Multimodal manual therapy vs. pharmacological care for management of tension type headache: A meta-analysis of randomized trials

Juan A Mesa-Jiménez¹,², Cristina Lozano-López², Santiago Angulo-Díaz-Parreño¹, Ángel L Rodríguez-Fernández¹, Jose L De-la-Hoz-Aizpurua² and Cesar Fernández-de-las-Peñas²,³

Abstract

Background: Manual therapies are generally requested by patients with tension type headache.

Objective: To compare the efficacy of multimodal manual therapy vs. pharmacological care for the management of tension type headache pain by conducting a meta-analysis of randomized controlled trials.

Methods: PubMed, MEDLINE, EMBASE, AMED, CINAHL, EBSCO, Cochrane Database of Systematic Reviews, Cochrane Collaboration Trials Register, PEDro and SCOPUS were searched from their inception until June 2014. All randomized controlled trials comparing any manual therapy vs. medication care for treating tension type headache adults were included. Data were extracted and methodological quality assessed independently by two reviewers. We pooled headache frequency as the main outcome and also intensity and duration. The weighted mean difference between manual therapy and pharmacological care was used to determine effect sizes.

Results: Five randomized controlled trials met our inclusion criteria and were included in the meta-analysis. Pooled analyses found that manual therapies were more effective than pharmacological care in reducing frequency (weighted mean difference –0.8036, 95% confidence interval –1.66 to –0.44; three trials), intensity (weighted mean difference –0.5974, 95% confidence interval –0.8875 to –0.3073; five trials) and duration (weighted mean difference –0.5558, 95% confidence interval –0.9124 to –0.1992; three trials) of the headache immediately after treatment. No differences were found at longer follow-up for headache intensity (weighted mean difference –0.3498, 95% confidence interval –1.106 to 0.407; three trials).

Conclusion: Manual therapies were associated with moderate effectiveness at short term, but similar effectiveness at longer follow-up for reducing headache frequency, intensity and duration in tension type headache than pharmacological medical drug care. However, due to the heterogeneity of the interventions, these results should be considered with caution at this stage.

Keywords

Tension type headache, manual therapy, medication, effectiveness

Date received: 26 November 2014; revised: 9 February 2015; accepted: 14 February 2015

Introduction

In the 21st century, around 42% of the adult population suffers from tension type headache (TTH). In fact, the disability attributable to TTH is larger worldwide than that due to migraine headache (1). Among the different headaches, probably TTH is one of the most common, but also the most neglected, forms (2).
Several therapeutic approaches are proposed for the management of TTH with pharmacological drugs, physical/manual therapy and relaxation/cognitive therapies the most commonly used (3). In fact some meta-analyses support a small benefit of tricyclic antidepressants (4), botulinum toxin A (5) and acupuncture for the management of TTH and migraine (6,7). Nevertheless, Eisenberg et al. concluded that alternative medicine use increased substantially in individuals with chronic pain conditions, including back problems and headaches (8), chiropractic, acupuncture and massage being the treatment most requested by patients with TTH (9). In fact, the clinical guidelines on the treatment of TTH by European Federation of Neurological Societies has concluded that physical therapy, although scientific basis is limited, should be considered for the management of this disorder in conjunction with pharmacological drugs (10).

Different systematic reviews have investigated the effectiveness of different physical therapy interventions including spinal manipulation, soft tissue therapies and dry needling for the management of TTH (11–15). All these reviews concluded that the effectiveness of physical therapy for TTH cannot be completely determined due to the heterogeneity in treatments applied and their comparison groups. To first estimate the effectiveness of physical/manual therapy, it is a determining factor to compare their results with the most commonly treatment applied for TTH, pharmacological medication.

To the best of the authors’ knowledge, no meta-analysis of manual therapies in TTH has been conducted yet. To establish whether manual therapies, without distinction of specific targeted-tissue therapeutic intervention, has specific efficacy compared with pharmacological drugs in the management of TTH, we undertook the first meta-analysis comparing efficacy of manual therapy in isolation or combined with exercises had been used for management of TTH; (ii) the comparison group had to receive medical pharmacological drug medication; (iii) the interventions should be properly described in the trial; (iv) the trial should report changes in at least one clinical headache parameter including headache frequency, headache intensity or headache duration as the main outcome.

**Inclusion criteria for article selection**

Articles chosen to go through the selection process were independently reviewed by two authors. All randomized controlled clinical trials (RCTs) investigating manual therapy vs. pharmacological medication care for treating TTH were included. Therefore, papers were included if they met the following inclusion criteria: (i) they had to describe a RCT in which any form of manual therapy in isolation or combined with exercises had been used for management of TTH; (ii) the comparison group had to receive medical pharmacological drug medication; (iii) the interventions should be properly described in the trial; (iv) the trial should report changes in at least one clinical headache parameter including headache frequency, headache intensity or headache duration as the main outcome.

**Data extraction**

Data from each study were extracted independently by two of the authors. A standardized data extraction form containing questions on population, interventions, study methods, results and outcomes was used according to the CONSORT statement (16). For each study, the following data were taken: inclusion and exclusion criteria; randomization; sample size; dropouts; blinding patients or assessors; outcome measures; interventions; results; follow-up periods. Finally, both authors had to achieve a consensus on each item of the data extraction form.

**Assessment of methodological quality**

The methodological quality of each trial was assessed using the PEDro critical appraisal scoring system by two reviewers. This scale scores studies depending on the presence/absence of 10 methodological criteria: random allocation; concealed allocation; baseline comparability; blinded assessors; blinded subjects; blinded therapists; adequate follow-up; intention-to-treat analysis; between-group comparisons; point estimates and variability (17). Foley et al. reported that the PEDro scale exhibits excellent inter-rater reliability for assessing methodological quality of RCT including...
pharmacological interventions (Intra-class correlation coefficient (ICC) 0.89, 95% confidence interval (CI) 0.78–0.95) and non-pharmacological interventions (ICC 0.91, 95% CI 0.84–0.95) (18).

**Statistical analysis**

Because headache outcomes varied among studies, we preferentially pooled data on headache clinical parameters in the following order, according to the recommendations of the reviewers of Cochrane protocol and following International Headache Society (IHS) recommendation: headache frequency; headache intensity; headache duration (19). Headache frequency was expressed as the number of days per month with pain; headache intensity was abstracted in the scale used by each trial; whereas headache duration was recorded as the hours per day with headache.

The meta-analytic comparison was based on the mean difference change in the headache clinical parameter (frequency, intensity or duration) from baseline to follow-up of individuals receiving manual therapy vs. those receiving pharmacological drug medications. We required outcomes to be self-reported by the patients. Outcomes were typically obtained from a headache diary or on examination. When both were available, we chose the average from the headache diary.

To combine outcomes, we used weighted mean difference (WMD) for each headache clinical outcomes. We performed a funnel plot by plotting the WMD against study weight for all trials included in the meta-analysis. The funnel plot was inspected visually and the Egger linear regression method (20) was used to test for plot symmetry. We assessed heterogeneity statistically with Q statistics (21). All analyses were performed using the STATA program (version 14.0).

**Results**

**Search**

Our search of the electronic databases located 80 publications for review. Fifty-six publications did not fit the inclusion criteria, based on examination of titles or abstracts. Another 19 studies were excluded based on full-text review particularly because manual therapies where combined with other physical therapeutic modalities. Therefore, five trials met all inclusion criteria and reported sufficient outcome data for a meta-analysis (Figure 1) (22–26).

**Included trials**

All the included trials used parallel group design and were in English. A total of 206 patients (mean size: 41 ± 23 patients, 79% female) were enrolled across the five studies (Table 1). Four studies used the 2004 criteria of the IHS for TTH (22–25), whereas one did not specify the criteria (26). Four studies included chronic headaches (22–24,26) and one was specifically conducted on frequent episodic TTH (25). Duration of treatment ranged from 4 to 6 weeks with 5–12 manual therapy sessions (mean: 7.6 ± 3 sessions). Manual therapy programmes included different treatment approaches: mobilization or manipulation of the spine; low-load stabilization exercises; soft tissue pressure release; postural correction/awareness (22–26). Pharmacological drug intervention followed accepted guidelines and was administered for the same time period than manual therapy. Most studies combined prophylactic treatment (i.e. tricyclic antidepressants) and acute therapy consisting of non-steroidal anti-inflammatory drugs. Outcomes included frequency ($n = 4$), intensity (all studies) and duration ($n = 4$) of the headache. All, except one trial (26), used a headache diary for 2 weeks to assess headache clinical parameters. All studies included an immediate follow-up period after the interventions, whereas three trials (22,24,26) included a follow-up period ranging from 18 to 24 weeks (mean: 21 ± 3 weeks) after the intervention. The details of all included trials are detailed in Table 1.
<table>
<thead>
<tr>
<th>Country</th>
<th>Setting</th>
<th>Diagnosis</th>
<th>Sample (n)</th>
<th>Treatments</th>
<th>Outcomes</th>
<th>Sessions</th>
<th>Follow-up</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Castien et al.,</td>
<td>The Netherlands</td>
<td>Chronic TTH</td>
<td>82 subjects</td>
<td>(A) Medication care (MC) intervention: following the Dutch general practice guideline for headache treatment: analgesics, NSAIDs or changed current pain medication</td>
<td>Primary: Headache frequency, intensity and duration (2 week diary)</td>
<td>2–3 visits during an 8-week period</td>
<td>Baseline, immediately after treatment</td>
<td>Primary: Significant differences in favour of the MT immediately after (8 weeks) for frequency (–6.4 days; 95% CI –8.3 to –4.6), duration (–5.3 hours, –9.5 to –1.2 hours) and intensity (–1.8, –3.1 to –0.7) of headache, and 26 weeks after for frequency (–4.9 days, –6.95 to –2.98) and intensity (–1.4, –2.7 to –0.2) of headache.</td>
</tr>
<tr>
<td>2011 (22)</td>
<td>Primary healthcare centres and private settings in an urban area</td>
<td>according to the IHS-II criteria</td>
<td>(18 men/64 women)</td>
<td></td>
<td>Secondary: HDI, HIT-6, active CROM, PPT upper trapezius, endurance of the neck flexors and GROC</td>
<td>(B) Manual therapy (MT): mobilizations of the cervical and thoracic spine, exercises and postural corrections</td>
<td>8–9 sess. max of 30 min (during 8-week period)</td>
<td>(8 weeks), and 26 week after randomization</td>
</tr>
<tr>
<td>De Hertogh et al.,</td>
<td>Belgium Outpatient clinics of neurology department of hospital</td>
<td>Chronic TTH</td>
<td>37 subjects</td>
<td>(A) MC intervention: following the Dutch general guideline for headache: NSAIDs or analgesics in a stepped progression</td>
<td>Primary: HIT-6, global perceived effect</td>
<td>2–3 visits during a 6-week period</td>
<td>Baseline, immediately after treatment</td>
<td>Primary: No significant differences between groups for HIT-6 (mean score between-group difference &lt; 3.5 points, ( P &gt; 0.05 )) at all follow-ups</td>
</tr>
<tr>
<td>2009 (24)</td>
<td>according to the IHS-II criteria (migraine was also permitted)</td>
<td></td>
<td>(9 men/28 women)</td>
<td></td>
<td>Secondary: Headache frequency (percentage)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(continued)
Table 1. Continued.

<table>
<thead>
<tr>
<th>Country</th>
<th>Setting</th>
<th>Diagnosis</th>
<th>Sample (n)</th>
<th>Treatments</th>
<th>Outcomes</th>
<th>Sessions</th>
<th>Follow-up</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hsieh et al., 2010 (26)</td>
<td>Taiwan Medical urban hospital</td>
<td>Chronic headache (no subtype specified)</td>
<td>28 subjects (11 men/17 women)</td>
<td>(A) MC intervention: analgesics NSAIDs or muscle relaxant at neurologist discretion</td>
<td>Primary: Headache intensity (visual analogue scale)</td>
<td>(A) 1–2 visits during a 4-week period</td>
<td>Baseline, immediately after treatment</td>
<td>Primary: Significant differences in favour of the MT immediately after (between-group diff.: –23, P = 0.047) and 24 weeks after between-group diff.: –42, P = 0.002) for headache intensity</td>
</tr>
<tr>
<td>Ghanbari et al., 2005 (25)</td>
<td>Iran Neurology clinic</td>
<td>Frequent Episodic TTH according to the IHS-II criteria</td>
<td>30 subjects (2 men/28 women)</td>
<td>(A) MC intervention: routine medication including NSAID as abortive drugs and tricyclic antidepressants as prophylactic drugs</td>
<td>Primary: Headache frequency, intensity and duration (2 week diary)</td>
<td>A) Routine medication for 4-week period</td>
<td>Baseline and immediately after the treatment phase</td>
<td>Primary: No significant differences between groups were found for frequency (between-group diff.: –3.7 days, P = 0.5), duration (between-group diff.: –3.9 hours, P = 0.5), and intensity (between-group diff.: –0.5, P = 0.064) of headache.</td>
</tr>
<tr>
<td>Foster et al., 2005 (23)</td>
<td>United States of America</td>
<td>Chronic TTH according to the IHS-II criteria (migraine was also permitted)</td>
<td>29 subjects (3 men/26 women)</td>
<td>(A) MC intervention: routine medication</td>
<td>Primary: Headache frequency, intensity and duration (2 week diary)</td>
<td>(A) Routine medication for 6-week period, no medical supervision</td>
<td>Baseline and immediately after the treatment phase</td>
<td>Primary: Significant difference in favour of the MT for headache duration (between-group diff.: –1.5 hours, P &lt; 0.05). A trend for decrease in headache frequency in favour of the MT was found (27.5% reduction). No changes in headache intensity were observed.</td>
</tr>
</tbody>
</table>

(continued)
Table 1. Continued.

<table>
<thead>
<tr>
<th>Country</th>
<th>Setting</th>
<th>Diagnosis</th>
<th>Sample (n)</th>
<th>Treatments</th>
<th>Outcomes</th>
<th>Sessions</th>
<th>Follow-up</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medicine Centre</td>
<td>from a School Medicine</td>
<td></td>
<td></td>
<td>(B) MC plus medical attention: routine medication regulated by the medical doctor</td>
<td>(B) Secondary: Headache-related quality of life, medication intake</td>
<td>(B) 1 session a week for 6-week period</td>
<td>(weekly for headache diary)</td>
<td>Secondary: Significant differences in favour of the MT group were found for headache quality of life ($P &lt; 0.01$) and medication usage ($P = 0.04$)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(C) MT: Trager therapy consisting of a movement-based educational process to help patients increase their body awareness, learn relaxation skills and practise pain-free, balanced movement. All process is induced by manual therapy conducted by the practitioner</td>
<td>(C) 6 sessions of 60 min (for 6-week period, 1 per week)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

TTH: tension type headache; NSAIDs: non-steroidal anti-inflammatory drugs; Mob: mobilization; Man: manipulation; HIT-6: Headache Impact Test-6; HDI: Headache Disability Inventory; GROC: general rate of change; CROM: cervical range of motion; PPT: pressure pain thresholds.
Methodological quality

Methodological quality scores ranged from 4 to 8 points (mean: 5.8 ± 1.6) from a maximum of 10 points (Table 2). Only two studies reported the method of allocation concealment (22,24). None was trial blinded patients or therapist, whereas only one blinded the outcome assessors (22). Table 2 shows the details of the PEDro scale items and the total score of all studies.

Treatment efficacy on headache outcomes

For the frequency of headache, only immediate effects of the intervention could be calculated. Manual therapy was more effective than pharmacological medical care in reducing headache frequency immediately after intervention (WMD –0.8036, 95% CI –1.66 to –0.44; three trials, Figure 2). The pooled data for headache days/month were statistically significant (P < 0.001) and passed the test of heterogeneity (Q = 1.943; P = 0.378).

For headache intensity, both immediate and short-term (20 weeks) effects were calculated. Similarly, manual therapy was more effective than pharmacological medical care in decreasing headache intensity immediately after (WMD –0.5974, 95% CI –0.8875 to –0.3073; five trials, Figure 3(a)), which was statistically significant (P < 0.001) and passed the test of heterogeneity (Q = 3.5022; P = 0.174).

Discussion

The results of the current meta-analysis suggest that manual therapy seems to be more effective than pharmacological medical care for reducing the frequency, intensity and duration of the headache at short term in individuals with TTH. Nevertheless, there were no differences at a longer follow-up period (24 weeks) on headache intensity.

It is difficult to directly compare our results with prior systematic reviews, because, to our knowledge, this is the first meta-analysis on this topic. Current

Table 2. PEDro score rates of randomized clinical trials included in the meta-analysis.

<table>
<thead>
<tr>
<th>Study</th>
<th>Random Alloc</th>
<th>Conce Alloc</th>
<th>Basel Comp</th>
<th>Blind Assessors</th>
<th>Blind Subjects</th>
<th>Blind Therapist</th>
<th>Follow up</th>
<th>Intention to treat analysis</th>
<th>Between-group Comp</th>
<th>Points estimates and Variability</th>
<th>Total score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Castien et al., 2011 (22)</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>NO</td>
<td>NO</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>8/10</td>
</tr>
<tr>
<td>De Hertogh et al., 2009 (24)</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>7/10</td>
</tr>
<tr>
<td>Foster et al., 2005 (23)</td>
<td>YES</td>
<td>NO</td>
<td>YES</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>5/10</td>
</tr>
<tr>
<td>Hsieh et al., 2010 (26)</td>
<td>YES</td>
<td>NO</td>
<td>YES</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>5/10</td>
</tr>
<tr>
<td>Ghanbari et al., 2005 (25)</td>
<td>YES</td>
<td>NO</td>
<td>YES</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>4/10</td>
</tr>
</tbody>
</table>

Alloc: allocation; Conce: concealed; Basel Comp: baseline comparability; Comp: comparisons; Varia: variability.

Figure 2. Effect of manual therapy on headache frequency for tension type headache compared with pharmacological medical care.
results disagree with previous systematic reviews conducted on different manual therapies in TTH (11–15). All these reviews concluded that the effectiveness of manual therapy is not justified by the literature due to the heterogeneity in the treatments applied and their comparison groups. In the current meta-analysis, we found a moderate effect size, only at short-term follow-up, in favour of manual therapy. These discrepancies can be related to the fact that previous studies included in these reviews used several comparison groups, whereas we only included pharmacological medical care as the comparative treatment. However, we recognize that we pooled data from several manual therapies, including exercises, targeting different tissues, so we cannot determine which particular intervention is more effective for the management of TTH.

Previous meta-analyses have investigated the effectiveness of pharmacological drugs vs. placebo for the management of TTH (4,5). The reported efficacy (WMD) for tricyclic antidepressants was –1.29 (95% CI –2.18 to –0.39) for decreasing headache frequency; however, tricyclics were more likely to cause adverse effects (1.53, 95% CI 1.11–2.12) than placebo (4). Conversely, botulinum toxin A was not significantly associated (–1.43; 95% CI –3.13 to 0.27) with a reduction in headache frequency (5). The effect sizes in our meta-analysis were all moderate (0.55 < WMD < 0.88) and significant, suggesting that manual therapy is associated with a higher benefit than pharmacological medical care for TTH, at least, at short term. Nevertheless, direct comparisons between different meta-analyses should be conducted with caution. In fact, the comparison group

<table>
<thead>
<tr>
<th>Study ID</th>
<th>Year</th>
<th>Exposed</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foster et al</td>
<td>11/43,4/17,1</td>
<td>6/39,7/21,6</td>
<td>8.46%</td>
</tr>
<tr>
<td>Hoieh et al</td>
<td>14/39,2/26</td>
<td>14/55,7/28,7</td>
<td>14.62%</td>
</tr>
<tr>
<td>Causten et al</td>
<td>41/3,6/1,9</td>
<td>41/4,8/1,5</td>
<td>42.26%</td>
</tr>
<tr>
<td>De Hertogh et al</td>
<td>18/15,3/24,3</td>
<td>19/31,9/29,4</td>
<td>19.30%</td>
</tr>
<tr>
<td>Ghanbari A et al</td>
<td>15/5/2,5</td>
<td>15/6,4/7,1</td>
<td>15.35%</td>
</tr>
</tbody>
</table>

Figure 3. Effect of manual therapy on headache intensity for tension type headache compared with pharmacological medical care immediately after the intervention (top) or at longer (24 weeks) follow-up (bottom).

<table>
<thead>
<tr>
<th>Study ID</th>
<th>Year</th>
<th>Exposed</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foster et al</td>
<td>11/41,5/17,1</td>
<td>14/57,3/17,7</td>
<td>21.02%</td>
</tr>
<tr>
<td>Causten et al</td>
<td>41/3,2/1,9</td>
<td>41/4,8/1,5</td>
<td>26.69%</td>
</tr>
<tr>
<td>De Hertogh et al</td>
<td>18/19,3/29,9</td>
<td>19/31,5/24,2</td>
<td>24.32%</td>
</tr>
<tr>
<td>Boline et al</td>
<td>70/4,3/2,7</td>
<td>56/3,2/3,3</td>
<td>27.77%</td>
</tr>
</tbody>
</table>

Figure 4. Effect of manual therapy on the duration of the headache for tension type headache compared with pharmacological medical care.
in most of the trials combined prophylactic and acute drug management; therefore, we cannot give clear conclusions on which pharmacological treatment was responsible for the changes in the outcomes.

We found that at a longer follow-up (20 weeks), no differences existed between manual therapy and pharmacological medical care for reducing headache intensity. This is expected since the effect of drug treatment seems to increase over time (4). Patients treated with manual therapy stopped the management at the end of the treatment period, but those receiving pharmacological medical care may continue with ‘needed’ intake.

Manual therapies included in the current meta-analysis were variable among the studies, but the following showed a common denominator: spinal manipulation/mobilization; soft tissue intervention/exercise. A combination of these interventions seems to be justified by several theories supporting the role of musculoskeletal disorders in TTH (3,27,28). This may explain why previous systematic reviews investigating the effectiveness of isolated interventions, i.e. spinal manipulation (11,12), did not reach firm conclusions.

Strengths of the current meta-analysis include its methodological rigor, the care taken in design (inclusion/exclusion criteria), data extraction, homogeneous comparison groups and data analysis. Nevertheless, some potential limitations should be recognized. First, there were relatively few studies and 75% of the studies included a small sample size. Second, four studies (75%) included patients with chronic headache whereas one included subjects with frequent episodic TTH. Considering the variation between TTH subtypes’ response to medication, further subgroup analysis is an area for potential future investigation of manual/physical therapy for TTH. Third, based on international guidelines (19), we chose the frequency of headache as the primary outcome. The restriction of our analysis to the specific clinical outcomes of headache frequency, intensity and duration is a potential limitation. The inclusion of additional pooled outcomes, such as analgesic consumption and measures of function or pressure pain sensitivity, would add likely relevant information for the review. Our review of the literature suggests that available trials do not provide sufficient data for pooling these outcomes at this time. Fourth, most trials included relatively short follow-up periods, particularly since TTH tends to be chronic. The average duration of the trials in our meta-analysis was 4 weeks and the longest only 30 weeks after randomization. Fifth, it is impossible to tell from our data what the optimal dose for either intervention is. Meta-analysis is limited by the problem of aggregate data. Optimal therapeutic dosing is a question that should be answered in future studies. Finally, as we have pointed out, due to the heterogeneity of both interventions, manual therapies and pharmacological drug, these results should be considered with caution at this stage.

Despite these limitations, our meta-analysis shows the efficacy of manual therapy in people with TTH. The benefit seems moderate to large in magnitude. Helpful studies would be those that determine whether particular subgroups of patients are more likely to respond to manual therapies, such as those with higher musculoskeletal disorders. It would also be useful to better define more effective manual therapy regimens, in terms of treatment sessions, treatment duration or interaction with other interventions.

**Conclusion**

This meta-analysis suggests that manual therapy seems to be more effective than pharmacological medical care for reducing the frequency, intensity and duration of the headache at short term in patients with TTH. No differences at longer follow-up period (24 weeks) on headache intensity were observed. However, due to the heterogeneity of both interventions, manual therapies and pharmacological drugs, these results should be considered with caution at this stage. Future research is needed to further determine the effectiveness of specific manual therapies for the management of TTH and to determine whether particular subgroups of TTH patients are more likely to respond to manual therapy or pharmacological drug management.

**Clinical implications**

- There is evidence suggesting that manual therapy seems to be more effective at short term but equally effective at longer follow-up than pharmacological drug treatment for reducing the frequency, intensity and duration of the headache in tension type headache.
- Future research is needed to determine the effectiveness of specific manual physical therapies for the management of tension type headache and to determine if particular subgroups of patients are more likely to respond to either intervention.
Conflict of interest
None declared.

Funding
This work received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

References
2. Bendtsen L and Jensen R. Tension type headache: the most common, but also the most neglected headache disorder. *Curr Opin Neurol* 2006; 19: 305–309.