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Research Submissions

The Impact of Spinal Manipulation on Migraine Pain and Disability: A Systematic Review and Meta-Analysis

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Background.—Several small studies have suggested that spinal manipulation may be an effective treatment for reducing migraine pain and disability. We performed a systematic review and meta-analysis of published randomized clinical trials (RCTs) to evaluate the evidence regarding spinal manipulation as an alternative or integrative therapy in reducing migraine pain and disability.

Methods.—PubMed and the Cochrane Library databases were searched for clinical trials that evaluated spinal manipulation and migraine-related outcomes through April 2017. Search terms included: migraine, spinal manipulation, manual therapy, chiropractic, and osteopathic. Meta-analytic methods were employed to estimate the effect sizes (Hedges' *g*) and heterogeneity (I^2) for migraine days, pain, and disability. The methodological quality of retrieved studies was examined following the Cochrane Risk of Bias Tool.

Results.—Our search identified 6 RCTs (pooled n = 677; range of n = 42-218) eligible for meta-analysis. Intervention duration ranged from 2 to 6 months; outcomes included measures of migraine days (primary outcome), migraine pain/intensity, and migraine disability. Methodological quality varied across the studies. For example, some studies received high or unclear bias scores for methodological features such as compliance, blinding, and completeness of outcome data. Due to high levels of heterogeneity when all 6 studies were included in the meta-analysis, the 1 RCT performed only among chronic migraineurs was excluded. Heterogeneity across the remaining studies was low. We observed that spinal manipulation reduced migraine days with an overall small effect size (Hedges' $g = -0.35$, 95% CI: −0.53, −0.16, $P < .001$) as well as migraine pain/intensity.

Conclusions.—Spinal manipulation may be an effective therapeutic technique to reduce migraine days and pain/intensity. However, given the limitations to studies included in this meta-analysis, we consider these results to be preliminary. Methodologically rigorous, large-scale RCTs are warranted to better inform the evidence base for spinal manipulation as a treatment for migraine.

Key words: spinal manipulation, migraine, pain, disability

Abbreviation: RCTs randomized clinical trials

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BACKGROUND

Thirty-eight million adults in the United States are estimated to be migraine sufferers; of these, 91% experience migraine-associated disability.[1-3] Traditionally, abortive and prophylactic medications are first-line treatment for migraine therapy, with most migraineurs treating their headaches at the onset of symptoms.[2] However, approximately 40% of those with episodic migraine have unmet treatment needs.[4] Of these patients, one-third report dissatisfaction with current treatment and about half report moderate or severe headache-related disability.[4] In addition, commonly prescribed rescue medications (eg, analgesics, ergots, triptans, and opioids) may increase the risk of medication overuse headaches, allodynia, and dependence.[5] The limitations to current pharmacological therapies have highlighted the need to explore alternative or integrative treatments for migraine.

One potential non-pharmacological approach to the treatment of migraine patients is spinal manipulation, a manual therapy technique most commonly used by doctors of chiropractic, but also practiced by some physical therapists and osteopathic physicians. A recent cross-sectional survey using data from the US National Health Interview Survey estimated that approximately 15.4% of individuals with migraine have used chiropractic care (which can include spinal manipulation) in the past 12 months.[6] Given the prevalence of migraine, this may translate into a substantial disease burden in chiropractic care clinics because 94% of spinal manipulation for which reimbursement is sought in the United States is delivered by chiropractors.[7] For example, a survey of Australian chiropractors found that 53% of chiropractors reported managing patients with migraine "often" and 40.9% of chiropractors reported managing patients with migraine "sometimes."[8] In the United States, approximately 12% of patients seeking treatment from a chiropractor report headache as their chief complaint.[9] Given the prevalence of migraine patients seeking chiropractic care and the need for evidence-based non-pharmacological approaches to treat migraine, there is a need to understand whether spinal manipulation, an integral component to chiropractic care, is an effective non-pharmacological approach for the treatment of migraine headaches.

Three systematic reviews have examined the effects of spinal manipulation on migraine,[10-12] but these reviews included only 3 randomized controlled trials[13-15] and did not include a meta-analysis of the effects seen in these studies. Since the publication of these reviews, additional randomized controlled trials on spinal manipulation have been conducted.[16-18] The aim of this study is to provide a synthesis of available clinical trials using a systematic review and to perform a preliminary meta-analysis examining the effects of spinal manipulation on migraine frequency, pain, and disability.

METHODS

Literature Search and Inclusion Criteria.—Our literature search strategy and inclusion criteria were specified a priori. In accordance with PRISMA guidelines, we searched the Cochrane Library and PubMed, which includes MEDLINE, for relevant articles from inception through April 2017. The following search terms were used: spinal manipulation, osteopathic, chiropractic, manual therapy, and migraine. The search was limited to articles identified as clinical trials in PubMed. To expand the selection, we also manually searched the reference lists of all retrieved articles.

Eligibility Criteria.—We included randomized clinical trials (RCTs) where the primary intervention

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was spinal manipulation and the primary disorder investigated was migraine headaches. No exclusions were made on the basis of provider type (eg, chiropractic vs osteopathic) or area of the spine manipulated.

Data Extraction and Syntheses.—Data were extracted independently by 2 researchers (AH, RS) utilizing a standardized template generated in Microsoft Excel. Admissible data included the study design, duration and frequency of the intervention, sample size, type of control, and outcome measures. The decisions about what data to extract were made a priori.

Quality Assessment.—Three authors (AH, KO, PR) individually assessed the methodological quality of RCTs using the 7-item Cochrane Collaboration Tool for assessing risk of bias.[19] The criteria were selected a priori and included: (1) random sequence generation, (2) allocation concealment, (3) blinding of participants, (4) blinding of outcome assessment, (5) incomplete outcome data, (6) selective reporting (including reporting of all outcomes and specifying a primary outcome), and (7) other bias. For "other bias," we evaluated the studies for the following criteria: group similarity at baseline with regard to the outcome measures, similarity in co-intervention, compliance, timing of outcome assessments, rationale for sample size, rationale for control group, and intervention description (see Supplemental Table 1 for full descriptions of these items). Per established criteria, the evaluated domains were judged as low risk, high risk, or unclear bias. In the case of evaluation discrepancies, the authors discussed and came to an agreement.

Safety Monitoring.—We reviewed the studies for the inclusion of formal protocols that methodically monitored adverse events, and whether any adverse events reported were a direct result of the intervention.

Data Analysis and Syntheses.—For each study, the mean and standard deviation (SD) values at baseline and post-intervention for the primary and secondary outcomes were extracted. Other data extracted included *t* score or *P* value between groups and the sample size (N) in each group. If such data were not available, the standard error values, confidence intervals, or medians with interquartile ranges were translated into mean and SD following suggested statistical formulas.[19,20] The most common outcomes assessed across all studies were migraine days and measures of migraine-related pain and disability. Migraine days was used as our primary outcome.

Effect sizes (Hedges' *g*) and 95% confidence intervals using random and fixed effects models were calculated by Comprehensive Meta-Analysis Version 3.0 software (CMA v3, Biostat, Inc., Frederick, MD, USA). Effect sizes of 0.2, 0.5, and 0.8 are considered small, medium, and large, respectively.[21] Heterogeneity was assessed by calculating the Q value and I^2 statistics. A low P value for the Q statistic or an I^2 ratio greater than 75% indicated heterogeneity across the studies. The pooled effect sizes for the most common outcomes were calculated. For the primary analyses, we calculated pooled effect sizes comparing the intervention group to all possible control groups. If an article had 2 different control groups, the sample size of the intervention group was divided by 2 to avoid overweighting the study. In secondary analyses, subgroup analyses were performed for active controls and passive controls.

RESULTS

Study Selection and Characteristics.—Our literature search is summarized in Figure 1. The initial search identified 76 clinical trials. The titles and abstracts were assessed for inclusion. After the removal of duplicate records, 48 remained for further assessment. Of those, 21 were not RCT studies and 1 text was unavailable in English. The remaining 26 studies were further assessed for eligibility. Of the remaining clinical trials, 19 did not use spinal manipulation as a treatment and 1 did not present original data. The 6 remaining clinical trials[13-18] were included in the overall quantitative synthesis, 3 of which have been included in previous systematic reviews.[13-15] Two of the trials were registered in clinicaltrials.gov.[16,17]

Participant Characteristics and Study Setting.—The 6 clinical trials identified in our literature review are summarized in Table 1. A total of 677 patients were randomized into these studies; 670 patients had baseline assessments and could be included in analyses. The average age of participants at baseline was

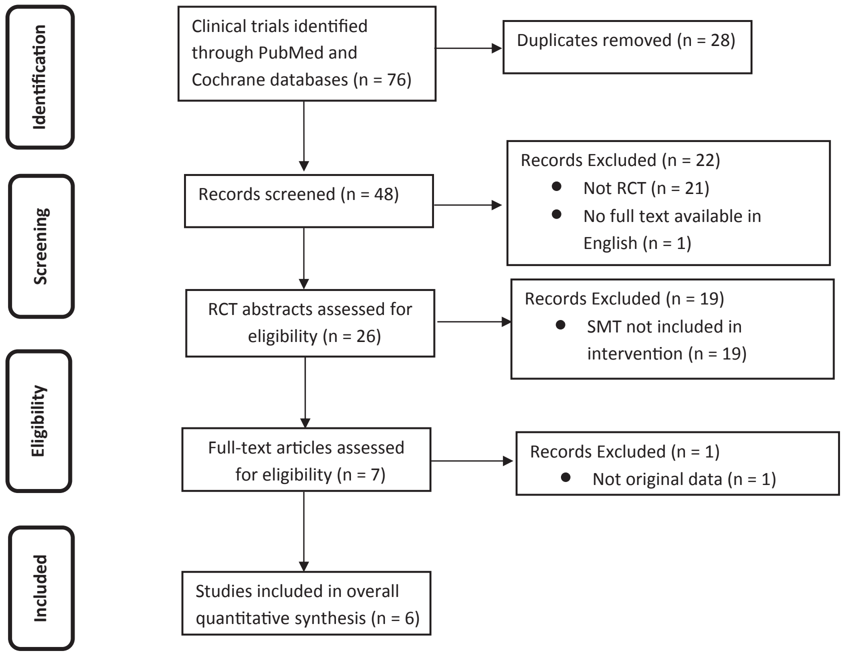

Fig. 1.—Study identification process following PRISMA guidelines. SMT = spinal manipulation therapy.

39.3 years and 75.0% were female. All studies allowed patients to continue use of their current medications. Five studies enrolled episodic migraine patients and the minimum number of migraine attacks per month needed to be eligible ranged from 1 to 4.[13-15,17,18] Only 1 study enrolled patients diagnosed with chronic migraine according to ICHD-II criteria.[16]

Intervention and Control Group Characteristics.— All studies used a parallel-arm design in which participants were assigned to a spinal manipulation treatment group or to a control group (either active or passive controls). While there was heterogeneity in the specific type of spinal manipulation techniques used in each study, the techniques used in the treatment groups were applied with the intent to influence the function of joints and the tautness of soft tissue. The spinal manipulations were performed by a chiropractor in 3 studies,[13,15,17] an osteopathic physician in 2 studies,[16,18] or by either a medical practitioner, physiotherapist, or chiropractor in 1 study.[14] The duration of the intervention ranged from 2 to 6 months, with the number of treatments ranging from 8 to 16. The type of control group used varied across the studies. Five of the 6 studies employed active controls where the intervention group was compared to sham therapy,[16,17] cervical mobilization (movement of joints within normal limitations),[14] detuned interferential therapy (which served as a "placebo" therapy),[15] or a combination of spinal manipulation and amitriptyline treatment.[13] In addition to having an active control, 3 studies also contained a second "passive" control arm where patients were allowed to either continue usual pharmacological therapy,[17] change medications as their physician directed,[16] or were assigned to take amitriptyline.[13] The sixth study only used a "passive" control group and compared those receiving the intervention to those not receiving spinal manipulation, sham treatment, or physical therapy.[18] In this study, all participants were allowed to continue their previously prescribed medications.[18]

Outcome Measures.—Of the 6 studies, 5 assessed their outcomes through the use of migraine diaries.[13-17] In addition to using migraine diaries, 2 studies also administered questionnaires to assess some outcomes at set time points during the study.[13,16] One study only assessed outcomes through questionnaires.[18] Migraine days per month or the frequency of migraine attacks was assessed in all studies and was our primary outcome. We also analyzed migraine intensity or migraine pain[13-18] and measures of migraine disability.[14-16,18]

Table 1.—Characteristics of Included Studies

Main Author (country)	Study Type	Sample	Gender (M/F)	Intervention	Number of Treatments	Duration (months)	Control Group	Measured Outcomes
Cerritelli 2015 (Italy)	RCT	105	36/69	SM	8	6	(1) Sham + medication (2) medication only	HIT-6*, migraine days, pain intensity, medication use, functional disability
Chaibi 2017 (Norway)	RCT	104†	14/83	SM	12	3	(1) Sham (2) Usual pharmacological management	Migraine days*, duration*, intensity, headache index*, medication use
Voigt 2011 (Germany)	RCT	42	00/42	SM	5	2.5	Usual pharmacological management	MIDAS*, SF-36 (some domains*), German "Pain Questionnaire"*, HRQOL, migraine days, pain intensity*
Tuchin 2000 (Australia)	RCT	123	39/86†††	SM	16	2	Detuned interferential therapy (placebo)	Migraine frequency*, intensity, duration*, disability*, associated symptoms, medication use*
Nelson 1998 (USA)	RCT	218††	46/172	SM	14	2	(1) Medication (2) spinal manipulation + medication	Headache Index score (including headache frequency and severity), SF-36, medication use
Parker 1978 (Australia)	RCT	85	33/52	SM	8-16	2	Cervical mobilization	Duration, pain, disability, migraine frequency

EPI = Eysenck Personality Inventory; HIT-6 = Headache Impact Test; HRQOL = Health-Related Quality of Life; MIDAS = Migraine Disability Assessment; RCT = randomized clinical trial; SF-36 = Short Form-36; SM = spinal manipulation.

*Outcome significantly improved comparing spinal manipulation to the control group.

†This is the number of participants who were randomized. One participant in the spinal manipulation group, 1 participant in the sham group, and 5 participants in the usual pharmacological management group dropped out prior to baseline assessment.

‡This is the number of participants who were randomized. Five participants in the medication group did not accept their treatment assignment.

§One hundred and twenty-seven subjects agreed to enter the trial and 123 subjects completed the trial. This study reported gender for 125 subjects.

Adverse Effects.—Of the 6 RCTs, only 2 studies explicitly reported adverse events or adverse effects.[16,17] The first reported that adverse effects were an item in headache diaries but provided no additional reporting details. No adverse effects were reported during this trial.[16] The second study reported that all adverse events were recorded after each intervention session but it was unclear how adverse events were recorded for those in the usual pharmacological management group. Few adverse events were observed and none were considered serious or severe.[17] A third study reported the prevalence of neck pain among those receiving spinal manipulation but not among the other groups and the authors did not report other adverse events.[15]

Risk of Bias Assessment.—Table 2 displays the results from our risk of bias assessment. Only 3 studies were judged to be low risk of bias for the random sequence generation and for allocation concealment.[13,16,17] Given the nature of the intervention and control treatment chosen, most studies were unable to blind participants.[13-15,18] Two studies did use a "sham" spinal manipulation for 1 of their control groups, which allowed blinding of participants in the intervention and "sham" groups but not those in medication only or usual pharmacological management control groups.[16,17] Both studies also provided information to demonstrate that blinding of participants in the "sham" group was successful.[16,17] One study found that none of the patients in the sham group were able to correctly guess the nature of their treatment.[16] The other study asked participants after each session whether they believed they had received spinal manipulation. Over 80% of participants believed they had received spinal manipulation regardless of group allocation.[17] Because participants self-reported all outcomes, lack of blinding of participants directly impacted our assessment of blinding of the outcomes. Only the 2 studies that used "sham" groups received low risk of bias scores for blinding of the outcomes.[16,17] Some studies did mention that the analyst was blinded to the treatment assignment of participants[17] or that the outcomes assessor was blinded.[16] Only 2 studies provided enough information to show low attrition rates during the course of the study ("incomplete outcome data" criteria).[14,16] All studies provided

Table 2.—Risk of Bias Summary for Included Studies

Study	Random Sequence	Allocation Concealment	Blinding of Participants	Blinding of Outcome Assessment	Incomplete Outcome Data	Selective Reporting – A	Selective Reporting – B	Differences at Baseline	Co-Interventions Similar	Compliance	Timing of Outcomes	Rationale for Sample Size	Rationale for Control Group	Intervention Description
Cerritelli 2015	L	L	L / H	L / UC	L	L	L	L	H	UC	L	L	L / H	L
Chaibi 2017	L	L	L / H	L / UC	L	L	L	L	L	L	L	L	L / L	L
Nelson 1998	L	L	H	UC	H	L	L	L	L	UC	L	L	L	L
Tuchin 2011	H	H	H	UC	UC	L	H	L	UC	UC	L	H	L	L
Voigt 2011	UC	UC	H	UC	UC	L	H	L	L	UC	L	H	UC	L
Parker 1978	UC	UC	UC	UC	UC	L	H	L	L	UC	L	H	L	L

H = high risk of bias; L = low risk of bias; UC = unclear (see Supplemental Table 1 for criteria for each rating); split boxes include rating for first and second control group as listed in Table 1.

information on all outcome measures mentioned in the methods section, but 3 studies did not specify a primary outcome.[14,15,18] For other biases, the most noticeable result was that 5 studies provided insufficient detail to determine participant compliance. Three studies did not provide sample size rationale.[14,15,18]

Effects of Spinal Manipulation on Migraine Days/ Frequency of Migraine.—All 6 studies provided information on migraine days per month[15-17] or in the past 3 months,[18] percentage of days with headache in the past 4 weeks,[13] or the "mean frequency of attacks."[14] The originally planned a priori meta-analysis including all 6 studies using a random effects model indicated that spinal manipulation had a greater impact on reducing the number of migraine days compared to controls with an overall large effect size (Hedges' g = −1.16, 95% CI: −1.94, −0.39, P = .003) (Supplemental Table 1). However, heterogeneity across the 6 studies was high (I^2 ratio = 93.80%) and appeared to be driven by the study by Cerritelli et al,[16] which only enrolled chronic migraineurs and showed effect sizes that were substantially larger than the other studies. Due to concerns that arose during peer review that even a random effects model would not adequately capture this between study heterogeneity across all 6 studies, we decided post hoc (ie, after performing our initial analyses) to exclude the study by Cerritelli et al from our main analyses. Results from analyses including this study can be found in the Supporting Information and generally were of stronger magnitude than those presented here. After excluding this study, heterogeneity across the remaining studies was low (Q statistic = 3.61, P value = .72; I^2 ratio = 0) and we decided post hoc to use a fixed effects model. The meta-analysis of the remaining 5 studies indicated that spinal manipulation had a greater impact on reducing the number of migraine days compared to controls with an overall small effect size (Hedges' g = −0.35, 95% CI: −0.53, −0.16, P value < .001) using a fixed effects model. As a sensitivity analysis, we also performed this analysis using a random effects model and observed the same results (Hedges' g = −0.35, 95% CI: −0.53, −0.16, P value < .001). The effect size was similar when the analysis was restricted to studies that compared the intervention group to active controls (4 studies; Hedges' g = −0.41, 95% CI: −0.64, −0.17, P value = .001). The overall effect size was slightly smaller when comparing the interventional group to passive controls (3 studies; Hedges' g = −0.25, 95% CI: −0.56, 0.06, P value = .117, Fig. 2).

Effect of Spinal Manipulation on Migraine Pain or Intensity.—A measure of migraine pain or intensity was used in all studies usually through a Likert scale or visual analog scale. However, 1 study[18] used MIDAS B and the German "Pain Questionnaire" to assess migraine pain. Analyses excluding the study by Cerritelli et al[16] observed that spinal manipulation had greater impact on reducing migraine pain or intensity with an overall small effect size (Hedges' g = −0.28, 95% CI: −0.46, −0.09, P value = .004) from a fixed effects meta-analysis (Q statistic = 3.26,

Model	Study	Comparison	Hedges' g	SE	95% CI		p-value	weight
	Chaibi 2017	active	-0.32	0.29	-0.89	0.26	0.284	20.19
	Tuchin 2000	active	-0.39	0.19	-0.77	-0.02	0.041	21.19
	Nelson 1998	active	-0.71	0.24	-1.17	-0.24	0.003	20.79
	Parker 1978	active	-0.13	0.26	-0.64	0.39	0.628	20.54
Fixed ES for active controls*			-0.41	0.12	-0.64	-0.17	0.001	
	Chaibi 2017	passive	-0.18	0.30	-0.76	0.42	0.561	25.59
	Voigt 2011	passive	-0.23	0.30	-0.82	0.37	0.459	25.57
	Nelson 1998	passive	-0.31	0.24	-0.77	0.15	0.192	25.97
Fixed ES for passive controls*			-0.25	0.16	-0.56	0.06	0.117	
Fixed ES for all control groups*			-0.35	0.10	-0.53	-0.16	<0.001	

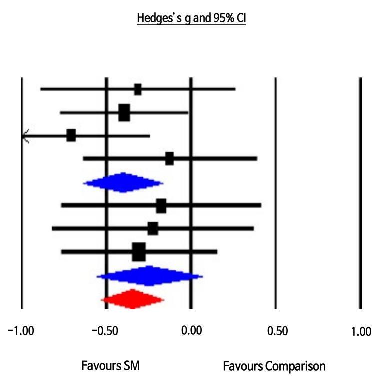

Fig. 2.—Results of meta-analysis evaluating spinal manipulation for migraine days. ES = effect size; SE = standard error; CI = confidence interval; SM = spinal manipulation. *These effect estimates exclude the study by Cerritelli et al. Effect estimates including that study can be found in the Supporting Information.

Model	Study	Subgroup	Hedges's	SE	95% CI		p	weight
	Chaibi 2017	active	-0.03	0.29	-0.61	0.54	0.909	18.77
	Tuchin 2000	active	-0.35	0.19	-0.73	0.02	0.066	22.80
	Nelson 1998	active	-0.14	0.23	-0.60	0.32	0.556	21.15
	Parker 1978	active	-0.29	0.26	-0.80	0.23	0.278	19.96
Fixed ES for active controls*		active	-0.23	0.12	-0.46	0.00	0.050	
	Chaibi 2017	passive	-0.41	0.30	-1.01	0.18	0.022	24.66
	Voigt 2011	passive	-0.18	0.30	-0.77	0.42	0.557	24.66
	Nelson 1998	passive	-0.25	0.24	-0.72	0.22	0.291	27.09
Fixed ES for passive controls*		passive	-0.36	0.16	-0.67	-0.04	0.027	
Fixed for all control groups*		Overall	-0.28	0.10	-0.46	-0.09	0.004	

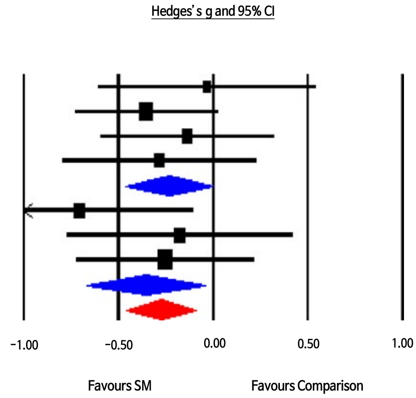

Fig. 3.—Results of meta-analysis evaluating spinal manipulation for migraine pain/intensity. ES = effect size; SE = standard error; CI = confidence interval; SM = spinal manipulation. *These effect estimates exclude the study by Cerritelli et al. Effect estimates including that study can be found in the Supporting Information.

P value = .77; I^2 = 0). This effect was similar when restricting analyses to active control groups (Hedges' *g* = −0.23, 95% CI: −0.46, 0, *P* value = .050) or to passive controls *t* (Hedges' *g* = −0.36, 95% CI: −0.67, −0.04, *P* value = .027, Fig. 3).

Effects of Spinal Manipulation on Migraine Disability.—Only 4 studies provided information on migraine disability. Measures of disability varied across studies and included assessments of number of hours before returning to work,[15] "mean disability,"[14] disturbance in occupation due to migraine and days of disablement from MIDAS 1,[18] and functional disability and the HIT-6.[16] After excluding the study by Cerritelli et al,[16] we observed a small effect size in a fixed effects meta-analysis (*Q* statistic = 0.34, *P* value = .84; I^2 = 0) (Hedges' *g* = −0.16, 95% CI: −0.43, 0.12, *P* value = .265). Due to the limited number of studies, we were not able to perform subgroup analyses among active and passive controls (Fig. 4).

DISCUSSION

Results from this preliminary meta-analysis suggest that spinal manipulation reduced migraine days and migraine pain or intensity with an overall small effect size and did not impact migraine disability compared to control interventions.

Subgroup analysis stratified by control group type (active vs passive) showed similar magnitudes of effects as the main analyses. Performing analyses stratified by the type of control group used is important because there is concern that beneficial effects of an "active" intervention, like spinal manipulation, may be due solely to the increased attention given to the intervention group. While use of an "active" control group (eg, sham manipulation or placebo therapy) may help to avoid this potential bias, developing sham manipulations that are nontherapeutic is a challenge. In this meta-analysis, spinal manipulation was associated with significant reductions in migraine days compared to those in active control groups which suggests

Model	Study	Subgroup	Hedges's	SE	95% CI		p	weight
	Voigt 2011	passive	-0.23	0.30	-0.83	0.37	0.448	49.87
	Tuchin 2000	active	-0.19	0.19	-0.57	0.19	0.319	36.06
	Parker 1978	active	-0.03	0.26	-0.54	0.49	0.920	33.27
Fixed ES for all control groups*		Overall	-0.15	0.14	-0.42	0.12	0.265	

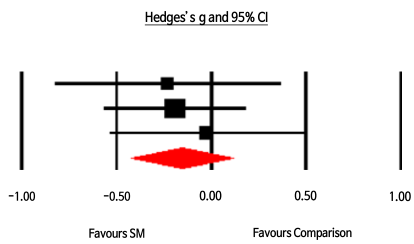

Fig. 4.—Results of meta-analysis evaluating spinal manipulation for migraine disability. ES = effect size; SE = standard error; CI = confidence interval; SM = spinal manipulation. *These effect estimates exclude the study by Cerritelli et al. Effect estimates including that study can be found in the Supporting Information.

that the results seen for the intervention group are not solely due to attention or expectation.

Our risk of bias assessment also indicated areas in which some studies received high bias scores (eg, random sequence generation, allocation concealment, blinding of participants and personnel, prespecifying a primary outcome, and reporting on compliance). Identifying areas where prior studies have shown limitations may help guide and strengthen the scientific rigor of future research in this field. For example, prespecifying the primary outcome as well as collecting and reporting on compliance over the course of a study should be implemented in all future trials of spinal manipulation. Blinding of participants in studies of spinal manipulation can be difficult depending upon the type of comparison group used in the trial. Two recent studies used sham therapy for one of their control groups. Both formally evaluated the blinding of participants and observed that it was possible to achieve blinding in trials of spinal manipulation.[16,17] Even if participants are unable to be blinded (eg, when spinal manipulation is compared to pharmacological treatment alone), individuals analyzing the data should be blinded to treatment group assignment.

The exact mechanisms by which spinal manipulation may influence migraine days, pain, and disability are not yet known but a few hypotheses have been proposed. Cerritelli et al suggested that spinal manipulation may affect migraine through the rebalance of the vegetative nervous system nuclei or by the reduction of proinflammatory substances.[16] Chaibi et al suggested that spinal manipulation may stimulate neural inhibitory systems by activating central descending inhibitory pathways.[17]

Although the results of this meta-analysis suggest that spinal manipulation may reduce migraine days and migraine pain/intensity, several important limitations should be discussed. Given the variation in study quality and specific study design features, we consider the results of these meta-analyses to be preliminary. Additional well-designed trials are needed before a definitive statement on the use of spinal manipulation for migraine can be made. Unfortunately, the low number of studies included in the meta-analysis prohibited us from using meta-regression to formally quantify the effects of different design features on our results. In addition, the populations enrolled in these studies varied. In particular, the study by Cerritelli et al enrolled a population of chronic migraineurs,[16] while other studies enrolled participants who experienced as few as 1 migraine per month. The study of chronic migraineurs observed larger effect estimates than any of the other studies included in our meta-analysis.[16] Until more studies of both chronic and episodic migraine are performed, we cannot determine if there are differences in the effect of spinal manipulation on chronic vs episodic migraine. Although all studies examined a measure of migraine days, there was often variability in the assessments of migraine pain/intensity or migraine disability. This limited our ability to determine the influence of spinal manipulation on other migraine outcomes. We were also unable to explore the effect of spinal manipulation on different follow-up lengths due to the limited number of studies and assessment time points in each trial. We limited our systematic review and meta-analysis to studies listed in PubMed which would exclude trials that were never published. This may result in publication bias if trials which were not able to be completed or which had null results were not published. A search of clinicialtrials.gov identified 2 additional ongoing trials (1 not yet recruiting and 1 currently recruiting) which should be included in future systematic reviews of spinal manipulation for migraine. We were unable to formally assess publication bias using a funnel plot due to the low number of studies included in this meta-analysis.

Only 2 studies explicitly collected adverse events. In order to fully understand the benefits and risks of spinal manipulation for migraineurs, more rigorous assessments of potential adverse events should be performed. Adequate monitoring of adverse events is particularly important in this population because of concerns that cervical manipulation may be associated with cervical artery dissection[22] and the increased risk of cervical artery dissection among migraineurs.[23,24] Further understanding of the potential risks and benefits of spinal manipulation for migraineurs may help migraineurs and their physicians determine the best course of care.

Most studies included in this review focused on spinal manipulation techniques. While spinal manipulation is one feature of chiropractic care, physical therapy, and osteopathy, current therapeutic models typically encompass a multimodal approach including but not limited to education, spinal stabilization exercises, soft tissue manipulation, breathing training, stretching techniques, nutrition, and ergonomic modifications.[25-27] It is currently unknown whether the wide variety of potential multimodal care models as practiced in clinical settings reduce migraine days, pain, or disability.

CONCLUSION

Results from this preliminary meta-analysis suggest that spinal manipulation may reduce migraine days and pain/intensity. However, variation in study quality makes it difficult to determine the magnitude of this effect. Methodologically rigorous, large-scale RCTs are warranted to better inform the evidence base for the role of spinal manipulation in integrative models of care provided by chiropractors, physical therapists, and osteopathic physicians as a treatment for migraine.

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