification of efficacy study 1 : 1 allocation ratio conducted at only 1 clinical center. No changes were made in the proposed methodology because the original protocol was not altered. Furthermore, the Consolidated Statement for Reporting Trials (CONSORT) statement and checklist were considered [48].

Ethical considerations and trial registry

The present study was designed and applied following the ethical principles for medical research involving human subjects established in the Declaration of Helsinki. The study protocol was approved by the Ethics Committee from La Viña Medical Center, Valencia, Venezuela (code CE0072015) and registered at ClinicalTrials (NCT02593721; October 26, 2015). Informed consent of all participants was obtained and the rights of subjects were protected.

Randomization and blinding

Subjects were assigned to 1 of the 2 groups using restricted block randomization through block computerized randomization software (www.randomizer.com) assuring that each block had a size

of 31 participants. Randomization and allocation to the trial group was carried out by computer software randomized printed cards contained in consecutively numbered opaque sealed envelopes that were handed to the participant by the physiatrist medical doctor (PMD). The outcome assessor (OA) was blinded to the randomization of group allocation. The principal investigator did not participate in the application of treatment or data collection.

Participants

Subjects were recruited from a group of voluntary consecutive individuals seeking treatment or assessment related to CP in the established medical center that was selected to apply the study, or by referral of 5 other private and public medical centers. A total of 133 individuals were screened from July to August 2015. MRI corroboration and other necessary medical assessment including the need for diagnosis were performed by a specialized PMD. A total of 62 participants were recruited and divided into 2 groups of 31 subjects by the PMD in concordance with the randomization schedule that the data analyst (DA) generated. Group A contained MNNM participants and group B contained OI participants.

All eligible participants were adults who belonged to both genders ranging from 18 to 45 years of age with a clinical diagnosis of cervicobrachial pain confirmed by magnetic MRI and presence of unilateral symptoms of arm pain, paresthesia or numbness in the upper limb and positive results in all of the following tests: Spurling, distraction, and upper limb during at least 3 continuous months previous to enrollment. Exclusion criteria of participants were contraindication for intake of NSAIDs, the use of any type of treatment (therapy, procedure or drug) to relieve pain, and presence in participants of vertebral instability, vertebral osteoporosis, vertebral or spine infection and neurologic diseases of genetic, infectious or neoplastic origin, cervical stenosis myelopathy, pregnancy, kinesiophobia, endocrine disorders and menopause, history of spine surgery, intellectual disability, severe mental illness, intoxication, severe sleep deprivation and Alzheimer's disease. Furthermore, patients with any neurological or neuromuscular disorders (different or not related to CP) diagnosed by the PMD were excluded.

Interventions

Eligible subjects who consented to participate were randomly allocated to receive 1 of the 2 proposed treatments. The first group was named group A and received a non-surgical non-invasive MNNM procedure. MNNM was applied continuously for 2 min on 5 different occasions with 1 min of rest between each 2-minute application of the MNNM procedure by a PT with at least 2 years of experience in manual therapy. The intervention was applied during a period of 6 weeks (from Monday to Friday). The maximum level of elbow extension movement without the reproduction of symptoms during the application of the MNNM treatment was determined through the baseline use of a universal hand held goniometer device. The MNNM intervention was applied according to the previously described principles of neural tissue mobilization for treating CP by Butler, Butler and Coppieters, Coppieters and Butler, and Elvey-Hall [14, 26–30].

The MNNM was performed by PT in the affected upper limb and consisted of initial supine neutral positioning of the patient, shoulder girdle depression, glenohumeral 90° abduction with a lateral rotation component, supination of the forearm, elbow and wrist flexion, thumb and finger extension followed by an immediate second movement of elbow extension with wrist, thumb, and finger flexion, while maintaining the initial shoulder girdle, glenohumeral and forearm positioning [12]. This passive movement sequence of upper limb flexion and extension was done repetitively at an approximate speed of 1 complete repetition of upper limb flexion and extension movement every 2 s without the reproduction of symptoms.

The second group of individuals was named group B and received an oral ibuprofen tablet treatment that was prescribed by the PMD who is familiar with the proper use and side effects of OI in CP. The PMD was responsible for modulating the OI dose to the subject's tolerance whilst trying to achieve the maximum hypoalgesic desired effect. The starting dose on the first day of treatment was a single dose of 400 mg. Doses were increased in case of subjects' adequate tolerance to a maximum dose of 1200 mg/day, divided into 3 doses every 8 h. Patients could leave the present study when they wanted to or if the PMD considered that symptoms worsened significantly; therefore at all times the free will of participants to continue or abandon the experiment was fully respected.

Outcome measurements

Both groups, MNNM and OI, were assessed in the same time frames. The primary outcome measure was change from baseline using the numeric rating scale for pain (NRSP). The time frame was at baseline and 1 h after the application of treatment, corresponding to intervention sessions 1, 15 and 30 (baseline, 4 weeks and 6 weeks, respectively). The NRSP is an 11-point scale for patient self-reporting of pain [49–51]. It was employed to

evaluate the presence and relief of cervicobrachial pain symptoms by a blinded PT outcomes assessor (PTOA). Secondary outcomes were related to individual physical function; the first secondary outcome measure was change from baseline of the physical function involving the affected upper limb using the QuickDASH (Disabilities of the Arm, Shoulder and Hand) scale. The time frame corresponded to intervention sessions 1 and 30 (baseline and 6 weeks, respectively). The QuickDASH test is a self-report short questionnaire designed to measure physical function and symptoms in people with any of several musculoskeletal disorders of the upper limb [52, 53]. The last secondary outcome measure was the change from baseline cervical rotation range of motion at 1 h. This outcome measure time frame was at baseline and 1 h after the application of treatment, corresponding to intervention sessions 1 and 30 (baseline and 6 weeks, respectively). Cervical rotation was assessed in units of rotation degrees, using a cervical range-of-motion device (CROM) [54, 55]. All secondary outcomes were assessed by the PTOA. No changes were made in the proposed outcomes because there was no deviation from the original protocol.

Sample size calculation

G*Power software 3.1.9.2 was used to set the sample size. For sample size determination the NRSP was used as the primary reference measurement. The effect size for the NRSP was estimated as 0.509. Assuming at least six measurements, correction of sphericity was determined as 0.5 with 0.95 power and a 0.05 α level; 20% of the sample was considered lost. Consequently a total sample size of 54 subjects was estimated to be randomly divided into two groups of 27 subjects. Criteria for participant removal were the presence of any exclusion criterion at the time of measurement or diagnosis and/or during the study period or monitoring process, failure to attend 2 sessions of treatment or evaluation, voluntary abandonment, death or removal by decision of the present study holders.

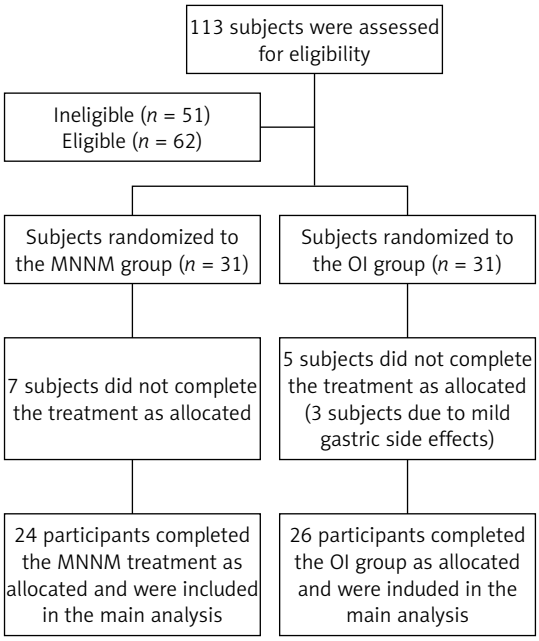

Figure 1. Participant flow diagram of voluntary participants through different study phases

n – number of subjects, MNNM – median nerve neural mobilization, OI – oral ibuprofen.

Statistical analysis

Demographic characteristics including age and gender of participants were analyzed. The Kolmogorov-Smirnov test was used to confirm a normal distribution of the sample. NRSP, CROM and QuickDASH mean, between-session variance percentages and confidence interval according to each session and type of treatment were performed. Student's *t* test was employed for between-group mean difference comparisons as well as for intragroup analyses. In addition, eta square values (η^2) of subjects' intereffect testing were added in both treatment groups. Box-plot graphics were developed in order to clarify the data. Finally, all data analyses were performed with commercially available software (SPSS 22.0, SPSS Inc, Chicago, IL) and a confidence interval (CI) of 95% (p-value < 0.05).

Results

Of the original 62 participants enrolled in the present study only 50 completed the trial. Of the 31 subjects who belonged to the MNNM group (group A) 24 subjects completed the trial: 6 subjects abandoned participation claiming personal reasons and 1 participant was removed by the study holders because of anticonvulsant intake concealment. In the OI group (group B) 5 participants of the original 31 abandoned the study; 2 participants were removed from the study because they missed evaluation sessions and a total of 3 participants were removed by the PMD because they showed mild signs of gastric side effects associated with OI. No important side effects were reported related to MNNM treatment (Figure 1).

There were no significant differences related to the size, age and sex of both groups' participants; therefore demographic values did not influence the primary and secondary outcomes of the present study (Table I). NRSP results of the MNNM group show significantly (p < 0.05) inferior mean values to those obtained by the OI group in all of the performed assessments. The MNNM

group had a constant decrease of NRSP scores that ranged between 6.9% and 15%, whereas the OI group did not exhibit a constant decrease in its NRSP values. It was observed that OI NRSP scores decreased dramatically 1 h after the drug was administered but OI NRSP scores had a tendency to increase back again at the baseline measure of the next session.

Because of this series of results we can clearly state that according to the applied protocol OI is more effective in reducing pain in terms of mean values than MNNM even though a tendency of constant pain reduction was observed in MNNM. The results of this investigation reveal that both MNNM and OI proved to be effective in treating CP. All ranges calculated for the confidence interval were contained within the lower and upper limits (between 1.13 and 1.45), implying that 95% differences in similar investigations would not exceed a higher value than 2 (Table II).

CROM outcome values showed an increase in the ipsilateral rotation range of cervical motion (IRRCM) in both treatment groups, but did not show a significant ($p > 0.05$) difference in between-group analysis. CROM device results reveal that MNNM and OI were equally effective in increasing IRRCM (Table III). Responses to the QuickDASH instrument in each study group expressed highly significant values ($p < 0.0004$ and

Table I. Demographic data of participants according to type of treatment

Demographic data	MNNM ($n = 24$)	OI ($n = 26$)	Statistical significance
Age [years]	32.3 ±3.7	30.8 ± 4.3	$p < 0.195$
Sex:			
Female	13 (54)	19 (73)	$p < 0.27$
Male	11 (46)	7 (27)	

**p < 0.05 was considered as statistically significant. Age – age in years of participants, Sex – biological sex of participants, MNNM – median nerve neural mobilization, n – number of participants, f – frequency, OI – oral ibuprofen.*

Table II. NRSP mean, between-session variance percentages and confidence interval according to each session and type of treatment

Session	MNNM ($n = 24$)	%	OI ($n = 26$)	%	MNNM – OI difference 95% CI (range IL – SL)
One	6.5 (0.9)	–	5.9 (1.0)	–	0.6 ($p < 0.033$)* 0.05–1.18 (1.13)
+ 1 h	5.9 (1.1)	–9.2	3.7 (1.4)	–37.3	2.2 ($p < 0.0001$)* 1.45–2.90 (1.45)
Two	4.9 (1.4)	–6.9	3.9 (0.9)	+5.4	1.0 ($p < 0.004$)* 0.36–1.77 (1.41)
+ 1 h	4.5 (1.4)	–8.2	2.1 (0.9)	–46.2	2.4 ($p < 0.0001$)* 1.75–3.17 (1.42)
Three	3.8 (1.3)	–15.5	2.9 (0.8)	+38.1	0.9 ($p < 0.009$)* 0.22–1.50 (1.28)
+ 1 h	3.5 (1.4)	–8.5	1.7 (0.7)	–41.2	1.8 ($p < 0.0001$)* 1.12–2.42 (1.30)

**p < 0.05 was considered as statistically significant. CI – 95% confidence interval, MNNM – median nerve neural mobilization, NRSP – numeric rating scale for pain, Session – time lapse when treatment was applied, OI – oral ibuprofen, One – time lapse corresponding to baseline assessment, (range IL – SL) – range lower limit minus range upper limit, +1 h – time lapse corresponding to 1 h after baseline application of treatment assessment, n – number of participants, % – between-session variance percentage.*

Table III. CROM device mean, between-session variance percentages and confidence interval according to each session and type of treatment

Session	MNNM ($n = 24$)	%	OI ($n = 26$)	%	MNNM – OI difference 95% CI (range IL – SL)
One	60.4 (7.0)	–	57.7 (5.6)	–	2.7 ($p < 0.143$) –0.94 – 6.31 (7.25)
+ 1 h	63.8 (7.7)	5.6	66.0 (7.4)	14.3	–2.2 ($p < 0.317$) –6.47 – 2.14 (8.61)
Two	65.0 (5.9)	1.8	66.1 (9.0)	1.5	–1.1 ($p < 0.489$) –5.94 – 2.88 (8.82)
+ 1 h	69.3 (7.4)	6.6	71.1 (4.5)	7.5	–0.84 ($p < 0.160$) –6.07 – 1.03 (7.10)

**p < 0.05 was considered as statistically significant. CI – 95% confidence interval, CROM – cervical range of motion, MNNM – median nerve neural mobilization, Session – time lapse when treatment was applied, OI – oral ibuprofen, One – time lapse corresponding to baseline assessment, (range IL – SL) – range lower limit minus range upper limit, +1 h – time lapse corresponding to 1 h after baseline application of treatment assessment, n – number of participants, % – between-session variance percentage.*

Table IV. QuickDASH mean, between-session variance percentages and confidence interval according to each session and type of treatment

Session	MNNM (n = 24)	%	OI (n = 26)	%	MNNM – OI difference 95% CI (range IL – SL)
One	60.8 (10.0)	–	52.2 (10.2)	–	8.6 ($p < 0.004$)* 2.85–14.43 (11.58)
Two	32.2 (12.6)	47.0	17.8 (7.6)	65.9	14.4 ($p < 0.0001$)* 8.32–20.39 (12.07)

**$p < 0.05$ was considered as statistically significant. CI – 95% confidence interval, DASH – The Disabilities of the Arm, Shoulder and Hand questionnaire, MNNM – median nerve neural mobilization, Session – time lapse when treatment was applied, OI – oral ibuprofen, One – time lapse corresponding to baseline assessment, (range IL – SL) – range lower limit minus range upper limit, n – number of participants, % – between-session variance percentage.*

$p < 0.0001$) in each of the QuickDASH assessment sessions. The improvement was greater in the OI treatment group, with a difference of 14.4 points and a 65.9% decrease compared to session one, while the MNNM group showed a 47.0% QuickDASH score decrease. Both treatments are capable of improving the physical condition of subjects who suffer CP according to QuickDASH instrument criteria (Table IV).

Eta squared values, expressed in percentages, show that the variations observed in the lower average values of the NRSP scale and increased degrees of CROM were the result of the applied treatments. In this regard, MNNM group average value explained variation of NRSP was 75.5%, whereas in the OI group the percentage was 81.6%; percentages for the CROM device were 61.2% and 82.1% respectively. These percentages reflect the percentage of variance in NRSP and CROM that was explained by the administration of treatments for each group (Table V).

Discussion

Therefore MNNM was not superior or equal to the OI treatment in reducing pain perception in subjects who suffer CP according to the applied protocol. Effectiveness values regarding NRSP and QuickDASH of MNNM proved to be significantly inferior ($p < 0.05$) than values obtained through the application of an OI treatment in achieving analgesia and improving function of the affected upper limb during CP.

Table V. Eta square values (η^2) of subjects intereffect testing*

Instruments and treatments	η^2	%
NRSP:		
MNNM	0.755	75.5
OI	0.816	81.6
CROM device:		
MNNM	0.612	61.2
OI	0.821	82.1

**NRSP scores and CROM device degrees results of MNNM and OI treatment sessions processed through eta^2 (η^2) subject intereffect testing related to repeated measure analysis of the general linear model. CROM – cervical range of motion, NRSP – numeric rating scale for pain, MNNM – median nerve neural mobilization, OI – oral ibuprofen, % – η^2 percentage value possibly related to treatment effect.*

The MNNM and OI outcomes of this study are believed to be of clinical importance according to Farrar *et al.* [56] and are in line with the pain reduction values (> 2 points) achieved by Cleland *et al.*, Allison *et al.* and Savva *et al.* [57–59]. Because of the novel nature of the applied protocol there was no available literature which could be used to compare specific parameters. All the available studies that applied MNNM had a mixed combination of MNNM with other types of treatments in the same group of subjects. The exclusive application and assessment of passive MNNM performed in this study may explain the smaller pain reduction effect of MNNM when compared to the results reported by De la Llave-Rincon *et al.,* Nee *et al.* and Savva *et al.* [12, 36, 59]. Pain reduction, function improvement and increase in IRRCM were continuous in the MNNM group mean while the OI group outcomes related to pain had a tendency to increase again after a time lapse. This event was linked to the extensively described pharmacokinetics and pharmacodynamics of OI [24].

CROM device outcomes revealed that both treatments applied in this investigation were significantly effective in increasing IRRCM in subjects who suffer CP, as seen in research by Cowell and Phillips [4]. Comparative analysis between the two treatment groups of the present study did not reveal a significant difference of effectiveness in increasing the IRRCM. This reveals that MNNM and OI are equally effective ($p < 0.05$) in increasing IRRCM according to the applied protocol. There was no evidence of side effects or an important exacerbation of symptoms related to MNNM resulting from the application of the protocol [36].

A discrepancy of results was found related to OI effectiveness in CP [60]. According to Sheather-Reid and Cohen [20] OI did not exert any analgesic effect in a group of subjects who suffered

CP [60–63]. It is important to state that although OI is recommended worldwide to treat CP, the research performed by Sheather-Reid and Cohen [20] in 1998 constitutes the only available study of OI effectiveness in CP. We believe that the reason for the discrepancy of results lies in the fact that the OI dose used to treat subjects in the Sheather-Reid and Cohen [20] investigation was only 800 mg/day, which, according to Rainsford and Portenoy and Kanner [35], is considered an inferior dosage to the recommended 1200 mg/day dose to properly achieve analgesia and reduce inflammation. This explanation is supported by a study performed by McQuay and Moore [63] which concludes that OI is a dose-dependent drug that may vary in its pain reduction effect according to the size of the dose administered to the subject. Another possible reason for the discrepancy of the results with the mentioned Sheather-Reid and Cohen [20] study was the small sample size (only 4 subjects completed the trial) and the inclusion criteria for participants.

The beneficial results of OI and MNNM obtained in the present study support the theory suggested by Allison *et al.* [58] that there is an inextricable link between articular, soft tissue and neural structures of the cervicobrachial anatomic region. The authors of the present study believe that CP is a multimodal condition where joint and neurogenic pain may coexist and overlap as proposed by Elvery and Hall [30]. This strong interrelation among joint and nervous tissue could explain the dual effectiveness of both OI and MNNM treatments in CP. We believe that OI exerted a systemic anti-inflammatory action on joints and soft tissue that could have reached a ceiling effect because the neural components were not specifically treated, whereas the MNNM treatment had a direct impact on CP by reducing peripheral and central neurogenic pain, which is widely known to be a source of local inflammation and nociception. This conjecture is consistent with the histological and Western blot findings of Santos *et al.* [64] which suggested that neurogenic and peripheral inflammation activated through dorsal horn sensitizing of glial cells is reversible by the application of neural mobilization and anti-inflammatory treatment.

A constant limitation faced during the present study was the lack of prior high quality research related to MNNM and OI in CP. Other limitations and potential sources of bias were found in the primary outcome and the participant blinding method. We believe that the NRSP results of this study cannot be used to determine whether pain was of neurogenic or musculoskeletal inflammatory origin. Nevertheless, special care was taken in the participants' inclusion criteria to ensure that pain of neural origin was also present. Furthermore, the time frames of the outcome measurements may have been influenced by the drug half-life and confounded the results between the groups. Blinding of participants was an additional challenge; in this regard, the study hypothesis, control group existence and group allocation blinding could have been the method of choice for subject masking, which is considered according to Boutron *et al.* [42] an effective blinding procedure. Furthermore, other conditions such as arthrogryposis [65] or coronary heart disease [66], which may influence CP, were not excluded. New approaches testing the feasibility and safety in orthopedic rehabilitation should be considered in future studies [67]. Due to the lack of dipper subgroup analysis and additional reproductions of the applied protocol, the authors considered that generalization of our study results was not possible.

In conclusion, OI may be superior to MNNM for pain reduction and upper limb function increase of subjects with CP according to the applied protocol in the present investigation. Nevertheless, it is important to acknowledge that both treatments may be effective in treating CP. MNNM may be considered an effective non-pharmaceutical treatment option in specific cases of CP.

Conflict of interest

The authors declare no conflict of interest.

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