Effects of a Physical Therapy Protocol in Patients with Chronic Migraine and Temporomandibular Disorders: A Randomized, Single-Blinded, Clinical Trial

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Aims: To investigate the effects of adding orofacial treatment to cervical physical therapy in patients with chronic migraine and temporomandibular disorders (TMD). **Methods:** A total of 45 participants with chronic migraine and TMD aged 18 to 65 years were randomized into two groups: a cervical group (CG) and a cervical and orofacial group (COG). Both groups continued their medication regimens for migraine treatment and received physical therapy. The CG received physical therapy only in the cervical region, and the COG received physical therapy in both the cervical and orofacial regions. Both groups received six sessions of treatment that consisted of manual therapy and therapeutic exercise in the cervical region or the cervical and orofacial regions. Scores on the Craniofacial Pain and Disability Inventory (CF-PDI) and the Headache Impact Test (HIT-6) were primary outcome variables, and the secondary outcome variables were scores on the Tampa Scale for Kinesiophobia (TSK-11), pain intensity measured on a visual analog scale (VAS), pressure pain thresholds (PPTs) in the temporal, masseter (2 points, M1 and M2) and extratrigeminal (wrist) regions, and maximal mouth opening (MMO). Data were recorded at baseline, posttreatment, and after 12 weeks of follow-up. The α level was set at .05 for all tests and two-way repeated-measures analysis of variance (ANOVA) for within- and between-group interactions. **Results:** There were 22 CG participants (13.6% men and 86.4% women) and 23 COG participants (13% men and 87% women). The ANOVA analysis revealed statistically significant differences for group $\times$ time interaction in CF-PDI, HIT-6 in the last follow-up, pain intensity, PPTs in the trigeminal region, and MMO ($P < .05$), with a medium-large magnitude of effect. No statistically significant differences were found in the PPTs of the extratrigeminal region or in the TSK-11 ($P > .05$). **Conclusion:** Both groups reported a significant improvement in CF-PDI, HIT-6, and pain intensity. Cervical and orofacial treatment was more effective than cervical treatment alone for increasing PPTs in the trigeminal region and producing pain-free MMO. Physical therapy alone was not effective for increasing the PPTs in the extratrigeminal region (wrist) or decreasing the level of TSK-11. *J Oral Facial Pain Headache 2018;32:137–150. doi: 10.11607/ofph.1912*

Keywords: *manual therapy, migraine, physical therapy, temporomandibular disorders, therapeutic exercise*

Temporomandibular disorders (TMD) and chronic migraine are common and important public health care concerns.[1–5] Patients presenting both disorders have reduced health-related quality of life (HRQoL) and severe disabilities that result in a significant economic burden and affect not only the individuals, but also their families and society.[6,7]

The association between migraine and TMD has been demonstrated in various studies.[8,9] These disorders present similar signs, symptoms, and pain mechanisms, including cutaneous allodynia and the sensitization of neurons in the trigeminocervical complex.[9–14] Previous studies have demonstrated that TMD is a risk factor for increased headache frequency and migraine chronification.[8,15] It has been suggested that these conditions are separate problems that might aggravate or sustain each other.[16]

Treatment of migraine can be more complicated when the patients present with comorbidities compared to those who do not. In clinical

practice, when migraine and TMD occur in the same person, each disorder is treated separately. In a recent study in women with migraine and TMD, the migraine improved when the two conditions were treated with medication and a stabilization splint. Additionally, better results were obtained when combined therapy was applied, which was better than pharmacologic treatment only, stabilization splints only, or placebo treatment.[17]

Physical therapy addressing the cervical region has demonstrated beneficial effects for patients with migraine. Several reviews of manual therapy for migraine have suggested that combined modalities of physical therapy—such as massage, myofascial release, trigger point treatment, stretching, mobilization, and manipulation techniques—provide significant improvements in headache intensity and frequency.[18–21] Therapeutic exercise has also been demonstrated to be beneficial for patients with migraine, given it results in reduction of pain intensity and frequency, drug use, and improvement of HRQoL.[22]

Manual therapy and therapeutic exercises in patients with TMD result in decreased pain and increased pain-free maximal mouth opening (MMO).[23–25] A previous study showed that manual therapy and therapeutic exercise in the cervical region in patients with myofascial TMD resulted in reduced facial pain, increased pressure pain thresholds (PPTs) in the masticatory muscle, and increased pain-free MMO.[26]

It has been suggested that if TMD can influence headache, TMD treatment could be used to help reduce headache.[27,28] In various studies, physical therapy in the cervical and orofacial regions decreased headache intensity in patients presenting both cervicogenic headache and TMD when compared to a control group that received only treatment in the cervical region.[27,28] There is a lack of information on manual therapy and therapeutic exercise on the combined orofacial and cervical regions for management of migraine and TMD; thus, it is important to evaluate the effects of physical therapy in these regions in patients with chronic migraine and TMD. Therefore, the aim of this study was to investigate the effects of adding orofacial treatment to cervical physical therapy in patients with chronic migraine and TMD.

Materials and Methods

Participants

The participants were recruited between July 2015 and March 2016 after specialized headache consultations in the Neurology Department of the Hospital Universitario Miguel Servet (HUMS). The inclusion criteria consisted of three main parameters: *(1)* diagnosis of chronic migraine by a neurologist specialized in headaches and based on the criteria of the International Classification Headache Disorders-III of the International Headache Society;[29] *(2)* age between 18 and 65 years; and *(3)* presence of myofascial TMD according to the Research Diagnostic Criteria for TMD (RDC/TMD).[11]

Participants were excluded if they presented with any of the following conditions: TMD due to disc displacement, osteoarthritis, or inflammatory arthritis of the temporomandibular joint (TMJ); other chronic diseases (respiratory, cardiovascular, and musculoskeletal disorders such as chronic polyarthritis, rheumatic muscular inflammation, osteoporosis, and osteoarthritis); other headaches, neurologic diseases, or dental problems; cognitive, emotional, or psychological disturbances; previous surgery or trauma in the orofacial region; and orthodontic or physical therapy treatment in the last 6 months. The intended sample size was 52 participants; however, the final sample was 45, as 7 participants were lost to the study for different reasons.

After consenting, the participants were randomized using a randomized computer program (randomization.com), grouped according to age and sex, and assigned by a study member who was not involved in the participant's assessment or treatment to either the cervical group (CG) or the cervical and orofacial group (COG). The assessor was blinded to the subject's group assignments, and the participants were asked not to make any comments about their treatment.

Study Design

The study was conducted as a randomized clinical trial. The sample consisted of two groups of participants diagnosed with chronic migraine and myofascial TMD. The CG received treatment only in the cervical region, and the COG received treatment in both the cervical and orofacial regions. All the procedures used in the study followed the ethical guidelines of the Declaration of Helsinki and were approved by the local ethics committee of the HUMS in Zaragoza, Spain, and Ethics Committee for Clinical Research of Aragon, Spain (approval date 18/02/2015). The study adhered to the CONSORT statement. All the participants provided written informed consent. The study is registered in ClinicalTrials.gov with the identifier: NCT02627014.

Interventions

Both groups received a total of six sessions of treatments delivered within a 3- to 6-week period. The duration of each treatment session was 30 minutes. The parameters for session distribution and the duration of each treatment session were in accordance with other studies.[27,28,30] Both groups had a similar

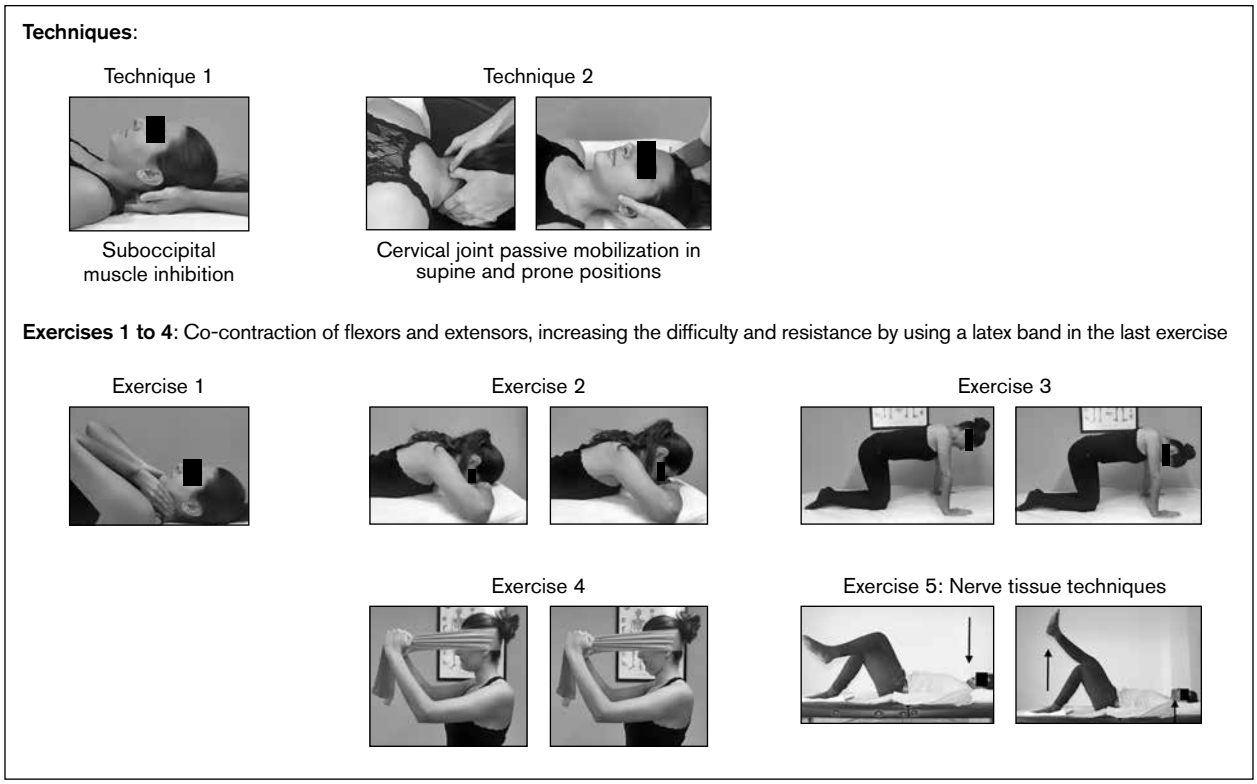

Fig 1 Techniques and exercises used in the cervical group.

distribution of treatment intervals. The treatment techniques were applied by the same physiotherapist (P.N.D.), who had more than 3 years of clinical experience in craniofacial techniques. This physiotherapist also received specific training for the study treatment. All the participants received a handout with exercises to be performed daily, which were explained in detail with images and a series of self-care techniques.

CG Intervention

Participants in the CG received treatment only in the cervical region.[28] In these sessions, participants were taught how to perform each exercise, and all the details of the training program were explained (sets, repetitions, rest periods, frequency, and common mistakes for each of the exercises). Treatment in this group combined manual therapy and both therapeutic and home exercises. Treatment consisted of several techniques, shown in Fig 1: *(1)* suboccipital muscle inhibition (Technique 1); *(2)* cervical joint passive mobilization in supine and prone positions (Technique 2); *(3)* co-contraction of flexors and extensors, increasing the difficulty and resistance by using a latex band (Thera-Band, Resistive Exercise Systems; Hygenic Corporation) (Exercises 1–4);[31] and *(4)* nerve tissue techniques (Exercise 5). Participants performed three sets of 10 repetitions for each exercise. In addition, these participants received self-care tips: *(1)* be aware of the position of the head during the day; *(2)* avoid working with the head tilted; and *(3)* maintain good cervical ergonomics. Exercises to be performed at home were explained and practiced in consultation with the physiotherapist and performed once a day for 5 days per week.

COG Intervention

Participants in this group underwent cervical treatment and also received an additional intervention in the orofacial region.[27,28] Participants were taught each exercise, and all the details of the training program were explained (sets, repetitions, rest periods, frequency, and common mistakes). The additional treatment included several techniques, shown in Fig 2: *(1)* longitudinal caudal bilateral technique in the TMJ (Technique 1);[32] *(2)* neuromuscular technique in the masseter and frontal muscles (Techniques 2 and 3);[33] and *(3)* coordination exercise of the masticatory muscles, increasing the difficulty and resistance (Exercises 1A–1E) with nerve tissue techniques (Exercise 2).[23] Participants performed three sets of 10 repetitions for each exercise. In addition, these participants received several self-care tips: *(1)* avoid eating hard foods; *(2)* avoid maximum mouth opening; *(3)* no chewing gum; *(4)* no sleeping

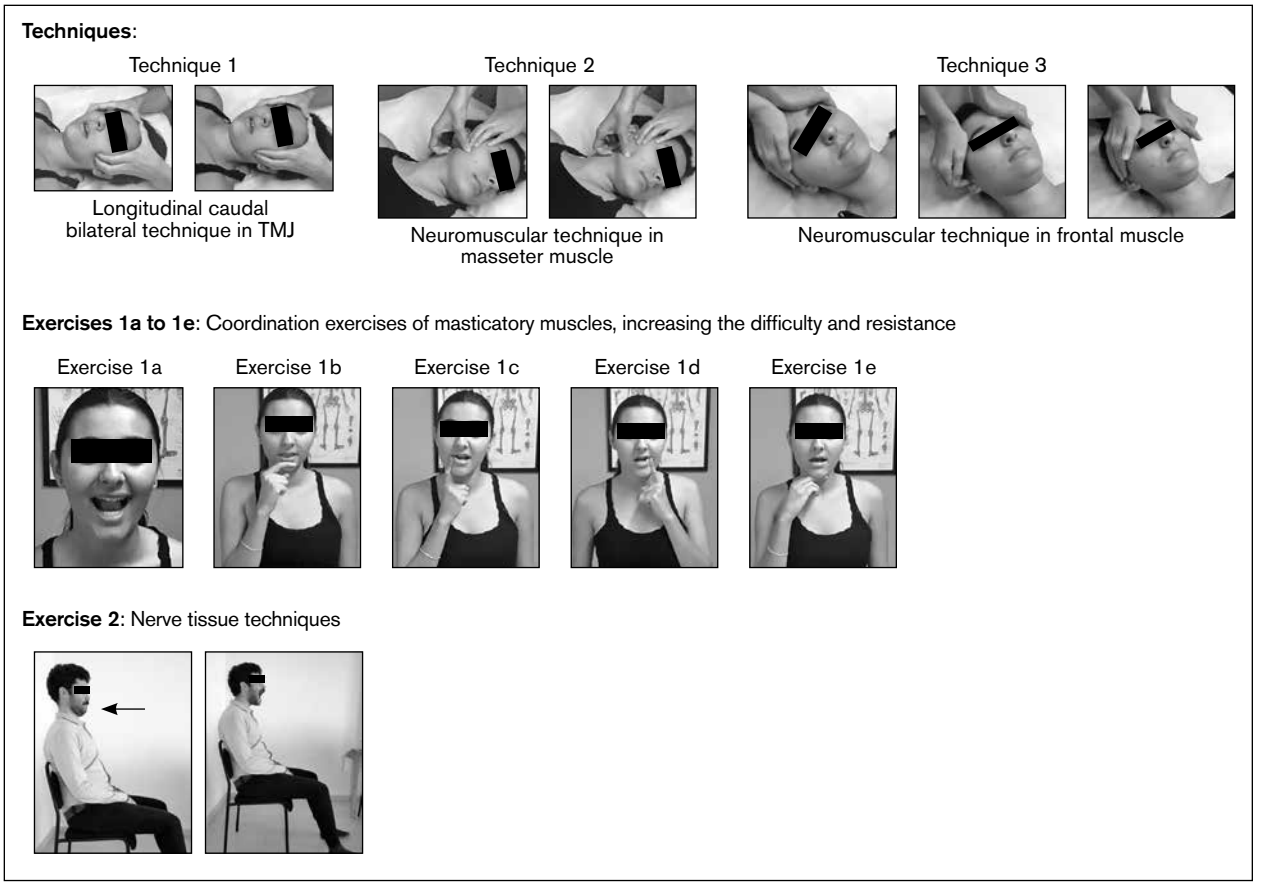

Fig 2 Techniques and exercises that were added to the cervical and were utilized in the cervical and orofacial group.
TMJ = temporomandibular joint.

on the affected side; *(5)* yawning with the tongue in the upper incisors; and *(6)* keep the tongue in the upper incisors. Home exercises were explained and practiced in consultation with the physiotherapist and performed once a day for 5 days per week.

Procedure

During the study period, both groups continued their medication regimens in accordance with previous studies.[20] For ethical reasons, the participants could not be withdrawn from pharmacologic treatment during the study. All had a similar intake of routine medication consisting of continuous preventive treatment and abortive pharmacologic treatment at the onset of migraine attacks prescribed by a headache specialist neurologist. Medication intake was equivalent in both groups.

A blinded investigator performed four assessments of all measurements, which included baseline (pretreatment), posttreatment, 6 weeks after the final treatment (follow-up 1), and 12 weeks after the final treatment (follow-up 2).

On assessment days, participants completed several questionnaires. These included various self-reports for pain-related variables. The baseline measures included a sociodemographic questionnaire that collected information regarding age, sex, height, weight, duration of the pain, educational level, and work status. Data on pain-related disability in the craniomandibular and facial regions were collected using the Craniofacial Pain and Disability Inventory (CF-PDI).[34] The impact and severity of headache were quantified using the Spanish version of the Headache Impact Test (HIT-6),[35,36] and the Spanish version of the Tampa Scale for Kinesiophobia (TSK-11) was used to assess the fear of pain and movement.[37]

Once the participants had completed all self-reports, the assessor proceeded to evaluate pain intensity with a visual analog scale (VAS), as well as PPTs and pain-free MMO. PPTs were measured bilaterally over the trigeminal region with the stimulus applied to the skin overlying the masseter and temporalis muscles and over the extratrigeminal region (wrist).

Primary Outcomes

The CF-PDI was used to assess pain, disability, and functional status of the mandibular and craniofacial regions. This self-administered questionnaire is an objective tool for assessing pain and disability

in patients with craniofacial pain and consists of 21 items that indicate increasing levels of pain and disability in the craniofacial region, with a possible overall score ranging from 0 to 63.[34]

The Spanish version of the HIT-6 was used to assess the impact and severity of headache on the patient's life.[35,36] This questionnaire consists of six items that assess headaches' interference with daily life and has demonstrated acceptable psychometric properties.[38] Furthermore, this instrument has been validated for patients with chronic migraine.[39] The total score can range from 36 to 78, and the results are stratified into four impact grades: *(1)* little or no impact (HIT-6 score 36–49); *(2)* moderate impact (HIT-6 score 50–55); *(3)* important impact (HIT-6 score 56–59); and *(4)* severe impact (HIT-6 score 60–78). The minimally important difference in the HIT-6 scores in patients with chronic daily headache was estimated to be between 2.3 and 2.7.[40,41]

Secondary Outcomes

The Spanish version of the TSK-11 was used to assess fear of reinjury due to movement. This questionnaire has an 11-item, 2-factor structure that includes activity avoidance and harm and demonstration of acceptable psychometric properties.[37] The total score can range from 11 to 44 points, and each item is rated on a 4-point Likert-type scale (1 = strongly disagree and 4 = strongly agree). High scores indicate greater fear of reinjury due to movement.

The VAS was used to measure the intensity of pain perceived by the participants.[42] The VAS was a 100-mm horizontal line anchored at one end with 0, indicating no pain, and at the other end with 10, indicating the worst pain imaginable. The participant placed a mark along the line corresponding to the intensity of their pain. This scale has been demonstrated to be a reliable and valid measure of pain intensity and is sensitive to clinical changes in pain.[43,44] Changes of 1.1 to 1.2 cm indicate a minimal clinical improvement.[45]

An analog algometer was used to assess PPTs (Wagner Instruments). This instrument consists of a 1-cm diameter hard rubber tip attached to the plunger of a pressure (force) gauge. The dial of the gauge is calibrated in kg/cm,^{2} and the range of the algometer is 0 to 10 kg with 0.1-kg increments.

PPTs were measured at three intratrigeminal sites. One was applied to the skin overlying the anterior fibers of the temporalis muscle (T1), and two were applied to the skin overlying the masseter muscle, 2.5 cm anterior to the tragus and 1.5 cm inferior to the zygomatic arch (the point of origin of the masseter muscle [M1]) and 1 cm superior and 2 cm anterior from the mandibular angle (the point of insertion of the masseter muscle [M2]).[46] The extratrigeminal point was established on the palmar region at the wrist in the middle point of the distal part between the ulnar and radius. Three measurements were taken by the same evaluator (M.G.P.) for each point, with an interval of 30 seconds between measurements. Bilateral data for each point were analyzed, and no significant differences were found. The PPTs corresponded to the mean of the three measures for each point and the mean of both sides of the participant.[46,47] During the measurements, the algometer was held perpendicular to the skin, and the participant was told to immediately alert the assessor when the pressure produced pain.[46,47] Previous research has shown a high reliability during this test (intraclass correlation coefficient = 0.91; 95% confidence interval [CI] 0.82 to 0.97).[46,48]

The pain-free MMO was registered using a digital calibrated caliper placed between the edges of the maxillary and mandibular incisors.[17,49] Measurements were made when the participant was seated with his/her back supported, with feet resting on the floor.[49,50] The instruction given to the participant was, "Open your mouth as wide as possible without causing pain or discomfort."[46,49] The vertical range of motion corresponded to the last measurement of the three opening movements made by the participant.[17,49]

Sample

The G* Power Software of the University of Düsseldorf was used to calculate the correct sample size.[51] Craniofacial disability was used as the main outcome variable. Considering an alpha error of 0.05 and a statistical power of 80%, a minimum of 22 participants was required to detect an effect size of 0.27, taking into account the mean difference and standard deviation (SD) of the result by using a pre- and a postmeasurement in each group. To detect the effects of size, data from a pilot study with six participants per group were used. Taking into account the possibility of a 20% loss, the sample size required for this study was 52 participants (26 per group).

Statistical Analyses

The Statistical Package for Social Sciences (SPSS 21, SPSS) software was used for the statistical analysis. The normality of the variables was evaluated by the Kolmogorov-Smirnov Test. Descriptive statistics were used to summarize the data for continuous variables and are presented as mean ± SD, 95% CI, and as absolute numbers and relative frequencies (percentages) for categorical variables. A chi-square test with residual analysis was used to compare categorical variables. Two-way repeated-measures analysis of variance (ANOVA) was used to compare continuous outcome variables. The factors analyzed were group (CG and COG) and time (baseline, posttreatment,

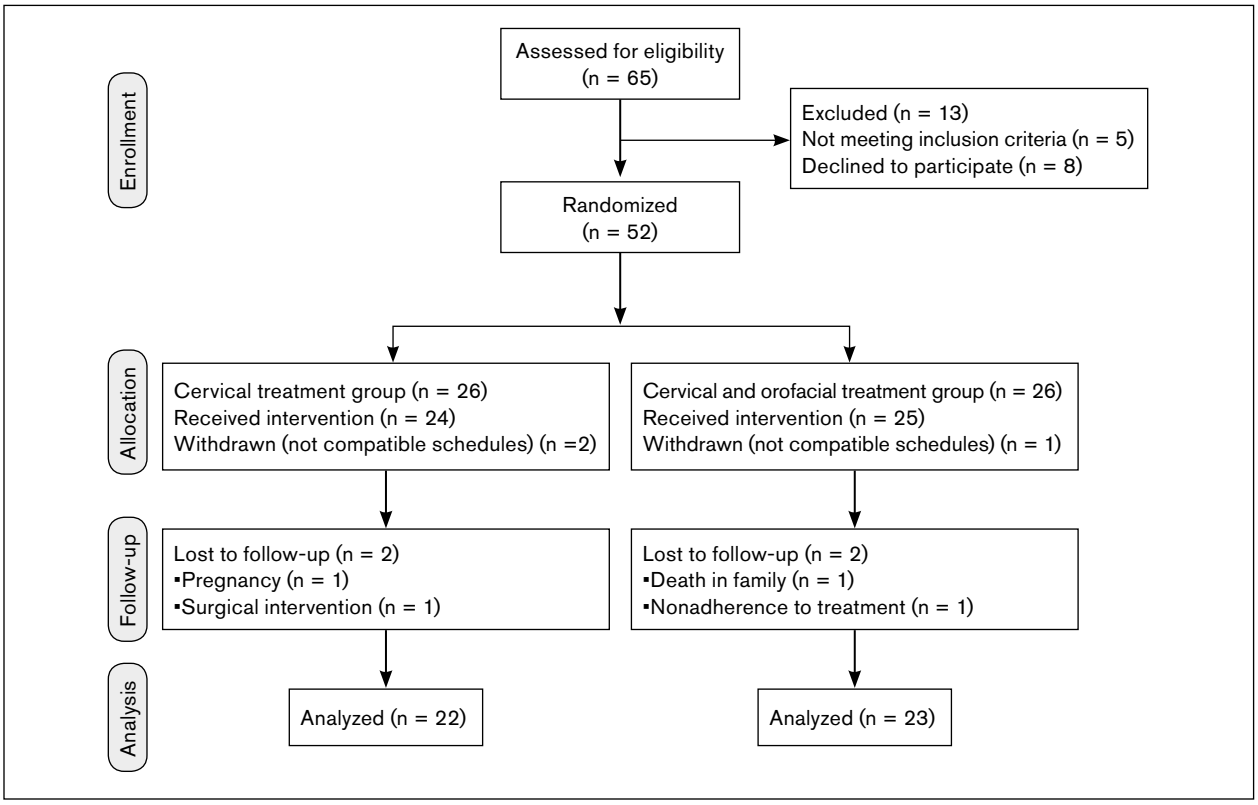

Fig 3 Flowchart of progression of participants through the study.

and follow-ups 1 and 2). The time × group interaction, which is the hypothesis of interest, was also analyzed. Partial eta-squared (η^2p) was calculated as a measure of effect size (strength of association) for each main effect and interaction in the ANOVA: 0.01 to 0.059 represented a small effect, 0.06 to 0.139 a medium effect, and > 0.14 a large effect.[52] Post hoc analysis with Bonferroni correction was performed in cases of significant ANOVA findings for multiple comparisons between variables. The post hoc analysis was performed to analyze changes in measurement time by comparing the baseline to follow-up data (posttreatment, follow-up 1, follow-up 2). Effect sizes (d) were calculated according to Cohen's method, in which the magnitude of effect was classified as small (0.20 to 0.49), medium (0.50 to 0.79), or large (≥ 0.8).[53] Cohen's d was calculated for the results of the multiple comparisons with the post hoc tests and for the comparison of the descriptive variables between groups. A P value < .05 was considered to reflect statistical significance.

Results

A total of 52 participants were included in the study and assigned to one of two groups: 26 participants to the CG, and 26 to the COG. In the CG, two participants did not receive treatment due to incompatible schedules and two participants were lost to follow-up due to pregnancy and surgical intervention. In the COG group, one participant did not receive treatment due to incompatible schedules and two participants were lost to follow-up due to death in the family and nonadherence to treatment. Finally, 45 participants (39 women and 6 men) with chronic migraine and TMD aged 18 to 65 years were included for the final analysis. Figure 3 shows the progression of participants throughout the study. No adverse effects were reported as a result of the intervention. Sociodemographic data of the samples did not present statistically significant differences (P > .05) between groups for age, weight, height, duration of pain, pain intensity, educational level, and employment status. The demographic and clinical data are summarized in Table 1. The descriptive statistics for psychological variables, PPTs, and MMO at baseline assessment revealed no significant differences between the two groups (Table 2).

Primary Outcomes

CF-PDI. ANOVA revealed statistically significant differences for the group × time interaction (F = 3.49; P = .027; η^2p = 0.075). In the CG, post hoc analysis

Table 1 Summary of Demographic and Clinical Data

Measure	CG (n = 22)	COG (n = 23)	*P* value
Age, mean (SD) (y)	48.2 (11.3)	46.0 (9.1)	.47
Gender, n (%)			
Male	3.0 (13.6)	3.0 (13)	1.00
Female	19.0 (86.4)	20.0 (87)	
Weight, mean (SD) (kg)	66.9 (11.9)	69.8 (12.6)	.43
Height, mean (SD) (cm)	164.1 (5.5)	165.7 (8.9)	.45
Body Mass Index, mean (SD) (kg/m^2)	24.6 (3.9)	25.4 (4.4)	.56
Duration of pain, mean (SD) (y)	28.1 (12)	22.6 (12)	.13
VAS, mean (SD) (mm)	69.6 (12.8)	73.5 (13)	.34
Educational level, n (%)			.32
Primary	7.0 (31.8)	3.0 (13)	
Secondary	9.0 (40.9)	12.0 (52.2)	
College	6.0 (27.3)	8.0 (34.8)	
Employment status, n (%)			.49
Active worker	12.0 (54.6)	10.0 (43.5)	
Unemployed	8.0 (36.4)	8.0 (34.8)	
Others (sick leave, unable, retired)	2.0 (9.1)	5.0 (21.7)	

CG = cervical group; COG = cervical and orofacial group; SD = standard deviation; VAS = visual analog scale.

Table 2 Descriptive Statistics for Psychological, Pain, and Disability Variables, PPTs, and Pain-free MMO at Baseline

Variables	CG (n = 22) Mean (SD)	COG (n = 23) Mean (SD)	Mean differences	95% CI	Effect size (d)	*P* value
HIT-6	66.59 (6.05)	65.52 (3.69)	1.07	(–1.93, 4.07)	2.22	.48
TSK-11	26.09 (9.19)	25.48 (9.15)	0.61	(–4.90, 6.13)	0.07	.82
CF-PDI	21.45 (8.37)	21.35 (11.68)	0.10	(–6.03, 6.24)	0.01	.97
VAS (mm)	69.32 (12.75)	76.30 (11.60)	–6.99	(–14.31, 0.34)	–0.57	.06
PPTs (kg/cm^2)						
T1	2.08 (0.50)	1.81 (0.45)	0.27	(–0.02, 0.56)	0.57	.06
M1	1.89 (0.54)	1.78 (0.43)	0.11	(–0.18, 0.41)	0.23	.45
M2	1.55 (0.36)	1.44 (0.31)	0.11	(–0.09, 0.31)	0.33	.27
CP	3.47 (1.18)	3.16 (0.85)	0.32	(–0.30, 0.93)	0.30	.31
Pain-free MMO (mm)	31.41 (8.75)	32.87 (7.16)	–1.46	(–6.26, 3.34)	–0.18	.54

CG = cervical group; COG = cervical and orofacial group; CF-PDI = Craniofacial Pain and Disability Inventory; HIT-6 = Headache Impact Test; TSK-11 = Tampa Scale for Kinesiophobia; VAS = visual analog scale; PPT = pressure pain threshold; T1 = temporalis muscle; M1 = origin of masseter muscle; M2 = insertion of masseter muscle; CP = control point; MMO = maximal mouth opening; CI = confidence interval; SD = standard deviation.

showed no statistically significant differences between baseline and posttreatment ($P > .05$), whereas statistically significant differences between baseline and follow-ups 1 and 2 ($P < .05$) were found. Additionally, in the COG, statistically significant differences were found between baseline and posttreatment ($P = .001$) and between baseline and follow-ups 1 and 2 ($P < .001$). Statistically significant differences were found between groups at follow-up 2 ($P = .042$). Descriptive data and post hoc results are shown in Table 3.

HIT-6. Statistically significant differences were found for the group × time interaction (F = 9.83; $P < .001$; $\eta^2p = 0.19$). In the CG, the post hoc analysis showed statistically significant differences between baseline and posttreatment ($P < .001$) and between baseline and follow-ups 1 and 2 ($P < .05$). Furthermore, in the COG, statistically significant differences were found between baseline, posttreatment, and follow-ups 1 and 2 ($P < .001$). Statistically significant differences were found between the groups at follow-up 2 ($P = .002$). Descriptive data and post hoc results are shown in Table 3.

Secondary Outcomes

TSK-11. ANOVA revealed no statistically significant differences for the group × time interaction (F = 1.01; $P = .37$; $\eta^2p = 0.023$). Descriptive data and post hoc results are shown in Table 3.

Pain Intensity (VAS). ANOVA revealed statistically significant differences for the group × time interaction (F = 21.41; $P < .001$; $\eta^2p = 0.33$). In the CG, the post hoc analysis showed statistically significant differences between baseline, posttreatment, and follow-up 1 ($P < .05$), whereas no statistically significant differences were found between baseline

Table 3 Descriptive Data and Multiple Comparisons of the Pain and Psychological Outcome Measures at Each Measurement Point With Respect to Baseline

Measure/group	Baseline Mean (SD)	Posttreatment Mean (SD)	Mean difference (95% CI); Effect size (d)
CF-PDI			
CG	21.45 (8.37)	18.95 (6.77)	2.5 (–1.05 to 6.05); d = 0.30
COG	21.35 (11.68)	16.22 (11.20)	5.13 (1.66 to 8.6);* d = 0.44
Mean difference (95% CI); Effect size (d)	0.10 (–6.03 to 6.24); d = 0.01	2.74 (–2.86 to 8.33); d = 0.29	
HIT-6			
CG	66.59 (6.05)	62.23 (6.23)	4.36 (1.61 to 7.12);** d = 0.72
COG	65.52 (3.69)	60.87 (6.68)	4.65 (1.96 to 7.35);** d = 1.26
Mean difference (95% CI); Effect size (d)	1.07 (–1.93 to 4.07); d = 2.22	1.36 (–2.53 to 5.25); d = 0.21	
TSK-11			
CG	26.09 (9.19)	25.05 (7.76)	1.04 (–2.23 to 4.33); d = 0.11
COG	25.48 (9.15)	23.30 (7.99)	2.18 (–1.03 to 5.38); d = 0.24
Mean difference (95% CI); Effect size (d)	0.61 (–4.90 to 6.13); d = 0.07	1.75 (–3.00 to 6.48); d = 0.22	
VAS (mm)			
CG	69.32 (12.75)	59.86 (16.21)	9.46 (2.38 to 16.54);* d = 0.74
COG	76.30 (11.60)	59.65 (14.26)	16.65 (9.73 to 23.58);** d = 1.31
Mean difference (95% CI); Effect size (d)	–6.99 (–14.31 to 0.34); d = –0.57	0.21 (–8.96 to 9.38); d = 0.01	

CG = cervical group; COG = cervical and orofacial group; CI = confidence interval; Follow-up 1 = 6 weeks posttreatment; Follow-up 2 = 12 weeks posttreatment; CF-PDI = Craniofacial Pain and Disability Inventory; HIT-6 = Headache Impact Test; TSK-11 = Tampa Scale for Kinesiophobia; VAS = visual analog scale; SD = standard deviation. *$P < .05$; **$P < .001$.

and follow-up 2. In the COG, statistically significant differences were found between baseline, posttreatment, and follow-ups 1 and 2 ($P < .001$). Statistically significant differences were found between groups at follow-up 2 ($P = .001$). Descriptive data and post hoc results are shown in Table 3.

PPTs in the Trigeminal and Extratrigeminal Regions. For T1, ANOVA revealed statistically significant differences for the group × time interaction (F = 15.12; $P < .001$; $\eta^2p = 0.26$). In the CG, the post hoc analysis showed no statistically significant differences ($P > .05$) over time. By contrast, in the COG, statistically significant differences were found between baseline and posttreatment ($P < .001$), baseline and follow-up 1 ($P = .002$), and baseline and follow-up 2 ($P < .001$).

For M1, ANOVA showed statistically significant differences for the group × time interaction (F = 6.83; $P = .001$; $\eta^2p = 0.14$). In the CG, post hoc analysis showed no statistically significant differences ($P > .05$) over time. Nevertheless, statistically significant differences between baseline and posttreatment ($P = .001$), baseline and follow-up 1 ($P = .018$), and baseline and follow-up 2 ($P = .001$) were found in the COG.

For M2, ANOVA revealed that significant differences were present for the group × time interaction (F = 10.67; $P < .001$; $\eta^2p = 0.20$). In the CG, the post hoc analysis showed no statistically significant differences ($P > .05$) over time. However, statistically significant differences between baseline and posttreatment ($P < .05$) and between baseline and follow-ups 1 and 2 ($P < .001$) were found in the COG. No statistically significant differences were found in the extratrigeminal region (wrist) for the group × time interaction (F = 2.79; $P = .55$; $\eta^2p = 0.061$).

When analyzing the three trigeminal points, statistically significant differences were found between groups at follow-up 2 ($P < .05$). The descriptive data and multiple comparisons are summarized in Table 4.

Pain-Free MMO. Statistically significant differences were found for the group × time interaction (F = 12.01; $P < .001$; $\eta^2p = 0.22$). In the CG, the post hoc analysis showed no statistically significant differences ($P > .05$) over time. However, in the COG, statistically significant differences were found

Follow-up 1 Mean (SD)	Mean differencs (95% CI); Effect size (d)	Follow-up 2 Mean (SD)	Mean difference (95% CI); Effect size (d)
16.86 (7.84)	4.6 (0.74 to 8.45);* d = 0.55	17.14 (8.12)	4.32 (0.43 to 8.21);* d = 0.52
13.78 (9.59)	7.57 (3.80 to 11.34);** d = 0.65	11.61 (9.49)	9.74 (5.94 to 13.54);** d = 0.83
3.08 (–2.20 to 8.36); d = 0.35		5.53 (0.21 to 10.85);* d = 0.63	
61.59 (8.12)	5.0 (1.24 to 8.76);* d = 0.83	61.50 (8.92)	5.09 (0.36 to 9.82);* d = 0.84
56.96 (8.73)	8.57 (4.9 to 12.24);** d = 2.32	51.83 (10.87)	13.70 (9.1 to 18.32);** d = 3.71
4.63 (–0.44 to 9.71); d = 0.55		9.67 (3.68 to 15.67);* d = 0.97	
23.95 (7.02)	2.14 (–1.92 to 6.19); d = 0.23	23.73 (6.23)	2.36 (–1.79 to 6.52); d = 0.26
22.30 (8.25)	3.18 (–0.79 to 7.14); d = 0.35	20.22 (9.01)	5.26 (1.20 to 9.33); d = 0.58
1.65 (–2.97 to 6.27); d = 0.22		3.51 (–1.17 to 8.19); d = 0.45	
59.55 (18.60)	9.77 (1.61 to 17.93);* d = 0.77	64.05 (19.82)	5.27 (–4.49 to 15.04); d = 0.41
53.83 (17.35)	22.48 (14.50 to 30.46);** d = 1.76	41.26 (21.50)	35.04 (25.50 to 44.59);** d = 2.75
5.72 (–5.09 to 16.53); d = 0.32		22.79 (10.34 to 35.23);** d = 1.10	

between baseline, posttreatment, and follow-ups 1 and 2 ($P < .001$). Statistically significant differences were observed between groups in posttreatment ($P = .014$) and follow-ups 1 and 2 ($P = .003$ and $P = .01$, respectively). Descriptive data and post hoc results are shown in Table 4.

Discussion

This study was designed to investigate the effects of adding orofacial treatment to cervical physical therapy in patients with chronic migraine and TMD, as well as to provide new evidence on the effects of manual therapy and therapeutic exercises in patients with this comorbidity.

In the case of pain-free MMO, the study revealed statistically significant differences only in the COG at each time point the measurements were carried out with respect to baseline, and statistically significant differences were also observed between the CG and COG at posttreatment and follow-ups 1 and 2. Previous evidence has shown that the application of orofacial and cervical physical therapy in patients with cervicogenic headache and TMD increases pain-free MMO.[27] A similar finding was shown when educational treatment, manual therapy, and therapeutic exercises in the cervical and orofacial regions were applied to patients with bilateral disc displacement without reduction of the TMJ.[50] Furthermore, a previous study demonstrated that only the application of manual therapy and exercises at the cervical spine increased MMO in patients with myofascial TMD.[26] A possible explanation for the different results could be differences in the type of patient.

In terms of trigeminal PPTs, statistically significant differences were found only in the COG. In addition, statistically significant differences were revealed between the CG and COG at the last follow-up period. This result is in agreement with a previous study showing increased PPTs in this region after cervicofacial physical therapy in patients with headache and TMD.[27] This result was also in agreement with findings in patients with migraine and cervical pain and also in patients with myofascial TMD after application of manual therapy and exercises at the cervical spine.[26,54]

Table 4 Descriptive Data and Multiple Comparisons of the Physical Outcome Measures at Each Measurement Time Point With Respect to Baseline

Measure/group	Baseline Mean (SD)	Posttreatment Mean (SD)	Mean difference (95% CI); Effect size (d)
PPT T1			
CG	2.08 (0.50)	2.03 (0.50)	0.06 (−0.12 to 0.23); d = 0.10
COG	1.81 (0.45)	2.18 (0.58)	−0.37 (−0.54 to −0.20);** d = −0.82
Mean difference (95% CI); Effect size (d)	0.27 (−0.02 to 0.56); d = 0.57	−0.15 (−0.48 to 0.17); d = −0.28	
PPT M1			
CG	1.89 (0.54)	1.96 (0.54)	−0.08 (−0.28 to 0.13); d = −0.13
COG	1.78 (0.43)	2.09 (0.63)	−0.31 (−0.51 to −0.11);* d = −0.72
Mean difference (95% CI); Effect size (d)	0.11 (−0.18 to 0.41); d = 0.23	−0.12 (−0.49 to 0.23); d = −0.22	
PPT M2			
CG	1.55 (0.36)	1.57 (0.44)	−0.02 (−0.19 to 0.15); d = −0.06
COG	1.44 (0.31)	1.69 (0.48)	−0.25 (−0.42 to −0.09);* d = −0.81
Mean difference (95% CI); Effect size (d)	0.11 (−0.09 to 0.31); d = 0.33	−0.12 (−0.40 to 0.16); d = −0.26	
PPT CP			
CG	3.47 (1.18)	3.44 (1.06)	0.04 (−0.29 to 0.36); d = 0.03
COG	3.16 (0.85)	3.47 (0.91)	−0.32 (−0.63 to −0.001); d = −0.37
Mean difference (95% CI); Effect size (d)	0.32 (−0.30 to 0.93); d = 0.30	−0.04 (−0.63 to 0.56); d = −0.03	
Pain-free MMO			
CG	31.41 (8.75)	31.64 (8.48)	−0.23 (−2.28 to 1.82); d = −0.03
COG	32.87 (7.16)	37.22 (5.98)	−4.35 (−6.35 to −2.34);** d = −0.61
Mean difference (95% CI); Effect size (d)	−1.46 (−6.26 to 3.34); d = −0.18	−5.58 (−9.98 to −1.19);* d = −0.76	

CG = cervical group; COG = cervical and orofacial group; Follow-up 1 = 6 weeks posttreatment; Follow-up 2 = 12 weeks posttreatment; CI = confidence interval; PPT = pressure pain threshold; T1 = temporalis muscle; M1 = origin of masseter muscle; M2 = insertion of masseter muscle; CP = control point (wrist); MMO = maximal mouth opening; SD = standard deviation. *$P < .05$; **$P < .001$.

In relation to the PPTs in the extratrigeminal region (wrist), studies have shown a general hypersensitivity in patients with concomitant migraine and TMD compared to patients having only migraine or TMD. This finding could be related to central modifications in pain pathways.[55] The present PPT findings indicated that physical therapy at either the cervical or in both the cervical and orofacial regions produced a localized hypoalgesic effect in the trigeminal region, but not in the extratrigeminal region.

In agreement with these results, previous studies obtained hypoalgesia only in the area where treatment was applied, and in these studies, the participants also presented with more than one disorder.[56,57] However, other studies in which the sample consisted of patients without comorbidities have shown that the application of manual therapy and therapeutic exercises produced generalized hypoalgesia.[58–61] These results have shown overall positive outcomes for muscle pain, given an increase in PPTs at the anterior temporalis (area of migraine pain) and at the masseter muscle (area of TMD pain).

Regarding pain intensity, HIT-6, and CF-PDI variables, the present study revealed statistically significant differences in both groups, although the improvement in these variables was higher in the COG. A statistically significant difference between groups was found at the last follow-up period. These results suggest that both treatments were effective for reducing pain, craniofacial disabilities, and the impact of headache on daily life in patients with chronic migraine and TMD.

In the case of pain intensity, these results are in agreement with other studies that demonstrated a reduction in pain after applying multimodal physiotherapy treatment in chronic tension-type headache,

Follow-up 1 Mean (SD)	Mean differencs (95% CI); Effect size (d)	Follow-up 2 Mean (SD)	Mean difference (95% CI); Effect size (d)
1.91 (0.46)	0.18 (–0.08 to 0.43); d = 0.34	1.85 (0.48)	0.24 (–0.03 to 0.50); d = 0.46
2.15 (0.59)	–0.34 (–0.59 to –0.10);* d = –0.76	2.32 (0.61)	–0.50 (–0.76 to –0.24);** d = –1.13
–0.25 (–0.56 to 0.07); d = –0.45		–0.47 (–0.80 to –0.14);* d = –0.85	
1.90 (0.59)	–0.01 (–0.28 to 0.26); d = –0.02	1.75 (0.57)	0.13 (–0.16 to 0.42); d = 0.26
2.08 (0.54)	–0.30 (–0.57 to –0.03);* d = –0.70	2.19 (0.63)	–0.42 (–0.70 to –0.13);* d = –0.95
–0.18 (–0.52 to 0.16); d = –0.32		–0.44 (–0.80 to –0.08);* d = –0.73	
1.53 (0.43)	0.02 (–0.17 to 0.21); d = 0.06	1.47 (0.39)	0.08 (–0.16 to 0.31); d = 0.22
1.74 (0.45)	–0.30 (–0.50 to –0.12);** d = –0.97	1.87 (0.48)	–0.43 (–0.66 to –0.20);** d = –1.39
–0.21 (–0.48 to 0.05); d = –0.48		–0.40 (–0.66 to –0.14);* d = –0.91	
3.34 (1.06)	0.13 (–0.31 to 0.58); d = 0.11	3.18 (1.01)	0.29 (–0.17 to 0.74); d = 0.25
3.35 (0.85)	–0.19 (–0.62 to 0.24); d = –0.22	3.42 (0.91)	–0.27 (–0.71 to 0.18); d = –0.31
–0.01 (–0.58 to 0.57); d = –0.01		–0.24 (–0.82 to 0.34); d = –0.25	
32.32 (8.76)	–0.91 (–3.32 to 1.50); d = –0.10	32.36 (9.58)	–0.96 (–4.33 to 2.42); d = –0.11
39.13 (5.67)	–6.26 (–8.62 to –3.90);** d = –0.87	41.13 (6.49)	–8.26 (–11.56 to –4.96);** d = –1.15
–6.81 (–11.23 to –2.40);* d = –0.93		–8.77 (–13.67 to –3.87);* d = –1.08	

cervical manual therapy in chronic neck pain, and cervical and orofacial treatment in TMD.[50,62,63] Nevertheless, the present results do not agree with those obtained by von Piekartz and Lüdtke, who compared cervical treatment to cervical and orofacial treatment in patients with cervicogenic headache and TMD.[27] They found that only the cervical and orofacial treatment significantly decreased pain as measured through a colored analog scale, which is a pain intensity scale similar to the VAS that was designed especially for patients with headache of various age categories.[27,64]

In relation to the HIT-6, the present findings are in agreement with previous studies. Multimodal physiotherapy in the cervical region in chronic tension-type headache and cervical and orofacial physical therapy in migraine and chronic neck pain decreased the impact of headache on patients' daily lives.[54,62]

Finally, the present study found that the physiotherapy treatment used, which was based on manual therapy, was not effective in reducing fear of movement. A previous study applying manual therapy in the cervical region in patients with neck pain have found similar results.[65] The authors of the present study believe that other physiotherapy treatments that focus on a biobehavioral perspective could be effective in decreasing kinesiophobia in patients with migraine and TMD. Previous scientific studies have indicated that treatments such as therapeutic education,[66–68] graduated exposure,[68,69] and graded activity[70–72] are effective in decreasing fear of movement in other chronic musculoskeletal disorders.

In terms of pharmacologic treatment, both groups continued their medication regimens during the study period in accordance with a previous study.[20] For ethical reasons, participants could not be withdrawn

from pharmacologic treatment during the study. All had a similar intake of routine preventive and abortive treatment at the onset of migraine attacks. The medication was prescribed by a headache specialist neurologist. These participants had been taking medication for many years without significant improvements, and so it is unlikely that the improvements found in this study would have been specifically due to the medication.

Practical and Scientific Implications

To the best of the authors' knowledge, this study is the first to investigate the effects of manual therapy and therapeutic exercises for the cervical and orofacial regions combined in patients suffering from chronic migraine and TMD.

The clinical implications are that physical therapy is able to improve sensorimotor variables, pain levels, and craniofacial disabilities. There is evidence that physical therapy can be effective in reducing nociceptive inputs from the cervicofacial regions. Therefore, this type of therapy should be considered as a preventive treatment for these patients. The results of the study suggest that patients suffering from a combination of both chronic migraine and TMD should receive treatment for both conditions, with the aim of improving the symptomatology. Future studies should include a multimodal program based on therapeutic education and physical therapy aimed at decreasing kinesiophobia.

Study Limitations

The major study limitation was the absence of a control group, which would have allowed a comparison with the natural course of the disease. Future studies should include a control group and a long-term follow-up, as the present study observed that most changes between groups were noted at the last follow-up. Another important limitation was that participants did not stop pharmacologic treatments (abortive and preventive treatment) during the course of the study and that the decrease/increase in drug intake was not recorded or analyzed; it is important that this be addressed in future studies. Another limitation was that details regarding compliance were not reported or analyzed.

Conclusions

Cervical and orofacial treatment was more effective than cervical treatment alone for increasing PPTs in the trigeminal region and producing pain-free MMO. Additionally, both treatments were effective for decreasing pain related to disability in the craniofacial region and the impact and severity of headache and pain. However, the physical therapy treatment alone was not effective for increasing the PPT in the extratrigeminal region (wrist) or decreasing the level of kinesiophobia.

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References

1. Lipton RB, Bigal ME, Diamond M, et al. Migraine prevalence, disease burden, and the need for preventive therapy. Neurology 2007;68:343–349.
2. Gonçalves DA, Dal Fabbro AL, Campos JA, Bigal ME, Speciali JG. Symptoms of temporomandibular disorders in the population: An epidemiological study. J Orofac Pain 2010;24:270–278.
3. Stovner LJ, Hagen K, Jensen R, et al. The global burden of headache: A documentation of headache prevalence and disability worldwide. Cephalalgia 2007;27:193–210.
4. Ciancaglini R, Radaelli G. The relationship between headache and symptoms of temporomandibular disorder in the general population. J Dent 2001;29:93–98.
5. Okeson JP, de Leeuw R. Differential diagnosis of temporomandibular disorders and other orofacial pain disorders. Dent Clin North Am 2011;55:105–120.
6. Blumenfeld AM, Varon SF, Wilcox TK, et al. Disability, HRQoL and resource use among chronic and episodic migraineurs: Results from the International Burden of Migraine Study (IBMS). Cephalalgia 2011;31:301–315.
7. Levin M. The International Classification of Headache Disorders, 3rd Edition (ICHD III)—Changes and challenges. Headache 2013;53:1383–1395.
8. Gonçalves DA, Camparis CM, Speciali JG, Franco AL, Castanharo SM, Bigal ME. Temporomandibular disorders are differentially associated with headache diagnoses: A controlled study. Clin J Pain 2011;27:611–615.
9. Bevilaqua-Grossi D, Lipton RB, Napchan U, Grosberg B, Ashina S, Bigal ME. Temporomandibular disorders and cutaneous allodynia are associated in individuals with migraine. Cephalalgia 2010;30:425–432.
10. Watts PG, Peet KM, Juniper RP. Migraine and the temporomandibular joint: The final answer? Br Dent J 1986;161:170–173.
11. Dworkin SF, LeResche L. Research diagnostic criteria for temporomandibular disorders: Review, criteria, examinations and specifications, critique. J Craniomandib Disord 1992;6:301–355.
12. Burstein R, Yarnitsky D, Goor-Aryeh I, Ransil BJ, Bajwa ZH. An association between migraine and cutaneous allodynia. Ann Neurol 2000;47:614–624.
13. Bigal ME, Ashina S, Burstein R, et al. Prevalence and characteristics of allodynia in headache sufferers: A population study. Neurology 2008;70:1525–1533.
14. Chichorro JG, Porreca F, Sessle B. Mechanisms of craniofacial pain. Cephalalgia 2017;37:613–626.
15. Bigal ME, Serrano D, Buse D, Scher A, Stewart WF, Lipton RB. Acute migraine medications and evolution from episodic to chronic migraine: A longitudinal population-based study. Headache 2008;48:1157–1168.

16. Franco AL, Gonçalves DA, Castanharo SM, Speciali JG, Bigal ME, Camparis CM. Migraine is the most prevalent primary headache in individuals with temporomandibular disorders. J Orofac Pain 2010;24:287–292.
17. Gonçalves DA, Camparis CM, Speciali JG, et al. Treatment of comorbid migraine and temporomandibular disorders: A factorial, double-blind, randomized, placebo-controlled study. J Orofac Pain 2013;27:325–335.
18. Chaibi A, Tuchin PJ, Russell MB. Manual therapies for migraine: A systematic review. J Headache Pain 2011;12:127–133.
19. Chaibi A, Šaltyté Benth J, Tuchin PJ, Russell MB. Chiropractic spinal manipulative therapy for migraine: A study protocol of a single-blinded placebo-controlled randomised clinical trial. BMJ Open 2015;5:e008095.
20. Hernandez-Reif M, Dieter J, Field T, Swerdlow B, Diego M. Migraine headaches are reduced by massage therapy. Int J Neurosci 2009;96:1–11.
21. Tuchin PJ, Pollard H, Bonello R. A randomized controlled trial of chiropractic spinal manipulative therapy for migraine. J Manipulative Physiol Ther 2000;23:91–95.
22. Gil-Martínez A, Kindelan-Calvo P, Agudo-Carmona D, Muñoz-Plata R, López-de-Uralde-Villanueva I, La Touche R. Therapeutic exercise as treatment for migraine and tension-type headaches: A systematic review of randomised clinical trials [in Spanish]. Rev Neurol 2013;57:433–443.
23. Michelotti A, de Wijer A, Steenks M, Farella M. Home-exercise regimes for the management of non-specific temporomandibular disorders. J Oral Rehabil 2005;32:779–785.
24. Moraes Ada R, Sanches ML, Ribeiro EC, Guimarães AS. Therapeutic exercises for the control of temporomandibular disorders. Dental Press J Orthod 2013;18:134–139.
25. Tuncer AB, Ergun N, Tuncer AH, Karahan S. Effectiveness of manual therapy and home physical therapy in patients with temporomandibular disorders: A randomized controlled trial. J Bodyw Mov Ther 2013;17:302–308.
26. La Touche R, Fernández-de-Las-Peñas C, Fernández-Carnero J, et al. The effects of manual therapy and exercise directed at the cervical spine on pain and pressure pain sensitivity in patients with myofascial temporomandibular disorders. J Oral Rehabil 2009;36:644–652.
27. von Piekartz H, Lüdtke K. Effect of treatment of temporomandibular disorders (TMD) in patients with cervicogenic headache: A single-blind, randomized controlled study. Cranio 2011; 29:43–56.
28. von Piekartz H, Hall T. Orofacial manual therapy improves cervical movement impairment associated with headache and features of temporomandibular dysfunction: A randomized controlled trial. Man Ther 2013;18:345–350.
29. Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd edition (beta version). Cephalalgia 2013;33:629–808.
30. De Hertogh WJ, Vaes PH, Devroey D, Truijen S, Duquet W, Oostendorp R. Management of headache disorders: Design of a randomised clinical trial screening for prognostic patient characteristics. BMC Musculoskelet Disord 2007;8:38.
31. van Ettekoven H, Lucas C. Efficacy of physiotherapy including a craniocervical training programme for tension-type headache; A randomized clinical trial. Cephalalgia 2006;26:983–991.
32. von Piekartz HJM. Craniofacial Pain: Neuromusculoskeletal Assessment, Treatment and Management. London: Elsevier, 2007.
33. Fernández de las Peñas C, Arendt-Nielsen L, Gerwin R. Cefalea tensional y de origen cervical: Fisiopatología, diagnóstico y tratamiento. Barcelona: Elsevier Masson, 2010.
34. La Touche R, Pardo-Montero J, Gil-Martínez A, et al. Craniofacial Pain and Disability Inventory (CF-PDI): Development and psychometric validation of a new questionnaire. Pain Physician 2014;17:95–108.
35. Bjorner JB, Kosinski M, Ware JE Jr. Calibration of an item pool for assessing the burden of headaches: An application of item response theory to the Headache Impact Test (HIT). Qual Life Res 2003;12:913–933.
36. Gandek B, Alacoque J, Uzun V, Andrew-Hobbs M, Davis K. Translating the Short-Form Headache Impact Test (HIT-6) in 27 countries: Methodological and conceptual issues. Qual Life Res 2003;12:975–979.
37. Gómez-Pérez L, López-Martínez AE, Ruiz-Párraga GT. Psychometric properties of the Spanish version of the Tampa Scale for Kinesiophobia (TSK). J Pain 2011;12:425–435.
38. Martin M, Blaisdell B, Kwong JW, Bjorner JB. The Short-Form Headache Impact Test (HIT-6) was psychometrically equivalent in nine languages. J Clin Epidemiol 2004;57:1271–1278.
39. Rendas-Baum R, Yang M, Varon SF, Bloudek LM, DeGryse RE, Kosinski M. Validation of the Headache Impact Test (HIT-6) in patients with chronic migraine. Health Qual Life Outcomes 2014;12:117.
40. Coeytaux RR, Kaufman JS, Chao R, Mann JD, Devellis RF. Four methods of estimating the minimal important difference score were compared to establish a clinically significant change in Headache Impact Test. J Clin Epidemiol 2006;59:374–380.
41. Yang M, Rendas-Baum R, Varon SF, Kosinski M. Validation of the Headache Impact Test (HIT-6) across episodic and chronic migraine. Cephalalgia 2011;31:357–367.
42. Huskisson EC. Measurement of pain. Lancet 1974;2: 1127–1131.
43. Bijur PE, Silver W, Gallagher EJ. Reliability of the visual analog scale for measurement of acute pain. Acad Emerg Med 2001;8:1153–1157.
44. Jensen MP, Turner JA, Romano JM, Fisher LD. Comparative reliability and validity of chronic pain intensity measures. Pain 1999;83:157–162.
45. Emshoff R, Bertram S, Emshoff I. Clinically important difference thresholds of the visual analog scale: A conceptual model for identifying meaningful intraindividual changes for pain intensity. Pain 2011;152:2277–2282.
46. La Touche R, París-Alemany A, von Piekartz H, Mannheimer JS, Fernández-Carnero J, Rocabado M. The influence of cranio-cervical posture on maximal mouth opening and pressure pain threshold in patients with myofascial temporomandibular pain disorders. Clin J Pain 2011;27:48–55.
47. La Touche R, Paris-Alemany A, Gil-Martinez A, et al. Masticatory sensory-motor changes after an experimental chewing test influenced by pain catastrophizing and neck-pain-related disability in patients with headache attributed to temporomandibular disorders. J Headache Pain 2015;16:20.
48. Chesterton LS, Sim J, Wright CC, Foster NE. Interrater reliability of algometry in measuring pressure pain thresholds in healthy humans, using multiple raters. Clin J Pain 2007;23:760–766.
49. Heredia-Rizo AM, Rodríguez-Blanco C, Oliva-Pascual-Vaca Á, et al. Masticatory mechanosensitivity, mouth opening and impact of headache in subjects with a history of orthodontics use: A cross-sectional study. Eur J Phys Rehab Med 2014;50:411–418.
50. Cleland J, Palmer J. Effectiveness of manual physical therapy, therapeutic exercise, and patient education on bilateral disc displacement without reduction of the temporomandibular joint: A single-case design. J Orthop Sports Phys Ther 2004; 34:535–548.

51. Faul F, Erdfelder E, Lang AG, Buchner A. G*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behav Res Methods 2007; 39:175–191.
52. Cohen J. Eta-squared and partial eta-squared in fixed factor ANOVA designs. Educ Psychol Meas 2016;33:107–112.
53. Cohen J. Statistical Power Analysis for the Behavioral Sciences. Hillsdale, New Jersey: Lawrence Erlbaum, 1988.
54. Bevilaqua-Grossi D, Gonçalves MC, Carvalho GF, et al. Additional effects of a physical therapy protocol on headache frequency, pressure pain threshold, and improvement perception in patients with migraine and associated neck pain: A randomized controlled trial. Arch Phys Med Rehabil 2016;97:866–874.
55. Chaves TC, Dach F, Florencio LL, et al. Concomitant migraine and temporomandibular disorders are associated with higher heat pain hyperalgesia and cephalic cutaneous allodynia. Clin J Pain 2016;32:882–888.
56. Costa YM, Porporatti AL, Stuginski-Barbosa J, Bonjardim LR, Speciali JG, Conti PC. Headache attributed to masticatory myofascial pain: Impact on facial pain and pressure pain threshold. J Oral Rehabil 2016;43:161–168.
57. Sterling M, Jull G, Wright A. Cervical mobilisation: Concurrent effects on pain, sympathetic nervous system activity and motor activity. Man Ther 2001;6:72–81.
58. Cleland JA, Childs JD, McRae M, Palmer JA, Stowell T. Immediate effects of thoracic manipulation in patients with neck pain: A randomized clinical trial. Man Ther 2005;10:127–135.
59. Cleland JA, Glynn P, Whitman JM, Eberhart SL, MacDonald C, Childs JD. Short-term effects of thrust versus nonthrust mobilization/manipulation directed at the thoracic spine in patients with neck pain: A randomized clinical trial. Phys Ther 2007; 87:431–440.
60. Vicenzino B, Collins D, Wright A. The initial effects of a cervical spine manipulative physiotherapy treatment on the pain and dysfunction of lateral epicondylalgia. Pain 1996;68:69–74.
61. Andersen LL, Andersen CH, Sundstrup E, Jakobsen MD, Mortensen OS, Zebis MK. Central adaptation of pain perception in response to rehabilitation of musculoskeletal pain: Randomized controlled trial. Pain Physician 2012;15:385–394.
62. Beltran-Alacreu H, Lopez-de-Uralde-Villanueva I, La Touche R. Multimodal physiotherapy based on a biobehavioral approach as a treatment for chronic tension-type headache: A case report. Anesth Pain Med 2015;5:e32697.
63. Izquierdo Pérez H, Alonso Perez JL, Gil Martinez A, et al. Is one better than another?: A randomized clinical trial of manual therapy for patients with chronic neck pain. Man Ther 2014;19: 215–221.
64. McGrath P, Seifert CE, Speechley KN, Booth JC, Stitt L, Gibson MC. A new analogue scale for assessing children's pain: An initial validation study. Pain 1996;64:435–443.
65. Lopez-Lopez A, Alonso Perez JL, González Gutierez JL, et al. Mobilizations versus manipulations versus sustain apophyseal natural glide techniques and interaction with psychological factors for patients with chronic neck pain: Randomized controlled trial. Eur J Phys Rehab Med 2015;51:121–132.
66. Burton AK, Waddell G, Tillotson KM, Summerton N. Information and advice to patients with back pain can have a positive effect. A randomized controlled trial of a novel educational booklet in primary care. Spine (Phila Pa 1976) 1999;24:2484–2491.
67. Coudeyre E, Tubach F, Rannou F, et al. Effect of a simple information booklet on pain persistence after an acute episode of low back pain: A non-randomized trial in a primary care setting. PLoS One 2007;2:e706.
68. de Jong JR, Vlaeyen JW, de Gelder JM, Patijn J. Pain-related fear, perceived harmfulness of activities, and functional limitations in complex regional pain syndrome type I. J Pain 2011;12: 1209–1218.
69. Leeuw M, Goossens ME, van Breukelen GJ, et al. Exposure in vivo versus operant graded activity in chronic low back pain patients: Results of a randomized controlled trial. Pain 2008;138:192–207.
70. George SZ, Fritz JM, Bialosky JE, Donald DA. The effect of a fear-avoidance-based physical therapy intervention for patients with acute low back pain: Results of a randomized clinical trial. Spine (Phila Pa 1976) 2003;28:2551–2560.
71. Lindström I, Ohlund C, Eek C, et al. The effect of graded activity on patients with subacute low back pain: A randomized prospective clinical study with an operant-conditioning behavioral approach. Phys Ther 1992;72:279–290.
72. van der Giessen RN, Speksnijder CM, Helders PJ. The effectiveness of graded activity in patients with non-specific low-back pain: A systematic review. Disabil Rehabil 2012;34:1070–1076.