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Original article

Effectiveness of a manual therapy protocol based on articulatory techniques in migraine patients. A randomized controlled trial

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ABSTRACT

Background: Physiotherapy is used as a non-pharmacological treatment for migraine. However, controversy exists over whether articulatory manual techniques are effective in some aspects related to migraine.
Objectives: To assess the effectiveness of a manual therapy protocol based on articulatory techniques in pain intensity, frequency of episodes, migraine disability, quality of life, medication intake and self-reported perceived change after treatment in migraine patients.
Design: Randomized controlled trial.
Methods: Fifty individuals with migraine were randomized into the experimental group, which received manual therapy based on articulatory techniques (n = 25), or the placebo group (n = 25). The intervention lasted 4 weeks and included 4 sessions. Patients were assessed before (T1), after (T2) and at a one-month follow-up following the intervention (T3). The instruments used were the Migraine Disability Assessment (MIDAS) questionnaire, the Short Form-36 Health Survey (SF-36), the medication intake and The Patients' Global Impression of Change scale.
Results: In comparison with placebo group, manual therapy patients reported significant effects on pain intensity at T2 ($p < 0.001$; $d = 1.15$) and at T3 ($p < 0.001$; $d = 1.13$), migraine disability at T3 ($p < 0.05$; $d = 0.69$), physical quality of life at T2 ($p < 0.05$; $d = 0.72$), overall quality of life at T2 ($p < 0.05$; $d = 0.60$), decrease in medication intake at T2 ($p < 0.001$; $d = 1.11$) and at T3 ($p < 0.05$; $d = 0.77$) and self-reported perceived change after treatment at T2 and T3 ($p < 0.001$). No serious adverse events were reported.
Conclusions: The application of a manual therapy protocol based on articulatory techniques reduced pain intensity, migraine disability, and medication intake, while improving quality of life in patients with migraine.

3. Introduction

Migraine is a primary headache that affects one in ten people worldwide with an upward trend (Woldeamanuel and Cowan, 2017), and is the leading cause of disability in the 15-49-year-old age group (Steiner et al., 2018; GBD 2016, 2017). Migraine has a significant individual impact on productivity, thus favoring both work and school absenteeism (Baigi and Stewart, 2015), not only due to the limitations associated with migraine symptoms, but also because of the possible side effects of the drugs used (Vicente-Herrero et al., 2013). As a result, migraine has a major impact on the patient's quality of life (QoL), and may become a public health problem with personal, work and economic implications (Leonardi and Raggi, 2019).

The most common treatment option is pharmacological, however, medication is sometimes ineffective or involves side effects (Becker et al., 2015; Capi et al., 2018). Indeed, excessive intake of medication is considered as a risk factor for chronic migraine (Xu et al., 2020; Schwedt, 2014). Therefore, non-pharmacological treatment may be a good option for some patients, considering that a number of processes such as stress (Pellegrino et al., 2018; Kelman, 2007), certain psychiatric comorbidities (Dresler et al., 2019) and musculoskeletal dysfunctions (Palacios-Ceña et al., 2017; Ferracini et al., 2017; Nahman-Averbuch et al., 2018; Szikszay et al., 2019) can contribute to the development of migraine, increase disability (Steiner et al., 2018; GBD 2016, 2017) and adversely affect quality of life (Abu Bakar et al., 2016).

Manual therapy may reduce pain intensity, frequency and duration

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of migraine episodes (Luedtke et al., 2016; Chaibi et al., 2011; Grant and Niere, 2000). In this regard, it has been proposed that articulatory techniques (i.e., those in which low velocity and moderate to high amplitude movements are employed to force joint's full range of motion) can contribute to improving the possible limitations of the range of motion of the affected joints and trigger systemic neurophysiological responses that lead to pain inhibition (Bialosky et al., 2009, 2018; Schmid et al., 2008; Voogt et al., 2015). Thus, it has been suggested that joint mobilization may reduce the intensity of pain (Gandolfi et al., 2018; Davidson et al., 2018; Chaibi et al., 2017) and the frequency of migraine (Davidson et al., 2018; Chaibi et al., 2017) up to six months after the intervention (Davidson et al., 2018; Chaibi et al., 2017), although given the variability in the quality of previous studies it is difficult to determine the magnitude of this effect (Rist et al., 2019). Furthermore, controversy exists over whether it is effective in migraine-associated disability compared to placebo interventions (Rist et al., 2019). A number of studies that have applied articulatory techniques combined with soft-tissue techniques have reported improvements in impact and functional disability after 24 weeks of intervention in patients with chronic migraine (Cerritelli et al., 2015), as well as on-the-job and household-associated disability after 10 weeks of intervention in patients with episodic migraine (Voigt et al., 2011); in contrast, others have achieved no significant effect on migraine-associated disability after four weeks of intervention and onabotulinum toxin A injection in patients with chronic migraine (Gandolfi et al., 2018). In addition, the effect of a treatment exclusively using articulatory spinal techniques has shown its effectiveness in disability and QoL associated with other primary headaches (Espí-López et al., 2014; Monzani et al., 2016). However, subjective perception of change after treatment in individuals with migraine has not been investigated to date.

The aim of this study was to compare the effectiveness of a manual therapy protocol based on articulatory techniques with a hands-on placebo intervention in pain intensity, frequency of episodes, migraine disability, physical, mental and overall QoL, medication intake and self-reported perceived change after treatment in individuals with migraine. We further aimed to assess whether the effects were maintained one month after the intervention.

4. Materials and methods

4.1. Participants

Fifty individuals diagnosed with migraine were recruited as a convenience sample from several primary care centers in Valencia (Spain) from June to July 2018. Individuals between 18 and 50 years of age diagnosed according the ICHD-3 criteria (Headache Classification Committee of the International Headache Society (IHS), 2018), with four or more episodes per month, and a migraine history of one or more years were included in the study; headache medication regimens should be stabilized for four weeks prior to enrolment. Exclusion criteria were: (i) patients with another type of primary or secondary headache, (ii) temporomandibular disorders, (iii) signs of vertebral artery or internal carotid artery commitment, (iv) spinal radiculopathy, (v) vertigo, (vi) decompensated blood pressure, (vii) pregnancy, or (vii) in the process of pharmacological adaptation. Participants could use symptomatic medication when required (Diener et al., 2019).

4.2. Study design

A randomized controlled trial was carried out (NCT03555214), from June to October 2018 at the University of Valencia. The sample was randomly divided into 2 groups: a) Articulatory group (AG) (n = 25), that received a manual therapy protocol based on articulatory techniques; and b) Placebo group (PG) (n = 25), who received a hands-on placebo intervention. Both treatments lasted 4 weeks and included 4 sessions (one per week). Patients were assessed before (T1), immediately after (T2), and at one-month follow-up after the intervention (T3).

All participants provided written informed consent, all procedures were conducted in accordance with the ethical standards of the Declaration of Helsinki and the protocols were approved by the Ethics Committee of the University of Valencia (H1509655117217).

4.2.1. Randomization, blinding and masking

An external investigator who was not involved in the assessment or treatment of the participants performed the randomized allocation by preparing sealed, sequentially numbered envelopes that contained the treatment assignments. The physiotherapist opened the lowest numbered envelope to reveal the patient's assignment just before the treatment was performed. Patients and statistician were blinded to the treatment allocation.

4.3. Interventions

All the participants underwent a careful clinical history (Chaibi and Russell, 2019) and pre-manipulative testing of the cervical spine (Côté et al., 1996) performed by the physiotherapist, to detect (and thus exclude) any possible cervical artery dissection. No participant was excluded due to this reason. All techniques were executed by the same experienced physiotherapist, who had over 7 years' experience in the application of manual therapy for headache patients and had received more than 5 years of postgraduate training. During each session, potential adverse effects or harms were recorded.

AG participants were applied all the defined articulatory techniques in all the potential restricted joints related to migraine (Chaibi et al., 2017). For that purpose, low velocity and moderate to high amplitude movements were conducted on the neck and upper-trunk joints and sacroiliac joints to force their full range of motion. Specifically, the following techniques were applied bilaterally in all treatment sessions (Dunning et al., 2016): occiput-atlas-axis articulatory manipulation, upper cervical spine (C0–C1) mobilization, middle cervical spine (C2–C7) mobilization in supine, middle cervical spine (C2–C7) mobilization in prone, cervicothoracic junction articulatory manipulation, upper thoracic spine (T2-T6) articulatory manipulation and global sacroiliac joint articulatory manipulation. These techniques are described in detail in Appendix A.

Regarding the PG, the physiotherapist performed a superficial hands-on placebo intervention by gently placing the palms of both hand under the occiput for 10 min. No force or movement was applied (Cardoso--de-Mello-E-Mello-Ribeiro et al., 2015).

4.4. Main outcome measures

Migraine disability was assessed by the Migraine Disability Assessment (MIDAS) questionnaire (Stewart et al., 1999), which is based on five questions about the number of days lost due to headaches in the last three months. Additionally, this questionnaire includes two questions related to pain intensity and frequency of the episodes. The between-group minimally important difference is a 5-point decrease (Buse et al., 2018). It is considered a valid (α de Cronbach = 0.73–0.76) and reliable instrument (r = 0.80). (Stewart et al., 2001).

Physical, mental, and overall QoL was assessed with the Short Form-36 Health Survey (SF-36) (Ware and Sherbourne, 1992), a 36-item instrument that assesses health-related QoL. The physical component of the SF-36 evaluates physical functioning, physical role functioning, bodily pain and general health perceptions, whereas its mental component assesses vitality, social role functioning, emotional role functioning and mental health. For each dimension, the items are given a code number, aggregated and transformed into a scale ranging from 0 to 100, with higher values indicating better health (Vilagut et al., 2005). Effects larger than 12% of baseline score can be detected as minimal clinically important difference (Perrot and Lantéri-Minet, 2019). The

questionnaire has shown to have good validity (Cronbach's α = 0.70–0.90) and reliability (ICC = 0.58–0.99). (Vilagut et al., 2005).

The amount of *symptomatic medication* was registered in a standardized migraine dairy, as number of pills per day (Gandolfi et al., 2018). The percentage of medication intake reduction was further calculated both at T2 and at T3.

Self-reported perceived change after treatment was assessed with the Patients' Global Impression of Change (PGIC) scale, which consists of a 7-point verbal scale, with the options "very much improved", "much improved", "minimally improved", "no change", "minimally worse", "much worse", "very much worse" (Angst et al., 2001; Dworkin et al., 2008). Clinically significant improvement is considered to be achieved when items "much improved" and "very much improved" are rated (Angst et al., 2001; Dworkin et al., 2008). The test-retest reliability of the global rating of change scales has been shown to be excellent (ICC = 0.90) (Kamper et al., 1999). This variable was recorded at T2 and T3.

4.5. Statistics

Statistical analyses were performed using SPSS v.24 (IBM SPSS, Inc., Chicago, IL, USA). The inferential analyses of the data were conducted using a two-factor mixed multivariate analysis of variance (MANOVA) having a between-subjects factor "treatment group" with two categories (AG and PG) and a within-subject factor "time measurements" with three categories (T1, T2 and T3) for all the variables except for medication intake, for which the mixed MANOVA included only two categories in the within-subject factor (T2 and T3). Post-hoc analyses were requested using the Bonferroni correction. We evaluated the assumption of homoscedasticity using Levene's test and the sphericity using Mauchly's test. A Chi-squared test was used to explore the relationship between the intervention (AG and PG) and the self-reported perceived change at each time measurement (T2 and T3). Additionally, we explored similarity between groups at baseline using the Independent Student's t-test for the continuous variables and a Chi-squared test for the categorical variables. The α level was set equal to or less than 0.05 for all tests. For the effect size of the continuous variables, Cohen's d was computed, whereby the effect size was rated as follows: small (0.20–0.50), medium (0.50–0.80), or large (>0.80) (Thalheimer and Cook, 2002). For the categorical variables, the effect size was reported with the contingency coefficient (CC).

4.5.1. Sample size calculation

For computing sample size, we considered that our study was composed of two groups and three measurements, and we set a power of 80% and an effect size of (d = 0.88) based on a previous study conducted by Espí-López et al. (2018), in which a similar approach was proposed. This generated a minimum sample size of 12 participants per group (a total of 24 participants). Nevertheless, we doubled the recruitment taking into consideration possible dropouts (i.e., 50 participants).

5. Results

5.1. Participants

Fifty participants were randomly allocated to the AG and the PG (25 participants in each group) and all of them completed the study (Fig. 1). The mean (standard deviation, SD) age of the participants was 38.5 (9.6) years. There were no significant differences between groups before the intervention in any variable (Table 1). No serious intervention-related side effects occurred.

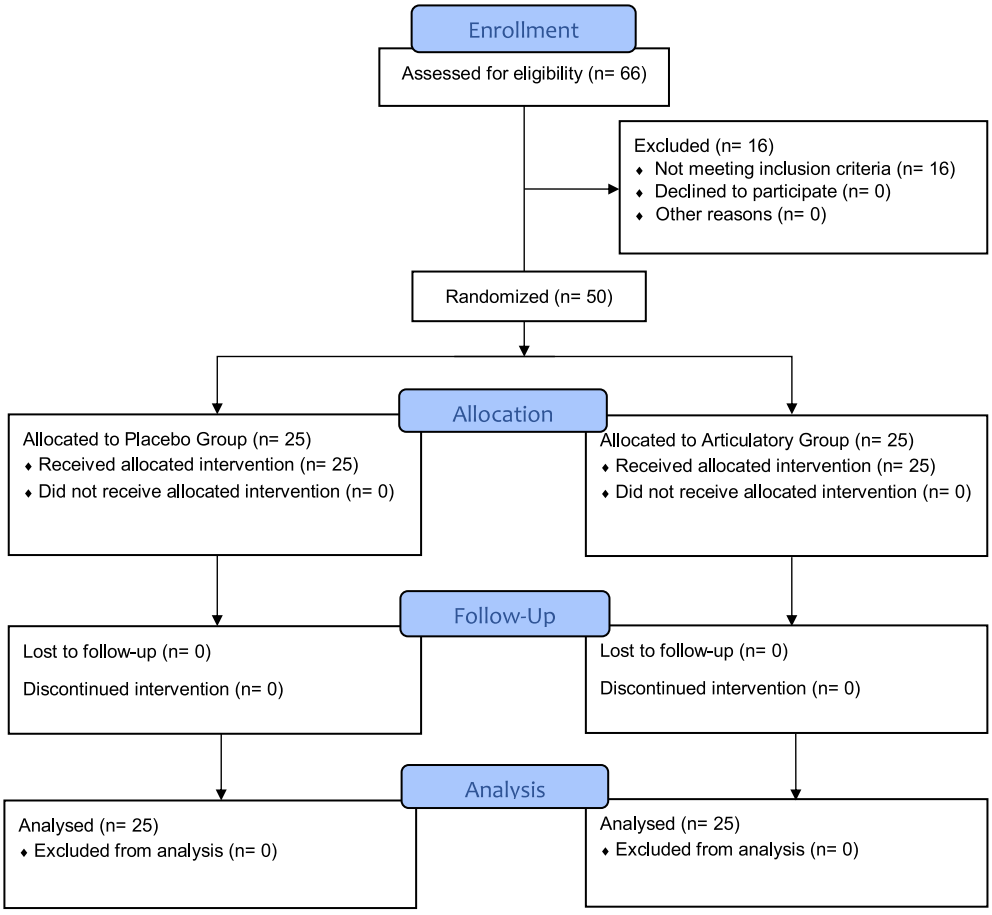

Fig. 1. Flowchart according to CONSORT Statement for the Report of randomized trials.

Table 1
Baseline demographic and headache characteristics.

Variables	PG (n = 25)	AG (n = 25)	p-value
Gender[a]			0.73
Female	20 (80)	19 (76)	
Male	5 (20)	6 (24)	
Migraine diagnose[a]			0.77
Episodic migraine	14 (56)	15 (60)	
Chronic migraine	11 (44)	10 (40)	
Family history[a]	17 (68)	18 (72)	0.76
Medication[a]			0.89
Preventive medication	2 (8)	3 (12)	
Symptomatic medication	22 (88)	21 (84)	
No medication	1 (4)	1 (4)	
Accompanying symptoms[a]			
Nausea/Vomiting	16 (64)	11 (44)	0.16
Aura	6 (24)	5 (20)	0.73
Photophobia	15 (60)	15 (60)	1.00
Phonophobia	10 (40)	12 (48)	0.57
Age[b]	37.6 (9.42)	39.1 (9.9)	0.95
Age of onset[b]	20.0 (10.7)	21.2 (10.3)	0.76
Period of evolution (years)[b]	17.7 (9.9)	17.9 (10.6)	0.57
Duration of the episodes (hours)[b]	22.2 (14.7)	23.2 (20.3)	0.08
Pain[b]	7.7 (1.0)	7.45 (1.3)	0.17

[a] Data shown as Absolute frequency (% relative frequency).
[b] Data shown as Mean (Standard deviation). PG: Placebo Group; AG: Articulatory Group.

5.2. General multivariate analysis results

MANOVA analysis showed a statistically significant interaction between factors "treatment groups" (AG and PG) and "time measurements" (T1, T2 and T3), Pillai's trace V = 0.8, F (22, 27) = 3.7, p = 0.001, $\eta^2 = 0.8$.

5.3. Effect of the treatment on intensity, frequency of the episodes, and migraine disability

There was a significant interaction between the two factors (i.e., treatment groups and time measurements) in pain intensity F (2, 96) = 12.2, p < 0.001, $\eta^2p = 0.2$, frequency of the episodes F (1.2, 58.3) = 13.3, p < 0.001, $\eta^2p = 0.2$, and migraine disability F (1.1, 52.8) = 32.9, p < 0.001, $\eta^2p = 0.4$.

There were significant intra-group mean differences [95% confidence interval] in AG in pain intensity, with a large effect size, at T1-T2 (1.0 [0.6 to 1.4]) and at T1-T3 (0.9 [0.5 to 1.3]); in frequency of the episodes, with a small size effect, at T1-T2 (2.8 [1.7 to 4.0]) and T1-T3 (4.2 [2.6 to 5.8]); and in migraine disability, with a small-medium effect size, at T1-T2 (4.5 [3.0 to 5.9]) and T1-T3 (10.4 [7.2 to 13.5]). There were no significant intra-group differences in PG in any of the variables (p ≥ 0.05).

In addition, the *post hoc* analysis revealed significant inter-group mean differences [95% CI] between AG and PG in pain intensity, with a large effect size at T2 (1.2 [0.6 to 1.9]) and at T3 (1.1 [0.6 to 1.7]); and in migraine disability, with a medium effect size at T3 (10.0 [1.8 to 18.2]). Table 2 shows the results of pairwise comparisons when the effect of the treatment was analyzed in each group.

5.4. Effect of the treatment on quality of life

There was a significant interaction between the two factors (i.e., treatment groups and time measurements) in Physical QoL F (2, 96) = 3.2, p < 0.05, $\eta^2p = 0.1$, and Overall QoL F (2, 96) = 3.8, p < 0.05, $\eta^2p = 0.1$; but not in Mental QoL (p ≥ 0.05).

As noted in Table 2, there were significant intra-group mean differences [95%CI] in AG in the scores for the variable Physical QoL at T1-T2 (−14.5 [-23.8 to −5.1]) and T1-T3 (−14.4 [-22.4 to −6.4]); Mental QoL at T1-T2 (−14.4 [-22.7 to −6.1]) and T1-T3 (−13.3 [-21.5 to −5.0]); Overall QoL at T1-T2 (−14.4 [-22.1 to −6.8]) and T1-T3 (−13.8 [-20.8 to −6.9]). Table 3 shows the results for SF-36 sub-scales. There were no significant intra-group differences in PG in any of the SF-36 questionnaire scores.

Regarding the differences between groups, there were significant inter-group mean differences [95% CI] in AG in the scores for the variables Physical QoL (−11.9 [-21.6 to −2.2]) and Overall QoL (−9.3

Table 2
Effect of the treatment on MIDAS and SF-36 scores (main variables) by time and group.

		Mean (Standard deviation)			Measurement times comparison Mean Difference (95%CI); Effect size (Cohen's d)		Groups comparison Mean Difference (95%CI); Effect size (Cohen's d)	
Variable	Group	T1	T2 (Week 4)	T3 (Week 8)	T1-T2	T1-T3	T2 (week 4)	T3 (Week 8)
Intensity (MIDAS)	PG	7.6 (0.8)	7.9 (1.1)	7.6 (0.9)	−0.1 (−0.5 to 0.3)	−0.02 (−0.4 to 0.4)	1.2 (0.6–1.9)***; d = 1.2	1.1 (0.6–1.7)***; d = 1.1
	AG	7.4 (1.1)	6.4 (1.0)	6.5 (1.0)	1.0 (0.6–1.4)***; d = 0.9	0.9 (0.5–1.3)***; d = 0.8		
Frequency of the episodes (MIDAS)	PG	24.0 (10.8)	23.2 (8.9)	23.4 (8.6)	0.9 (−0.3 to 2.0)	0.6 (−1.0 to 2.2)	1.2 (−4.5 to 6.8)	2.8 (−2.6 to 8.2)
	AG	24.8 (12.3)	22.0 (10.9)	20.6 (10.3)	2.8 (1.7–4.0)***; d = 0.3	4.2 (2.6–5.8)***; d = 0.4		
Migraine disability (MIDAS)	PG	34.1 (14.4)	33.9 (13.9)	34.3 (14.6)	0.2 (−1.2 to 1.7)	−0.2 (−3.3 to 3.0)	3.7 (−5.5 to 12.9)	10.0 (1.8–18.2)*; d = 0.7
	AG	34.6 (20.2)	30.2 (18.1)	24.3 (14.2)	4.5 (3.0–5.9)***; d = 0.2	10.4 (7.2–13.5)***; d = 0.6		
Physical QoL (SF-36)	PG	52.4 (14.2)	54.8 (20.2)	55.7 (17.2)	−2.4 (−11.8 to 6.9)	−3.4 (−11.4 to 4.6)	−11.9 (−21.6 to −2.2)*; d = 0.7	−10.9 (−22.0 to 0.2)
	AG	52.3 (20.7)	66.7 (13.1)	66.6 (21.6)	−14.5 (−23.8 to −5.1)**; d = 0.9	−14.4 (−22.4 to −6.4)***; d = 0.7		
Mental QoL (SF-36)	PG	55.9 (16.5)	60.5 (15.1)	60.8 (17.1)	−4.6 (−12.9 to 3.8)	−4.9 (−13.1 to 3.4)	−6.6 (−16.2 to 3.0)	−5.1 (−16.8 to 6.5)
	AG	52.7 (26.0)	67.1 (18.4)	65.9 (23.3)	−14.4 (−22.7 to −6.1)***; d = 0.7	−13.3 (−21.5 to −5.0)**; d = 0.5		
Overall QoL (SF-36)	PG	54.2 (12.1)	57.7 (15.8)	58.3 (14.9)	−3.5 (−11.1 to 4.1)	−4.1 (−11.0 to 2.8)	−9.3 (−18.0 to −0.5)*; d = 0.6	−8.0 (−18.4 to 2.4)
	AG	52.5 (21.6)	66.9 (15.0)	66.3 (21.1)	−14.4 (−22.1 to −6.8)***; d = 0.8	−13.8 (−20.8 to −6.9)***; d = 0.7		

CI indicates confidence interval; PG: placebo control group; AG: articulatory group. MIDAS: Migraine Disability Assessment. QoL: Quality of Life. T1: Pre-treatment; T2: Post-treatment: T3: Follow-up; *: p < 0.05; **: p < 0.01; ***: p < 0.001; d: Cohen's effect size (only for the significant comparisons).

Table 3
Effect of the treatment on the SF-36 scores (sub-dimensions) by time and group.

		Mean (Standard deviation)			Measurement times comparison Mean Difference (95%CI); Effect size (Cohen's d)		Groups comparison Mean Difference (95%CI); Effect size (Cohen's d)	
Variable	Group	T1	T2 (Week 4)	T3 (Week 8)	T1-T2	T1-T3	T2 (week 4)	T3 (Week 8)
Physical Functioning	PG	76.0 (13.5)	76.6 (23.2)	79.2 (18.5)	−0.6 (−9.9 to 8.7)	−3.2 (−11.1 to 4.8)	−6.0 (−18.1 to 6.1)	−3.1 (−13.8 to 7.7)
	AG	76.8 (24.5)	82.6 (19.1)	82.2 (19.4)	−5.8 (−15.1 to 3.5)	−5.4 (−13.4 to 2.6)		
Physical role functioning	PG	28.9 (28.6)	32.9 (41.3)	33.5 (40.1)	−4.0 (−24.1 to 16.1)	−4.6 (−25.6 to 16.4)	−22.1 (−40.4 to −3.8)*; d = 0.7	−24.5 (−46.2 to −2.9)*; d = 0.6
	AG	29.0 (31.2)	55.0 (19.1)	58.0 (35.9)	−26.0 (−46.1 to −5.9)**; d = 1.0	−29.0 (−50.0 to −8.1)**; d = 0.9		
Bodily pain	PG	49.2 (25.2)	49.3 (19.8)	50.2 (20.1)	−0.1 (−14.1 to 13.9)	−1.0 (−11.5 to 9.5)	−13.6 (−23.9 to −3.3)**; d = 0.8	−10.1 (−24.1 to 3.9)
	AG	48.6 (26.3)	62.9 (16.2)	60.3 (28.3)	−14.3 (−28.3 to −0.3)*; d = 0.7	−11.7 (−22.2 to −1.2)*; d = 0.4		
General health perception	PG	55.4 (23.6)	60.4 (23.2)	60.1 (24.6)	−5.0 (−18.1 to 8.1)	−4.7 (−10.32 to 0.9)	−6.0 (−17.0 to 5.0)	−5.9 (−18.2 to 6.4)
	AG	54.6 (21.5)	66.4 (14.3)	66.0 (18.3)	−11.8 (−24.9 to 1.3)	−11.4 (−17.0 to −5.8)***; d = 0.6		
Vitality	PG	48.4 (15.4)	51.6 (15.3)	52.8 (15.0)	−3.2 (−13.6 to 7.2)	−4.4 (−12.9 to 4.1)	−4.8 (−13.7 to 4.1)	−4.0 (−14.4 to 6.4)
	AG	47.0 (25.3)	56.4 (16.0)	56.8 (21.1)	−9.4 (−19.8 to 1.0)	−9.8 (−18.3 to −1.3)*; d = 0.4		
Social role functioning	PG	62.9 (16.9)	68.0 (18.1)	66.8 (21.5)	−5.1 (−15.1 to 4.9)	−3.9 (−12.9 to 5.1)	−3.5 (−15.6 to 8.7)	−3.8 (−17.3 to 9.7)
	AG	61.9 (32.61	71.5 (24.1)	70.6 (25.9)	−9.6 (−19.6 to 0.4)	−8.7 (−17.7 to 0.2)		
Emotional role functioning	PG	53.3 (46.2)	62.1 (33.0)	62.7 (38.9)	−8.8 (−28.8 to 11.2)	−9.3 (−28.7 to 10.1)	−15.2 (−32.7 to 2.3)	−8.0 (−29.8 to 13.8)
	AG	46.7 (46.2)	77.3 (28.4)	70.7 (37.7)	−30.7 (−50.7 to −10.6)**; d = 0.8	−24.0 (−43.4 to −4.6)*; d = 0.6		
Mental health	PG	59.1 (14.0)	60.2 (14.5)	60.8 (15.0)	−1.1 (−9.7 to 7.5)	−1.8 (−10.8 to 7.3)	−2.8 (−13.1 to 7.5)	−4.8 (−16.1 to 6.6)
	AG	55.1 (25.9)	63.0 (21.1)	65.6 (23.8)	−7.9 (−16.5 to 0.7)	−10.5 (−19.5 to −1.4)*; d = 0.4		

CI indicates confidence interval; PG: placebo control group; AG: articulatory group. SF-36: Short Form-36 Health Survey. QoL: Quality of Life. T1: Pre-treatment; T2: Post-treatment: T3: Follow-up; *: $p < 0.05$; **: $p < 0.01$; ***: $p < 0.001$; d: Cohen's effect size (only for the significant comparisons).

[-18.0 to −0.5]) at T2, with a medium effect size.

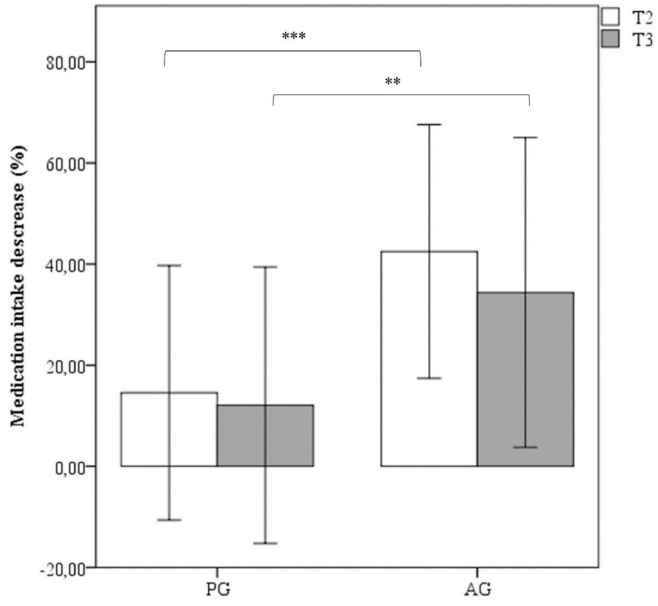

Fig. 2. Bars represent mean and standard deviation of the percentage of decrease in medication intake in the two groups at T2 and T3, and comparisons between groups. PG: placebo control group; AG: articulatory group; T2: Post-treatment; T3: Follow-up; **: $p < 0.01$; ***: $p < 0.001$.

5.4.1. *Effect of the treatment on medication intake*

Fig. 2 shows that the percentage of decrease in medication intake was greater in the AG (42.5%) than in the PG (14.5%) at T2 $t(46) = 3.9$, $p < 0.001$, $d = 1.1$, with a large effect size, and at T3 (34.4% and 12.1%, respectively) $t(46) = 2.7$, $p < 0.05$, $d = 0.8$, with a moderate effect size. There were no differences between T2 compared to T3 in either group ($p \geq 0.05$).

5.5. *Perceived change after treatment*

There was a significant relationship between the scale categories and the groups at both T2, χ^2 (Steiner et al., 2018)(4) = 18.7, p = 0.001, CC = 0.5, and T3, χ (Steiner et al., 2018)(3) = 24.5, $p < 0.001$, CC = 0.6. There were no differences between T2 compared to T3 in either group ($p \geq 0.05$). As shown in Fig. 3A, at T2, 60% of the PG felt no change, while 84% of the AG felt minimally or much improved. At T3 (Figs. 3B), 80% of the PG felt no change, while 76% of the AG felt minimally or much improved.

6. Discussion

The present protocol based on articulatory techniques was effective in reducing pain intensity, migraine disability and medication intake, while improving physical QoL and self-reported perceived change after treatment; these changes were maintained after one month. Furthermore, significant differences were observed in terms of frequency of episodes and mental QoL at T2 and T3 compared to the placebo intervention. To date, to the best of our knowledge, this is the first study to evaluate the therapeutic effect of articulatory techniques on QoL and

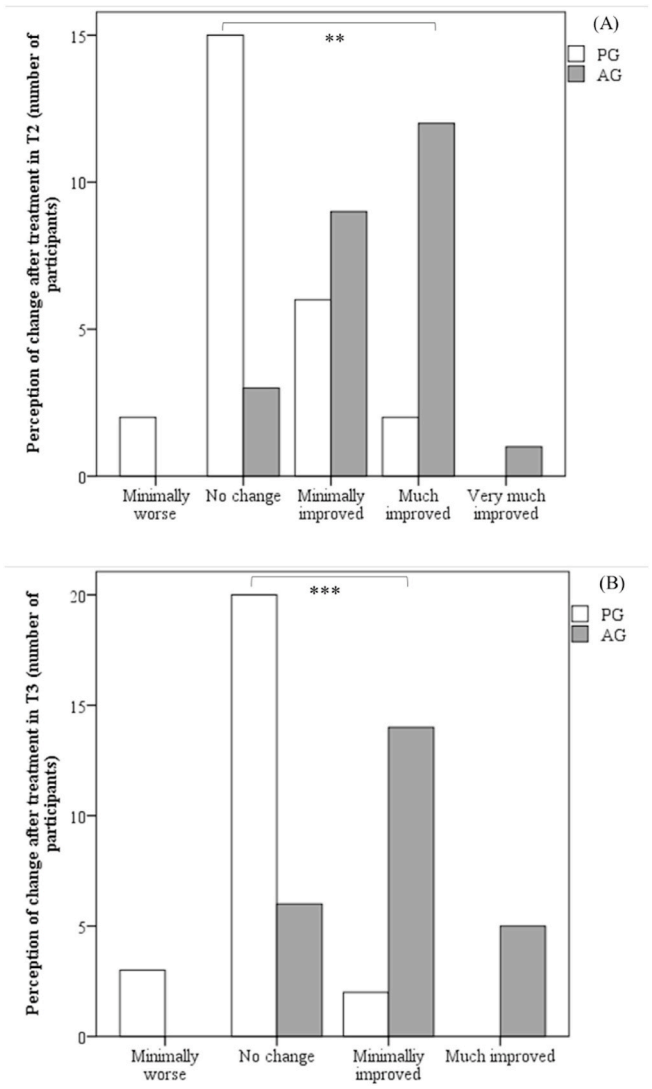

Fig. 3. Number of participants rating each category of the PGIC scale at T2 (A) and T3 (B). PGIC= Patients' Global Impression of Change; PG: placebo group; AG: articulatory group; T2: Post-treatment; T3: Follow-up; **: $p < 0.01$; ***: $p < 0.001$.

perceived change after treatment in patients with migraine, these being essential aspects associated with this pathology (Diener et al., 2019; Falsiroli-Maistrello et al., 2019).

Our results showed that pain intensity was reduced in AG individuals by 13.0% at T2 and 11.9% at T3. This could be because the joint mobilization techniques used in the AG may trigger systemic neurophysiological responses in the peripheral and central nervous system that lead to pain inhibition (Bialosky et al., 2009, 2018; Schmid et al., 2008; Voogt et al., 2015). In this regard, our results are consistent with a previous study showing that the mobilization of cervical segments C0 – C3 improved the intensity of migraine pain after one, three and six months following intervention, although without significant differences with respect the control group (Davidson et al., 2018). The difference in study results may be explained by the treatment protocol applied in the present study which targets several regions of the spinal column that may be involved in patients with migraine (von Piekartz et al., 2007).

Regarding the frequency of episodes, the AG intervention improved this variable, with a reduction of 11.4% at T2 and 16.9% at T3. Even greater changes were observed in a study that applied a 3-month treatment based on articulatory techniques (40% after treatment, 30.8% at one-month follow-up, 36.9% after six months, and 32.3% after 12 months) (Chaibi et al., 2017). These results suggest that a longer intervention could be more effective in reducing the frequency. However, it is interesting to evaluate the effectiveness of short-term treatments, such as the one proposed in this article, related to this variable, since long treatments may lead to a higher probability of drop-outs (Jack et al., 2010). In fact, a study that assessed the feasibility of mobilization of cervical segments C0 – C3 to reduce headache in migraine sufferers during four weeks (Davidson et al., 2018) obtained a 25.8% decrease in the frequency, a slightly larger change than ours, which may be explained by the greater number of sessions, namely, six instead of four.

In terms of migraine disability, this improved in the AG both at T2 (12.9%) and at T3 (29.9%), while improvements were significant compared to the PG at T3. Furthermore, the between-group minimally important difference was achieved at T2 and T3 (Buse et al., 2018). This result is important considering that migraine causes disability in those affected (GBD 2016, 2017; Baigi and Stewart, 2015). However, the possible effects of manual therapy based on articulatory techniques on this variable have been scarcely studied among these patients. A previous study observed that a manual therapy treatment using soft tissue and articulatory techniques in the cervical region was effective in reducing disability in patients with chronic migraine and associated temporomandibular disorders (7.1%), the results being maintained six and twelve weeks (13.1% and 20.9% respectively) after the intervention (Garrigós-Pedrón et al., 2018). However, such results are not entirely comparable to ours, as headaches associated with temporomandibular disorders may develop and respond to therapies differently (Headache Classification Committee of the International Headache Society (IHS), 2018).

Primary headaches have a negative impact on QoL (Abu Bakar et al., 2016), and manual therapy is considered an effective approach to improve QoL in patients with migraine (Falsiroli-Maistrello et al., 2019). However, this is the first study to evaluate the influence of a protocol based solely on articulatory techniques in these patients. The results point to an improvement in the physical, mental and overall QoL of 27.7%, 27.3% and 27.5 respectively at T2, and 27.5%, 25.1% and 26.3%, respectively at T3, achieving clinically important difference (Perrot and Lantéri-Minet, 2019), which could be partly explained by the reduced pain intensity and frequency (Wang et al., 2001). It is not surprising that the physical component improved to a greater extent than the mental factor, since patients with migraine tend to suffer associated mood disorders (Dresler et al., 2019; Seng and Seng, 2016). Voigt et al. (2011) evaluated the efficacy of a ten-week manual therapy program in patients with migraine, and similar results were reported for the physical component (22.3%), while a poorer outcome was noted for the mental component (16.8%). However, they did not have a placebo group, so the improvements could not be directly attributed to the intervention (Diener et al., 2019).

Another study applied manual therapy combined with therapeutic exercise in patients with primary headaches and obtained better results than those of the present study (43.9% in the physical QoL and 27.6% in the mental QoL after the intervention, and 42.6% and 21.0% respectively, after nine months follow-up) (Uthaikhup et al., 1016). However, such study was not migraine-specific and the evidence suggests that QoL differs among headache diagnoses (Wang et al., 2001). On the other hand, physical exercise may be contraindicated in some patients (Headache Classification Committee of the International Headache Society (IHS), 2018), so the results of this study showing that patients improve the physical sphere only through manual therapy are extremely interesting.

A significant improvement in medication intake at T2 (42.5%) and T3 (34.4%) was also observed in AG compared to PG, which is essential due to the well-documented side effects of the medication (Becker et al., 2015; Capi et al., 2018), as well as its influence on the chronification of migraine (Xu et al., 2020). Gandolfi et al. (2018) observed that manual therapy treatment with mobilization techniques of the cervical and thoracic joints together with myofascial therapy was effective for

reducing by 28.9% the consumption of symptomatic relief medication. However, a study including lumbosacral techniques achieved even greater improvements (approximately 50%) (Chaibi et al., 2017) similar to ours, which may suggest that combining cervicothoracic and lumbosacral techniques could be more effective in reducing medication intake.

In connection with perceived change after treatment, 52% of AG participants felt that they had much improved or very much improved after the treatment and 20% maintained this improvement at T3, i.e., a clinically significant improvement was achieved for this variable (Angst et al., 2001; Dworkin et al., 2008). Despite its importance in clinical trials on migraine (Diener et al., 2019), this variable has not been evaluated in previous studies addressing manual therapy based on articulatory techniques in migraine, therefore the study results cannot be compared with those attained by other authors.

However, this study has some limitations. Most participants were women, although this seems reasonable since migraine is twice as prevalent in women than in men (Woldeamanuel and Cowan, 2017). Also, given the variety of techniques used, the improvement cannot be entirely attributed to just one of them.

7. Conclusions

A manual therapy protocol based on articulatory techniques reduces pain intensity, frequency of migraine, migraine disability, and medication intake, while improving QoL in patients with migraine. Furthermore, the results were maintained after one month.

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Clinical trial registration number

NCT03555214

Declaration of competing interest

The authors declare they do not have any potential conflict of interest with regard to the investigation, authorship, and/or publication of this article.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.msksp.2021.102386.

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