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Effectiveness of a Treatment Involving Soft Tissue Techniques and/or Neural Mobilization Techniques in the Management of the Tension-Type Headache: A Randomized Controlled Trial

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EFFECTIVENESS OF A TREATMENT INVOLVING SOFT TISSUE TECHNIQUES AND/OR NEURAL MOBILIZATION TECHNIQUES IN THE MANAGEMENT OF THE TENSION-TYPE HEADACHE: A RANDOMIZED CONTROLLED TRIAL

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Clinical trial registration number: the study was approved by the Ethical Committee of the Balearic Island /CEI-IB) and was registered in the Australian New Zealand Clinical Trial Registry (ANZCTR) with the registration number ACTRN12615000698572. This study began in 2013, so a retrospective registration was made.

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ABSTRACT

Objective: To evaluate the effects of a protocol involving soft tissue techniques and/or Neural Mobilization Techniques in the management of patients with Frequent episodic tension-type headache (FETTH) and Chronic tension-type headache (CTTH).

Design: Randomized controlled, double blind, placebo control and before-after trial.

Setting: Rehabilitation area of Son Llatzer Hospital and Fisioplanet Centre

Participants: Ninety-seven patients (78 women; 19 men) diagnosed with FETTH or CTTH, were randomly assigned to groups A, B, C or D.

Interventions: (A) placebo superficial massage; (B) soft tissue techniques; (C) neural mobilization; (D) a combination of (B) and (C).

Main Outcomes Measures: The pressure pain threshold (PPT) in the temporal muscles (PPT_1, PPT_2) and supraorbital region (PPT_3), the frequency (Freq) and maximal intensity (Int) of the pain crisis, and the punctuation using the Hit-6 questionnaire (Hit6) were evaluated. All variables were assessed before, at the end of the treatment and 15 days and 30 days post-intervention.

Results: Groups B, C, and D had an increase of PPT and a reduction of Freq, Int, and Hit-6 in all time-points after the intervention compared to baseline and Group A (p <

0.001 in all cases). Group D had the highest PPT values and the lowest values in Freq and Hit-6 after the intervention.

Conclusions: The application of soft tissue techniques and neural mobilization in FETTH or CTTH patients induces significant changes in pressure pain threshold, the characteristics of the pain crisis, and its impact on daily life activities compared to the application of these techniques as isolated interventions.

Keywords: tension-type headache; musculoskeletal manipulations; soft tissue; nerve tissue.

Abbreviations:

Tension-type headache: TTH

Frequent episodic tension-type headache: FETTH

Chronic tension-type headache: CTTH

Neural mobilization techniques: NMT

Soft Tissue techniques: STT

Pressure pain threshold in the temporal muscles: PPT_1, PPT_2

Pressure pain threshold in supraorbital region: PPT_3

Frequency: Freq

Maximal Intensity: Int

Hit-6 questionnaire: Hit6

Trigeminal Caudal Nucleus: TCN

Evaluation before the beginning of the study: Pre

Evaluation one hour after the latest session: Post

Evaluation fifteen days later: Post15days

Evaluation thirty days later: Post30days

Introduction

Tension-type headache (TTH) is the most prevalent form of benign primary headache[1]. The prevalence for episodic TTH is 33.8% in a year and 2.3% for chronic TTH[2], being TTH the second most prevalent pathology in the world[3]. These situations make the TTH a shocking pathology in its social and economic aspects[4].

To explain the whole symptomatology, authors refer to peripheral sensitization that involves myofascial pain in the cranio-cervical musculature, as well as higher mechanical sensitivity in the nerve trunks[5, 6]. However, as a consequence of the continuous nociceptive afferents, previous studies also suggest a central sensitization with an alteration in the processing and/or the inhibitory mechanisms of pain that set the chronic character of this pathology, being the Trigeminal Caudal Nucleus (TCN) one of the structures that can be sensitized[7-9].

Despite the great impact of the TTH, studies to date have not established the best treatment to manage the symptomatology[10]. Although previous studies reported benefits of manual therapy by including soft tissue techniques (STT) to manage the myofascial pain, these studies were often low-quality, making it difficult to draw clear conclusions[11].

Neural mobilization techniques (NMT) intend to improve the adaptability, reduce mecanosensitivity and activate analgesic mechanisms by mechanically stimulating the nerves with palpation, elongation, and sliding[12-14]. In this regard, previous studies have shown that increases in the mechanosensitivivity may induce pain with neuropathic, nociceptive and mixed characteristics[14] and increases in the muscle contraction[15, 16]. For this reason, the therapies that mechanically stimulate the nervous tissue could decrease the local mechanosensitivity and increase the mechanic tolerance as consequence of activating the central mechanisms of analgesia [12-14, 17-20]. However, to the current authors' knowledge, no studies to date have included this type of intervention in the management of the TTH.

Based on these arguments, the present study aimed to analyze the effects of a protocol involving STT combined or not with NMT in the management of patients with Frequent episodic tension-type headache (FETTH) and Chronic tension-type headache (CTTH). It was hypothesized that the combination of both therapies is more effective in decreasing the sensitivity of the neuromusculoskeletal structures and thus, improves the central sensitization and chronic trend of this pathology, compared to the isolated techniques.

Methods

Design

The present study refers to a randomized, double-blind, controlled trial, with four intervention groups.

Participants

Participants were recruited randomly from the local hospital and other health centers from the region.

Criteria for inclusion in this study were: patients aged between 18 and 65 years and diagnosed with FETTH and CTTH with increased pericranial tenderness on manual palpation by neurologists according the International classification of headache disorders[21].

Criteria for exclusion in this study were: patients with impossibility of receiving manual therapy; patients with previous physiotherapy treatment for their TTH; and patients receiving pharmacologic prophylactic treatment two months before beginning the study.

Patients were told not to take medication unless they had an increase in symptoms with a VAS value 6-7, then they could take ibuprofen 400mg, one or two doses maximum to go through the crisis.

This study was performed between December 2013 and March 2015 in the Local Hospital and a private physiotherapy clinic. Before the beginning of the study all participants signed an informed consent, according to the declaration of Helsinki[22]. The study was approved by the Clinical Investigation Ethical Committee of the Balearic Island (CEI-IB)

Interventions

Six 15 minutes´ sessions were applied to every patient: two the first week, two the second week, and one more the third and the fourth weeks. The patients were randomly assigned to group A (placebo superficial massage: n=25), group B (n=25: STT), group C (n=25: NMT) or group D (n=25: combined treatment involving soft tissue and NMT). Epidat software v.4.0 was used to randomize the intervention to each participant. The randomization sequence was guarded by an independent collaborator who guaranteed its concealment. Also, every intervention was blinded for both participants and evaluators, and the physiotherapists who applied the treatment were blinded to the objectives of the investigation.

Protocol: placebo superficial massage

A physiotherapist applied a soft and superficial massage, while patients were in prone position. The physiotherapist used ultrasound gel to minimize the skin stimulation while performing multidirectional gliding in the thoracic region of the patients' back, without overstepping the D1 spinous process in cranial direction. The protocol lasted 15 minutes.

Protocol: Soft tissue techniques

A physiotherapist expert in manual therapy treated five muscles in the cranio-cervical region. The protocol lasted 15 minutes (three minutes each pair of muscles). Patients should not feel pain higher than two according to the EVA scale (0-10). The techniques were randomly included in the following order: Sternocleidomastoid muscle, Temporal muscle, Suboccipital musculature, Masseter muscle and Upper trapezius muscle (Figure 1).

Protocol: Neural mobilization techniques

A physiotherapist expert in manual therapy performed three NMT, whose performance was always mild, progressive, and slow. The protocol lasted 15 minutes (five minutes every mobilization). Patients should not feel pain higher than two according to the EVA scale (0-10). The techniques were included in the following order:

- Mobilization in cranio-cervical flexion: the physiotherapist performed an anterior rotation of the head, which stimulates the meninges [23]. To increase the mechanical stress in the nervous system, the patient was asked to do a descent and retropulsion of the shoulders, while gradually extending both elbows (Figure 2).

- Lateral cervical sliding: based on the technique described by Elvey [24], the physiotherapist laterally slide the cervical region of the patient. The purpose of this movement was to stimulate the brachial plexus. Patients were allowed to move their shoulders. To increase the mechanical stress in the nervous system, patients were asked to progressively extend their elbows, followed by forearm supination and a dorsal flexion of the carpal and fingers (Figure 3).

- Opening the mouth in cranio-cervical flexion: the physiotherapist passively held the cranio-cervical flexion with one hand, while the other hand opened the mouth (passive-assisted). The opening of the mouth increases the deformation of the trigeminal nerve, mainly the mandibular branch[25]. To increase the mechanical stress in the nervous system, patients were asked to progressively extend their elbows, followed by forearm supination and a dorsal flexion of the carpal and fingers (Figure 4).

Protocol: Combined protocol: Soft tissue and NMT.

A physiotherapist expert in manual therapy performed a combination of both protocols: soft tissue and NMT. The protocol lasted 15 minutes. The techniques included were the same as those added in the previous protocols, however the duration was shorter to adjust the total duration of the protocol to 15 minutes and avoid skewing this protocol's effects: seven and a half minutes of NMT and seven and a half minutes of STT.

Outcome measures

Frequency of the crisis: patients were given 15-days diaries. One diary was given two weeks before the first session (pre-measurement[26]), another one after the fourth session (Post), another one after the sixth session ($Post_{15days}$) and the last one 15 days after the sixth session ($Post_{30days}$). The diary had to be filled every day in the morning, afternoon and night to inform if they had headache.

Maximal Intensity of the pain: patients informed about this variable according to a Visual Analogical Scale (0: no pain; 10: maximum pain) placed in the diaries of headache frequency. If they felt headache, while filling this information in the diary, they had to record the maximal intensity of that pain perceived during that crisis, using the Visual Analogue Scale. As performed for the frequency, it had to be recorded three times every day (morning, afternoon and night). The maximal intensity of pain was obtained from the average of the three highest values in each diary[27].

Pressure pain threshold (PPT): We used an electronic pressure algometer Commander J-TECH with a stimulation surface area of 1 cm^2. The reliability and validity have been proved previously[28]. The pressure pain threshold was analyzed in three points:

- Temporal muscle (point 1) (PPT_1): three cm above the upper margin of the ear, vertical to the ear canal[29].

- Temporal muscle (point 2) (PPT_2): one cm in front of point 1[29].

- Supraorbital nerve emerging (point 3) (PPT_3): it can be located between the medial third and the middle third of the frontal bone edge[6].

The PPT was assessed three times in each point, with an interval of 30 seconds of rest. To obtain the final measure, the highest trial was discarded and the other two trials in each point were averaged[6, 29-31] This variable was evaluated before the beginning of the study (Pre), one hour after the latest session (Post), fifteen days later ($Post_{15days}$), and thirty days later ($Post_{30days}$).

Impact test-6 (Hit-6): its reliability has been shown in previous studies[32] to evaluate the impact of the headache on patients' daily life activities. Consists of 6 items with 5 response options; never: 6 points, rarely: 8 points, sometimes: 10 points, very often: 11 points, always: 13 points, with a total score ranging from 36 to 78 points[33]. This variable was evaluated before the beginning of the study (Pre), one hour after the latest session (Post), 15 days later ($Post_{15days}$), and 30 days later ($Post_{30days}$).

Statistical analysis

The sample size calculation was performed with Granmo v.7.12 software for the punctuation in the Hit-6 questionnaire because of its capacity to evaluate the impact of the headache on patients' daily life activities, and its relationship with key aspects of the symptomatology such as headache severity and quality of life[33]. An alpha level of 0.05 and a desired power (β) of 80% with a bilateral contrast were assumed. These assumptions generated a sample size of at least 23 participants per group to detect a minimal difference of six between two groups and a standard deviation of 5.52. Losses during the follow-up were estimated at 10%.

Demographic and clinical characteristics of the groups were compared with one-way ANOVA for quantitative variables, and Chi-squared (x2) for categorical variables.

Mixed-model repeated measures ANOVA was used to determine whether any change in PPT, the frequency, and maximal intensity of the crisis of pain, and the HIT-6 questionnaire is the result of interaction between the type of intervention (no treatment, soft tissue treatment, neural mobilization treatment, and combined treatment) and time. Analysis included within-subject variables (the time of measurement with four levels: before, immediately after, 15 days and 30 days after the intervention) and between-subjects variables (the intervention with four levels: no treatment, soft tissue treatment, neural mobilization treatment, and combined treatment).

Cohen's d was used to calculate and interpret the effect size of the mean differences. The effect size was rated as follows: small (0.2 – 0.5), medium (0.5 – 0.8) and large (> 0.8).

The percentage of individual patients achieving improvements equal to or greater than 50% for every group was calculated to determine the clinical relevance of the improvements in the frequency of the crisis.

Results

Ninety-seven participants (78 women; 19 men) aged 19 to 60 years (39.7 ± 11.5 years; 25.0 ± 3.2 kg/m^2) and diagnosed with TTH were included in this study (Table 1). All the groups were comparable in the clinical and anthropometric variables (p >0.05). The flow diagram is presented in Figure 5.

The mixed model linear analysis revealed significant group*time interaction for PPT in points 1, 2, and 3 (p <0.001), in which patients treated with NMT (group C), soft tissue (group B), or the combination (group D), experienced an increase of 41.7% (d = 0.79), 48.6% (d = 0.71), and 63.5% (d = 0.91), respectively, compared to baseline in PPT1, 44.8% (d = 0.73), 54.0 (d = 0.80), and 63.4% (d = 0.97) in PPT2, respectively, and 63.0% (d = 0.86), 48.6% (d = 0.72), and 67.5% (d = 0.90) in PPT3, respectively (p <0.001). The between-group differences showed that the control group (group A) had statistically significant lower values in all post-intervention measurements compared to the rest of the groups (p <0.001). Also, in PPT_2 and PPT_3, the patients treated with the combined protocol (group D) experienced a significant increase compared to the rest of the groups by the Post, $Post_{15days}$, and $Post_{30days}$ time points (p <0.001) (Table 2). No difference in PPT was found only respect to group B or group C (p>0.05 in all cases).

The mixed model linear analysis revealed significant group*time interaction for frequency and maximal intensity of the crisis of pain (p <0.001), in which patients treated with NMT (group C), STT (group B), and the combined protocol (group D), experienced a maximum reduction of 45.2% (d = 1.7), 47.5% (d = 2.1), and 57.2% (d = 2.1), respectively, compared to baseline measurements in frequency (p <0.001) and a maximum reduction of 37.2% (d = 1.6), 30.0% (d = 1.9), and 43.6% (d = 2.2), respectively, compared to baseline in maximal intensity. The between-group differences showed that the control group had higher values of frequency and maximal intensity compared to the rest of the groups in all the post-intervention measurements (p <0.001) and the group receiving the combined treatment had statistically significant lower values compared to the soft tissue treatment group (p <0.01) (Table 3). Participants who received the sham intervention (group A) also showed significant differences compared to the baseline in frequency, with a reduction of 6.9% (d = 0.2), and maximal intensity, with a reduction of 4.1% (d = 0.2) (p >0.05). No difference in frequency, maximal intensity or Hit-6 was found only respect to group C (p>0.05 in all cases).

Additional analysis to calculate the percentage of individual improvements in frequency of crisis showed that 13 from group B, 14 participants from group C, and 24 participants from group D achieved improvements equal to or greater than 50% in the frequency of crisis after the intervention. No participant from group 1 achieved 50% of improvements in the frequency of the crisis.

Table 3 also shows that the mixed model linear analysis revealed significant group*time interaction for punctuation in the impact questionnaire ($p < 0.001$), with subjects receiving STT (group B), NMT (group C), or the combined treatment (group D) experiencing a maximum reduction of 13.1% (d = 1.48), 13.5% (d = 1.48), and 16.3% (d = 1.57), respectively, compared to baseline measurements. Furthermore, participants who received the sham intervention also showed significant differences, with a reduction of 4.7% (d = 0.53) compared to the baseline ($p < 0.05$). The between-group differences showed that the control group (A), had statistically significant lower values than the rest of the groups in all the post-intervention measurements ($p < 0.001$).

Out of the twenty-one participants who took medication in their crisis episodes during the study period, nine belonged to control group, three to the NMT group, five to the STT group, and four to the combined protocol group. All of these twenty-one patients took medication just once during the study, except four participants in the control group, who took medication during two crisis (3 subjects) or three crisis (1 subject).

Discussion

The main finding of the present study was that four weeks of treatment, combined or not, of soft tissue and NMT, is effective in improving the pressure pain threshold in the head region, maximal intensity and frequency of the pain crisis, and Hit-6 of the TTH patients. However, results showed that the combined treatment is a more effective option in the management of the TTH than these techniques applied separately. These findings support previous studies that determined the combination of SST and mobilization techniques as the best option to manage TTH patients[34] and other types of headaches[35]. In this regard, the NMT combined with SST stimulates the peripheral and central receptors, producing an interaction of the mechanic and neurophysiologic factors that could lead to improvements in the mechanosensitivity of these structures and thus, a reduction in the pain level of patients with TTH[36].

In contrast with previous studies[36-39], a neural mobilization component to the mobilizations was included due to the NMT' ability to activate inhibitory mechanisms that modulate the mechanosensitivity of the neuromusculoskeletal tissues[12-14, 17-20].

In this regard, the most extended theory about the TTH refers to a peripheral process for the episodic TTH, in which one or more neuromusculoskeletal structures are sensitized and send nociceptive inputs to the central nervous system.[40, 41]. This nociceptive inputs from trigeminal nerve and cranio-cervical muscles are integrated in the TCN[42], whose continuous stimulation will sensitize the TCN and the central nervous system[8, 43-46].

Therefore, mechanical stimulation of the neuromusculoskeletal tissues, that send their inputs to the TCN, could decrease these nociceptive inputs and thus the nociceptive information to the central nervous system. Also, this stimulation would activate the inhibitory mechanisms, normalizing the TCN. Also, the decrease of the mechanosensitivity of the nervous tissue can reduce the muscle responses, which intend to protect the nerve tissue against tension and deformation stimulus due to the movement[15, 16].

Previous studies report clinical relevance of the findings when frequency reduction reaches 50%[47]. Therefore, it is important to highlight the number of subjects who achieved a reduction equal or greater than 50% in the frequency of crisis in any of the post-intervention measurements, where group D had the higher number with 24/25 subjects and group A the lower with 0/24 subjects. It must be also taken into account the large effect size and the 57% reduction shown in the frequency of the crisis in patients receiving the combined protocol, in contrast with the 47% and 45% obtained in patients who received soft tissue and NMT separately, respectively. Despite the fact that groups receiving the techniques separately did not reach clinical significance according to previous studies[47], they equaled and even overcame the reduction of 40% that is normally achieved thanks to pharmacologic treatment[48]. Similar results were found in Hit-6 questionnaire, where previous studies reported that the reduction should reach eight points to be clinically relevant[49]. In the present study, the groups receiving the NMT or STT separately reached eight points on the impact questionnaire, while the combined treatment group experienced a reduction of 9.8 points.

Improvements were found even in the control group in variables such as the frequency of the crisis and Hit-6, although with less significant differences and small effect sizes. These improvements could be explained by the observational effect (patients being observed in strict investigations may report better outcomes), the placebo effect, a simple random variation or the normal course of the disorder. These same reasons support similar results obtained in previous studies where the control group also improved in some variables[36, 39].

Apart from the variability of the techniques applied, the nature and location of the structures where the treatment is applied seems to be important[50]. In this way, the current study managed more types and number of structures than most studies involving combined protocols. In this regard, the inclusion of the neural mobilization component may be other important mechanism to reduce the mechanosensitivity of the TCN, but future studies are needed to confirm its importance.

Study limitation

As limitations, our sample included mainly women, which may influence the results. However, epidemiologic studies have determined women are the more prevalent population to suffer any type of tensional-type headache and even a risk factor for this pathology[51]. Therefore, the present study sample may refer to the most representative population suffering TTH. Other limitations refer to the follow-up, which may have been short if taking into account the chronic character of the TTH. Another limitation of our study is the impossibility to blind to the physiotherapists with respect to the interventions that they were applying.

With respect to the medication consumption, we highlight that it mainly referred to the initial days of the intervention period in the groups who received intervention protocols. In this regard, we suggest the local effects of the techniques that could remain any minimal inflammatory process as main reason, or even due to any misunderstanding about the level of pain that the patients should feel. Conversely, on the control group the ibuprofen intake happened during the whole period of the study.

For future studies, it is recommended to increase the duration of follow-up to identify the long-term effects of the treatment, apart from including the NMT in combination with other frequent treatments, such as manipulation or even therapeutic exercise, to obtain the most effective clinical approach to the TTH.

Conclusions

A protocol combining soft tissue and NMT is more effective in the management of FETTH and CTTH patients than the application of these techniques separately.

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FIGURE LEGEND

Figure 1. Soft tissue techniques: (A) Sternocleidomastoid, (B) Upper trapezius, (C) Temporal, (D) Masseter.

Figure 2. Progression of the mobilization in cranio-cervical flexion.

Figure 3. Progression of the lateral cervical sliding.

Figure 4. Opening the mouth in cranio-cervical flexion.

Figure 5. Flow diagram.

Appendix 1. Improvements in individual patients for the frequency of crisis. Those improvements equal to or greater than 50% are showed in red colour.

	Improvement in the frequency of crisis compared to baseline (%)		
Subject Group A	Post	$Post_{15days}$	$Post_{30days}$
#1	0.0	20.0	0.0
#2	20.0	0.0	0.0
#3	28.6	28.6	14.3
#4	-20.0	-10.0	-10.0
#5	7.7	7.7	7.7
#6	-33.3	0.0	-33.3
#7	0.0	0.0	0.0
#8	0.0	16.7	0.0
#9	-25.0	0.0	-25.0
#10	28.6	14.3	0.0
#11	22.2	22.2	11.1
#12	0.0	-20.0	0.0
#13	11.1	22.2	33.3
#14	27.3	18.2	27.3
#15	10.0	0.0	10.0
#16	28.6	14.3	28.6
#17	-40.0	-20.0	0.0
#18	0.0	25.0	0.0
#19	-25.0	-25.0	-75.0
#20	16.7	16.7	33.3
#21	25.0	12.5	12.5
#22	0.0	0.0	12.5
#23	16.7	0.0	0.0
#24	0.0	9.1	0.0

Table 1. Individual percentage of improvement in the frequency of crisis compared to baseline in subjects of group A.

	Improvement in the frequency of crisis compared to baseline (%)		
Subject Group B	Post	$Post_{15days}$	$Post_{30days}$
#1	36.4	45.5	36.4
#2	**60.0**	40.0	**60.0**
#3	**71.4**	**57.1**	**57.1**
#4	45.5	36.4	36.4
#5	44.4	44.4	55.6
#6	**60.0**	**60.0**	**50.0**
#7	41.7	**50.0**	41.7
#8	25.0	37.5	25.0
#9	45.5	45.5	45.5
#10	16.7	33.3	**50.0**
#11	20.0	40.0	40.0
#12	**66.7**	**55.6**	**55.6**
#13	37.5	37.5	37.5
#14	**54.5**	**54.5**	45.5
#15	20.0	40.0	40.0
#16	27.3	27.3	36.4
#17	**50.0**	37.5	25.0
#18	**55.6**	**55.6**	**66.7**
#19	**60.0**	40.0	**60.0**
#20	25.0	25.0	25.0
#21	**70.0**	**60.0**	**50.0**
#22	36.4	45.5	45.5
#23	42.9	**57.1**	42.9

Table 2. Individual percentage of improvement in the frequency of crisis compared to baseline in subjects of group A.

	Improvement in the frequency of crisis compared to baseline (%)		
Subject Group C	Post	$Post_{15days}$	$Post_{30days}$
#1	44.4	44.4	44.4
#2	**66.7**	33.3	16.7
#3	30.0	40.0	40.0
#4	**50.0**	37.5	25.0
#5	40.0	**60.0**	**80.0**
#6	37.5	**50.0**	**50.0**
#7	**77.8**	**55.6**	**55.6**
#8	**80.0**	**80.0**	**60.0**
#9	**57.1**	**57.1**	**71.4**
#10	36.4	36.4	45.5
#11	**85.7**	**71.4**	**57.1**
#12	33.3	33.3	25.0
#13	28.6	42.9	**57.1**
#14	**50.0**	**50.0**	**50.0**
#15	**75.0**	**75.0**	**50.0**
#16	25.0	33.3	33.3
#17	**85.7**	**71.4**	**85.7**
#18	37.5	37.5	37.5
#19	**75.0**	**50.0**	**50.0**
#20	**54.5**	**54.5**	**54.5**
#21	**66.7**	33.3	33.3
#22	22.2	33.3	22.2
#23	27.3	36.4	45.5
#24	46.2	38.5	46.2

Table 3. Individual percentage of improvement in the frequency of crisis compared to baseline in subjects of group A.

	Improvement in the frequency of crisis compared to baseline (%)		
Subject Group D	Post	$Post_{15days}$	$Post_{30days}$
#1	**83.3**	**66.7**	**83.3**
#2	**62.5**	**62.5**	**62.5**
#3	46.2	**53.8**	**61.5**
#4	**60.0**	**60.0**	**80.0**
#5	**62.5**	**50.0**	**50.0**
#6	**57.1**	42.9	**57.1**
#7	44.4	**55.6**	**55.6**
#8	**66.7**	**66.7**	**55.6**
#9	**66.7**	**50.0**	**66.7**
#10	42.9	42.9	42.9
#11	**50.0**	**50.0**	**50.0**
#12	**71.4**	**57.1**	**57.1**
#13	**58.3**	**50.0**	41.7
#14	**60.0**	40.0	**60.0**
#15	**50.0**	**66.7**	**50.0**
#16	41.7	41.7	**50.0**
#17	**54.5**	45.5	36.4
#18	**62.5**	**75.0**	**62.5**
#19	**80.0**	**80.0**	**80.0**
#20	**50.0**	**66.7**	**83.3**
#21	45.5	**54.5**	45.5
#22	**50.0**	33.3	**50.0**
#23	**75.0**	**100.0**	**100.0**
#24	**72.7**	**72.7**	**63.6**
#25	44.4	**55.6**	**55.6**

Table 4. Individual percentage of improvement in the frequency of crisis compared to baseline in subjects of group A.

Variable		Group A (n = 24)	Group B (n=23)	Group C (n=25)	Group D (n=25)
		Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD
Gender	Women	20	17	20	21
	Men	4	6	5	4
TTH	FETTH	14	15	14	13
	CTTH	10	8	11	12
Age (y)		40.5 ± 12.0	38.1 ± 10.9	39.4 ± 11.0	40.8 ± 12.1
Height (m)		1.70 ± 0.07	1.66 ± 0.01	1.64 ± 0.08	1.63 ± 0.06
Weight (kg)		69.2 ± 10.2	68.2 ± 11.8	67.9 ± 12.1	66.3 ± 7.8
BMI (kg/m^2)		25.3 ± 3.0	24.7 ± 3.4	25.1 ± 3.3	24.9 ± 3.0

Group A = no treatment; Group B = soft-tissue treatment; Group C = neural mobilization treatment; Group D = combined treatment; BMI = Body mass index; SD = Standard Deviation.

Table 1. Anthropometric characteristics of participants.

Variable		Group A (n = 24)	Group B (n=23)	Group C (n=25)	Group D (n=25)
		Mean ± DE	Mean ± DE	Mean ± DE	Mean ± DE
PPT_1 (kg/cm^2)	Pre	1.9 ± 0.3	2.1 ± 0.4	2.0 ± 0.3	2.0 ± 0.4
	Post	2.0 ± 0.4*	3.1 ± 0.4¥	2.9 ± 0.3¥	3.2 ± 0.4¥
	$Post_{15days}$	2.0 ± 0.4*	3.1 ± 0.4¥#	2.9 ± 0.4¥	3.2 ± 0.4¥
	$Post_{30days}$	1.9 ± 0.4*	3.0 ± 0.4¥	2.9 ± 0.4¥	3.2 ± 0.4¥
PPT_2 (kg/cm^2)	Pre	1.8 ± 0.3	1.9 ± 0.4	1.9 ± 0.4	2.0 ± 0.3
	Post	1.8 ± 0.4*	2.9 ± 0.5¥	2.8 ± 0.4¥	3.3 ± 0.3*¥
	$Post_{15days}$	1.8 ± 0.4*	2.9 ± 0.5¥	2.8 ± 0.4¥	3.3 ± 0.4*¥
	$Post_{30days}$	1.8 ± 0.4*	2.8 ± 0.5¥	2.8 ± 0.4¥	3.3 ± 0.4*¥
PPT_3 (kg/cm^2)	Pre	1.0 ± 0.3*	1.1 ± 0.3	1.0 ± 0.3	1.2 ± 0.3
	Post	1.0 ± 0.3*	1.6 ± 0.3¥	1.6 ± 0.3¥	2.0 ± 0.4*¥
	$Post_{15days}$	1.0 ± 0.3*	1.6 ± 0.3¥	1.6 ± 0.3¥	2.0 ± 0.4*¥
	$Post_{30days}$	1.0 ± 0.3*	1.6 ± 0.3¥	1.6 ± 0.3¥	2.0 ± 0.4*¥

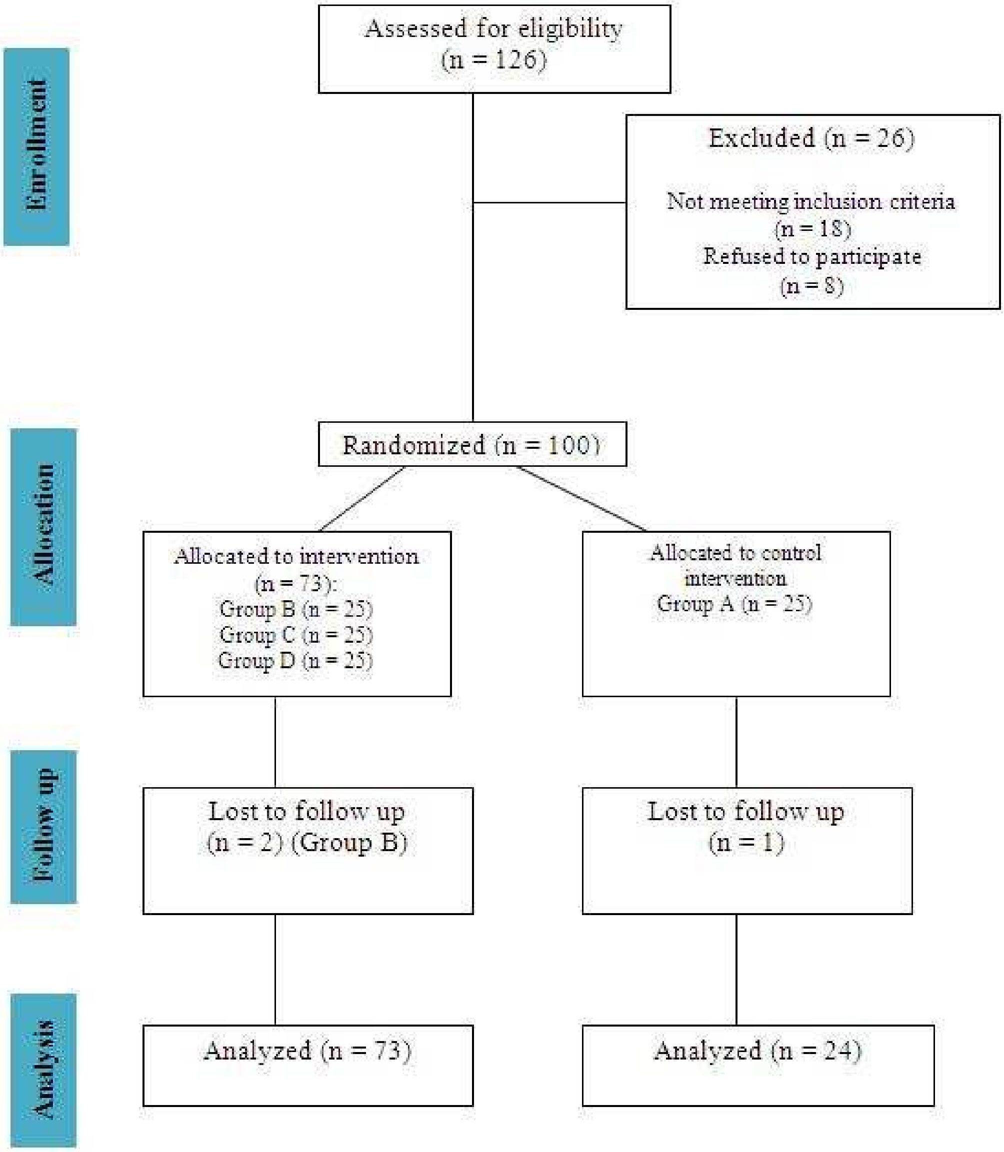
Pre = measurement previous the intervention period; Post = measurement one hour after the intervention period; $Post_{15days}$ = measurement fifteen days after intervention period; $Post_{30days}$ = measurement thirty after the intervention period; Group A = no treatment; Group B = soft-tissue treatment; Group C = neurodynamic treatment; Group D = combined treatment; PPT_1 = Pressure pain threshold in point 1 of the temporal muscle; PPT_2 = pressure pain threshold in the point 2 of the temporal muscle; PPT_3 = Pressure pain threshold in the supraorbital region; * = differences compared to the rest of the groups $p < 0.001$; ¥ = differences compared to the baseline measurement $p < 0.001$; #= differences compared to the previous measurement $p < 0.01$.

Table 2. Values of the pressure pain threshold test in the three points.

Variable		Group A (n = 24)	Group B (n=23)	Group C (n=25)	Group D (n=25)
		Mean ± DE	Mean ± DE	Mean ± DE	Mean ± DE
Frequency (d/15 days)	Pre	7.2 ± 2.7	8.6 ± 2.3	7.9 ± 2.7	8.0 ± 2.6
	Post	6.7 ± 2.5*	4.7 ± 1.7¥	4.2 ± 1.7¥	3.5 ± 1.7¥ ψ
	$Post_{15days}$	6.9 ± 2.5*¥	4.7 ± 1.4¥	4.3 ± 2.2¥	3.5 ± 1.7¥ ψ
	$Post_{30days}$	6.8 ± 2.3*	4.8 ± 1.7¥	4.3 ± 2.2¥	3.4 ± 1.9¥ ψ
Intensity (0-10 points)	Pre	5.6 ± 1.1	4.4 ± 1.1	5.7 ± 0.8	5.1 ± 1.0
	Post	5.4 ± 1.2*¥	2.8 ± 1.0¥	4.0 ± 1.0¥	2.9 ± 1.0¥
	$Post_{15days}$	5.4 ± 1.0*¥	2.8 ± 0.8¥	4.0 ±0.9¥	2.9 ± 1.0¥
	$Post_{30days}$	5.4 ± 1.1*¥	2.8 ± 1.0¥	4.1 ± 0.9¥	3.0 ± 1.1¥
Hit6 (36-78 points)	Pre	60.0 ± 5.9	60.8 ± 5.7	59.0 ± 5.3	59.7 ± 6.0
	Post	57.2 ± 4.5*¥	52.8 ± 5.1¥	51.0 ± 5.5¥	50.0 ± 6.2¥
	$Post_{15days}$	57.5 ± 4.8*¥	52.9 ± 4.7¥#	51.8 ± 5.2¥	50.0 ± 5.7¥
	$Post_{30days}$	57.7 ± 5.5*¥	52.9 ± 5.1¥	51.7 ± 5.4¥	50.3 ± 5.4¥

Pre = measurement previous the intervention period; Post = measurement one hour after the intervention period; $Post_{15days}$ = measurement fifteen days after intervention period; $Post_{30days}$ = measurement thirty after the intervention period; Group A = no treatment; Group B = soft-tissue treatment; Group C = neural mobilization treatment; Group D = combined treatment; d/15 days = days with pain every 15 days; Hit6 = Impact Hit-6 questionnaire; * = differences compared to the rest of the groups $p < 0.001$; ¥ = differences compared to the baseline measurement $p < 0.001$; # = differences compared to the previous measurement $p < 0.001$; ψ = differences compared to group B $p < 0.01$.

Table 3. Values of the frequency and intensity of the crisis of pain and punctuation in the Impact Hit-6 questionnaire.


Enrollment
Allocation
Follow up
Analysis
Assessed for eligibility
(n = 126)
Excluded (n = 26)
Not meeting inclusion criteria
(n = 18)
Refused to participate
(n = 8)
Randomized (n = 100)
Allocated to intervention
(n = 73):
Group B (n = 25)
Group C (n = 25)
Group D (n = 25)
Allocated to control
intervention
Group A (n = 25)
Lost to follow up
(n = 2) (Group B)
Lost to follow up
(n = 1)
Analyzed (n = 73)
Analyzed (n = 24)