SYSTEMATIC REVIEW UPDATE

Efficacy and safety of spinal manipulative therapy in the management of acute neck pain: a systematic review and meta-analysis

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Abstract

Background Spinal manipulative therapy (SMT) is frequently used to manage neck pain; however, its efficacy and safety in treating acute neck pain (ANP) remain uncertain and require further investigation.

Objectives This study aims to comprehensively evaluate the efficacy and safety of SMT in the treatment of ANP.

Databases and data treatment A thorough search was conducted in PubMed, Embase, Web of Science, PEDro, and Cochrane Library databases, covering all studies from inception to March 20, 2023. Mean differences (MD) with 95% confidence intervals (CIs) were calculated to assess outcomes such as pain intensity, cervical range of motion (CROM), and disability. The PEDro Scale and the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach were utilized to evaluate the methodological quality and strength of evidence.

Results Eight randomized controlled trials (RCTs) with 965 patients were included. Their PEDro scores ranged from 4—9 (mean: 6.38, SD: 1.25). Forest plot analysis showed SMT was better than the control in reducing pain (MD=-1.53, 95% CI [-2.22, -0.83]) and improving CROM in all measured aspects. It also significantly reduced disability scores (MD=-6.20, 95% CI [-9.81, -2.59]). No serious adverse events were reported.

Conclusions The evidence supports the use of SMT as an effective and safe intervention for reducing pain, improving CROM, and decreasing disability in patients with ANP. These findings provide valuable insights for clinical practitioners and highlight the potential of SMT as a viable therapeutic option in managing ANP.

Systematic review registration PROSPERO CRD42021264411.

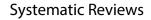
Keywords Spinal manipulative therapy, Acute neck pain, Systematic review, Meta-analysis, Musculoskeletal rehabilitation

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Introduction

Acute neck pain (ANP) can occur suddenly and rapidly progress, resulting in severe pain and detrimental effects on the patient's well-being [1]. Neck pain ranks as the fourth most common cause of disability worldwide, with an annual prevalence exceeding 30% [2]. The neck, a flexible structure that supports the weight of the head, is susceptible to pain and restricted movement. While many cases of ANP resolve either with or without treatment, approximately half of the affected individuals continue to experience chronic or episodic pain [2–4]. Moreover, neck pain imposes a financial burden, associated with high treatment costs, reduced productivity, and work-related challenges for employees [5]. Routine activities involving stretching, loading, and particularly twisting increase the likelihood of developing neck pain [1, 6, 7].

The clinical practice guidelines established by the American Physical Therapy Association (APTA) outline conservative treatment approaches for neck pain, which include coordination, strengthening, and endurance training [3]. Additionally, guidelines from APTA, the Canadian Chiropractic Association, and the Danish Health Authority incorporate manipulative techniques as part of the recommended treatment protocol [3, 8, 9]. Beyond these organizations, several other clinical practice guidelines have also endorsed the use of SMT for managing acute or subacute neck pain, typically within a multimodal treatment strategy. For instance, Bryans et al. [8] provided evidence-based guidelines emphasizing the role of chiropractic treatment in addressing neck pain, while Bussieres et al. highlighted SMT as an integral component for treating neck pain-associated disorders and whiplash-associated disorders [10]. Similarly, Kjaer et al. [9] and Whalen et al. [11] underscored the value of combining SMT with other therapies, such as exercise and education, to optimize patient outcomes. These comprehensive guidelines reflect a growing consensus on the efficacy and safety of SMT when used alongside complementary interventions for managing neck pain effectively.

Spinal manipulative therapy (SMT) is a"handson"therapeutic approach that applies force to spinal joints to alleviate neck pain [12]. Both thrust and nonthrust spinal motor segment manipulation techniques are employed as interventions for patients with ANP and recurrent neck pain [3]. By targeting dysfunctional areas of the spine, SMT aims to restores structural integrity, reduces pain, and stimulates the body's natural [13]. In addition, SMT is generally considered safe. Serious adverse events potentially associated with SMT are exceedingly rare, with incidence rates ranging from 1 case per 2 million procedures to 13 cases per 10,000 patients, and no life-threatening or fatal adverse events have been reported [14, 15]. However, despite the well—documented clinical benefits of SMT, the exact magnitude of its efficacy in alleviating pain, reducing disability, and enhancing overall functional outcomes remains inadequately explored. More rigorous studies are required to clarify these effects and gain better understanding of the factors that influence its therapeutic potential.

Although a meta-analysis on SMT for neck pain exists, it mainly concentrated on chronic neck pain instead of ANP [12]. The previous review methods had notable limitations. For example, they often included heterogeneous populations. Some prior meta-analyses on SMT for neck pain combined patients with acute, sub-acute, and chronic neck pain without proper discrimination. Given the significant differences in pathophysiology, treatment responses, and prognosis among these groups, this heterogeneity could have distorted the results, making it hard to draw accurate conclusions specifically for ANP. Also, there was a lack of differentiation between acute and chronic neck pain in previous reviews [16]. Acute and chronic neck pain have distinct natural courses and treatment responses. Reviews that failed to distinguish between them might have grouped studies with diverse outcomes, leading to an inaccurate understanding of SMT's true efficacy and safety for ANP, as SMT's effects can vary depending on the neck pain stage. However, numerous RCTs [16-23] related to this research have been identified. These trials offer different insights compared to those in the previous meta-analysis [12, 24], and they serve as a solid basis for synthesizing new research evidence directly applicable to ANP. Building on this growing body of research, a systematic review and meta-analysis were undertaken, incorporating a formal grading of evidence to ensure methodological rigor and transparency. Specific outcome measures such as pain, improvement in CROM, and reduction in disability are directly related to the key aspects of body function, activity limitations, and participation restrictions in patients with ANP. Therefore, the primary objective of this study is to evaluate the efficacy of SMT in alleviating pain in patients with ANP. Pain is regarded as the primary outcome, while improving CROM and reducing disability are considered as secondary outcomes.

Additionally, the review systematically assessed the safety profile of SMT, aiming to provide a comprehensive understanding of its clinical utility. This approach not only addresses the limitations of prior reviews but also seeks to offer clearer guidance for clinical application and future research directions.

Methods

Study design and registration

This research protocol adheres to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines, ensuring transparency and comprehensive reporting. Additionally, the protocol has been registered in the PROSPERO database with the registration number CRD42021264411 [25].

Data sources and searches

For this systematic review and meta-analysis, the researchers responsible for conducting the literature search and selection process are YXD and JXP. They searched several databases, including PubMed, Embase, Web of Science, PEDro, and Cochrane Library, to identify relevant literature published up until March 20, 2023. The purpose of this extensive search was to ensure that no recent reviews had covered the topic in the past five years. All the identified literature was imported into Endnote for classification and organization. To narrow down their search and focus on relevant content, the researchers utilized a combination of keywords, including"osteopathic manipulation,""chiropractic/ orthopedic manipulation,""spinal manipulation,""manual therapy,""sham/placebo manipulation,""acute pain, neck,""acute neckache,""acute cervicalgia,""acute cervicodynia,"and"randomized controlled trial."These keywords were applied in different combinations to retrieve the most relevant studies. The Supplemental Files contain the specific search terms used for each database. To assess the eligibility of the retrieved articles, YXD and JXP independently reviewed the titles and abstracts. They checked for the presence of the predefined criteria, which will be described in the upcoming section. Additionally, the reference lists of the selected RCTs [16-23] were reviewed, and earlier systematic reviews and meta-analyses were cross-referenced to identify any additional relevant studies. This comprehensive search strategy aims to capture all eligible RCTs for inclusion in the systematic review and meta-analysis.

Inclusion and exclusion criteria

This meta-analysis specifically includes RCTs that aimed to improve CROM, reduce pain, and minimize disability in patients with ANP. The participants in these studies were required to be 18 years or older and have a clinically diagnosed acute whiplash injury or ANP, defined as symptoms lasting less than 3 months, with or without radiating pain. The literature search process began by manually retrieving 1,882 records from multiple database. In the experimental groups, participants received SMT, which encompassed manipulation of the cervical, thoracic, and/or other spinal regions. These interventions could be administered either as a single-modal intervention or in combination with other therapies (multimodal intervention). The control group participants, on the other hand, received alternative therapies such as exercise, physical agents therapy, or placebo therapy. The primary outcome measures utilized to evaluate the effects of SMT on patients with ANP were pain severity, CROM, and disability. Pain intensity was assessed using visual analogue scales (VAS) and numeric pain rating scales (NPRS). The impact of ANP on patients' daily lives was evaluated through CROM measurements to assess cervical spine activity and disability measurements using the Neck Disability Index (NDI) and the Northwick Park Neck Pain Questionnaire (NPQ).

The following types of studies were excluded from this meta-analysis: non-RCTs, studies not focusing on ANP or whiplash injury, studies with unavailable full text or missing data, duplicate publications, poor-quality research, non-English literature, and editorials, letters, comments, or conference abstracts. These exclusion criteria ensure the inclusion of studies that meet the specific objectives and quality standards of the meta-analysis.

Literature quality assessment

To ensure a comprehensive assessment of the eligible studies, two evaluators (JMC and JHP) employed the Physical Therapy Evidence Database (PEDro) scale. The PEDro scale is a recognized tool for evaluating the risk of bias in RCTs and is widely used for this purpose [26]. The PEDro scale consists of 10 items that aim to identify potential weaknesses in the methodology of the studies. Each item is scored as either 1 (presence) or 0 (absence). The total score on the scale ranges from 0 to 10, with higher scores indicating stronger methodology. The scoring criteria for the PEDro scale are as follows: 9-10 = excellent, 6-8 = good, 4-5 = fair, and less than 4 = poor[26]. The evaluators assigned scores to each study based on the PEDro scale criteria. These scores help assess the quality of the studies. Studies with high scores and good or excellent methodology, or with a sample size greater than 50, are considered to have level 1 evidence. Conversely, studies with low scores, fair or poor methodology, or a sample size of less than 50 are categorized as level 2 evidence [27]. In addition, two researchers (JMC and JHP) rigorously examined the funding sources of the eight RCTs to check for potential biases related to influencing study results and reporting. Whenever there were differences in ratings between the two evaluators, th were resolved through discussions with the lead researcher (LRL). This iterative process ensures consistency and accuracy in the evaluation of the included studies.

Data extraction

To ensure the accuracy and reliability of the extracted data, two researchers (HL and MXL) independently used standardized forms to extract data in duplicate. Following this, they cross-checked their results to confirm consistency and resolve any discrepancies, ensuring that the extracted data was both accurate and consistent. The following data were extracted using the standardized forms: study characteristics (such as authors'names and publication year), patient characteristics (including the number of participants, their age, and gender), descriptions of the experimental and control interventions, duration of follow-up, types of outcome measures assessed, preand post-treatment results, and the authors'findings and conclusions. The extracted data were then entered into a Microsoft Excel spreadsheet, which facilitated the comparison of participant characteristics, interventions, and outcome measures across the included studies. This systematic organization of data enables a comprehensive analysis and synthesis of the findings. In cases where differences of opinion arose during the data extraction process, discussions were led by the lead researcher (LRL) to resolve any discrepancies. This collaborative approach ensures the accuracy and reliability of the extracted data.

Rating the body of evidence

Two reviewers (JHP and JMC) independently evaluated the quality of the available evidence using the GRADE criteria [28]. In cases where disagreements arose between the two reviewers, they resolved the differences through discussion. If consensus was not achieved, a third reviewer (LRL) was consulted to mediate and make the final decision. This approach ensured that the assessment of evidence quality was consistent, accurate, and unbiased. The GRADE system enables evaluation of the quality of evidence according to specific criteria such as the study design, bias risk, accuracy, consistency, indirectness, and effect size. In the GRADE system, symbols or letters are used to denote the appropriate grades; the strength of recommendations is classified into two levels-strong and weak-and the quality of the evidence is classified into four grades-high, medium, low, or very low [29]. We created outcome summary tables for the ratings of pain intensity, CROM, and disability conditions. We created summary of findings tables using the GRADE criteria in accordance with the Cochrane Handbook for Systematic Reviews of Interventions [30, 31].

Data analysis and synthesis of results

We only conducted meta-analyses when it was logical to do so, such as when the participants, treatments, and potential clinical issues could be pooled together. When comparing the control/placebo (sham) with SMT alone or in combination with other interventions, we used the standardized mean difference in pain intensity. When comparing differences within and between groups, as well as the corresponding MD and 95% confidence interval (CI), analysis was done using Review Manager (RevMan 5.4). The Cochrane Handbook [30] advises calculating either the MD between the two groups by using post-intervention measures or the mean change in each group by subtracting the post-intervention mean from the baseline mean. I^2 statistics were used to determine the heterogeneity of the results, with values of 25%, 50%, and 75% denoting low, medium, and high heterogeneity, respectively [32]. To address the possibility of clinical and methodological heterogeneity that might have affected the results, given the features of the included studies, in case the heterogeneity was lower than 50%, the fixed effects model would be adopted; conversely, if it exceeded 50%, the random effects model was utilized to combine the data.

Results

Search results

The literature search initially yielded 1,882 records retrieved manually from multiple databases. After removing duplicate entries, 927 unique studies were identified for further assessment. Subsequently, the titles and abstracts of these studies were screened, leading to the exclusion of 910 studies that were determined to be irrelevant based on their content. From the remaining 17 studies, nine were excluded due to unrelated outcome measures (n = 3), non-randomized controlled trial design (n = 4), or interventions that did not involve SMT (n = 2). Finally, after this rigorous screening process, eight RCTs [16–23] were selected based on their relevance to the research objectives and meeting the predefined inclusion criteria (Fig. 1).

Methodological quality

The quality scores for the included studies were primarily obtained from the PEDro database, where they are assessed by independent reviewers using standardized criteria. For studies without available PEDro scores, two researchers independently evaluated the methodological quality using the same criteria, resolving any discrepancies through discussion. The findings are displayed in Table 1, which shows that the methodological quality scores of the included studies ranged from 4 to 9 points (mean: 6.38, SD: 1.25). The participants and therapists were blinded to the group allocations in only one [17] and none of the studies, respectively. Three of the studies received fair-quality ratings [16, 18, 19], four received good-quality ratings [20–23], and only one received an excellent-quality rating [17]. Only one study had a sample

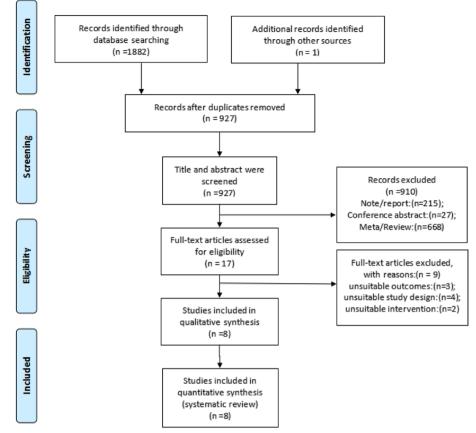


Fig. 1 PRISMA Flow Diagram of the inclusion process of the review

size of less than 50 [23]. Four studies were considered to provide level 1 evidence [17, 20–22], and the other four studies were considered to provide level 2 evidence [16, 18, 19, 23]. Overall, the certainty of evidence ranged from low to very low, primarily due to concerns regarding risk of bias, substantial heterogeneity combined with small sample sizes, indirectness of the included populations or interventions, and imprecision. (Table 2). Among the eight studies included in this review, only one reported public funding support, specifically from the National Center for Complementary and Alternative Medicine (NIH). The other seven studies did not specify any funding. We found no apparent association between funding status and reported outcomes or risk of bias (Table 3).

Characteristics of included studies

The eight RCTs [16-23] included a total of 965 patients, with sample sizes ranging from 36 to 323 (median [interquartile range] = 227 [45, 272]). The participants in the included studies had presented with ANP or whiplash injuries. Specifically, three RCTs [16, 19, 20] involved populations of patients with whiplash injuries, and the remaining studies [17, 18, 21-23] involved

patients with ANP. Regarding the different types of SMT applied to patients with ANP, SMT was applied to the entire spine (upper cervical spine, cervicothoracic junction, thoracic spine, thoracolumbar junction, and pelvic girdle) in one RCT, to the thoracic vertebra in three RCTs [16, 17, 22], to the cervical vertebra in three RCTs [18, 21, 23], and to the first rib in one RCT [20]. Participants in the experimental group received SMT alone or in combination with other forms of physiotherapy, while those in the control group received sham SMT or other forms of physiotherapy; in only one study [18], participants in the control group received drug therapy. The frequency of SMT treatment in the included RCTs [16–23] ranged from 1 to 15 sessions, and the duration of treatment did not exceed 4 weeks.

The outcome measures were pain, disability, CROM, fear, and quality of life. The VAS and NPRS were used to evaluate pain. Four studies [16, 19, 21, 22] used the VAS and three [17, 18, 23] used the NPRS to quantify pain. Neck disability was assessed using the NPQ [17, 22], and CROM (neck) was assessed in three studies [17, 21, 22].

ltem ^b	Fernández- de-las-Peñas et al. (2004a) [16]	Gonzá lez- Iglesias et al. (2009a) [17]	McReynolds et al. (2005) [18]	Fernández- de-las-Peñas et al. (2004b) [19]	Peña-Salinas et al. (2017) [20]	Bronfort et al. (2012) [21]	Gonzá lez- Iglesias et al. (2009b) [22]	Puentedura et al. (2011) [23]
1	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
3	No	Yes	No	No	Yes	Yes	Yes	Yes
4	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes
5	No	Yes	No	No	No	No	No	No
6	No	No	No	No	No	No	No	No
7	No	Yes	No	No	Yes	No	Yes	Yes
8	Yes	Yes	Yes	No	Yes	Yes	Yes	No
9	No	Yes	No	No	Yes	Yes	No	Yes
10	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
11	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Total PEDro score	4	9	5	4	8	7	7	7
Sample size ≥50	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
Level of evi- dence	2	1	2	2	1	1	1	2

Table 1 Risk of bias of included trials according to the PEDro Scale^a

Abbreviation: PEDro Physiotherapy Evidence Database

^a All quality scores were downloaded from the PEDro website. Item 1 is not included in the scoring calculation

^b Items: 1, Eligibility criteria were specified; 2, Subjects were randomly allocated to groups; 3, Allocation was concealed; 4, The groups were similar at baseline; 5, There was blinding of subjects; 6, There was blinding of therapists; 7, There was blinding of assessors; 8, There were measures of key outcomes from more than 85% of subjects; 9, Analyses were performed by intention-to-treat principles; 10, Between-group statistical comparisons were performed; 11, The study provided point measures and measures of variability

Meta-analysis

Effects of SMT on pain intensity

Seven studies assessed pain intensity using either the VAS or NPRS [16–19, 21–23] involving a total of 821 participants across the SMT and control groups. The results exhibited a high level of heterogeneity, with an I^2 value of 95%. This indicates substantial variability among the included studies, likely due to differences in study designs, populations, or interventions. Despite this heterogeneity, the pooled analysis revealed that SMT significantly reduced pain intensity compared to control treatments, with a MD of -1.53 (95% Cl: -2.22, -0.83; p < 0.001). These results suggest that SMT is effective in alleviating pain in individuals with ANP (Fig. 2).

Effects of SMT on CROM

Three studies [17, 21, 22], including 271 participants, assessed the effects of SMT on CROM. Improvements were seen in neck flexion (MD =11.01, 95% CI [9.10, 12.93], $I^2 = 0\%$, p < 0.001; Fig. 3A), neck extension (MD =10.23, 95% CI [7.77, 12.69], $I^2 = 0\%$, p < 0.001; Fig. 3B), left lateral flexion (MD =7.31, 95% CI [3.08, 11.54], $I^2 =$ 81%, p = 0.0007; Fig. 3C), right lateral flexion (MD =8.14, 95% CI [6.34, 9.95], $I^2 = 76\%$, p < 0.001; Fig. 3D), left rotation (MD =8.34, 95% CI [4.56, 12.12], $I^2 = 65\%$, p < 0.001;

Fig. 3F)and right rotation (MD = 8.95, 95% CI [4.33, 13.56], l^2 = 70%, p = 0.0001; Fig. 3F). The results indicate that SMT is effective in enhancing CROM across all measured dimensions.

Effects of SMT on disability

Disability was assessed using the NPQ in two studies [17, 22], while the NDI was utilized in another two studies [21, 23]. 295 patients were enrolled in the SMT group and the control group and the I^2 value was 89%. Meta-analysis of two studies that compared control group revealed a significant effect favoring the SMT group (MD = -6.20, 95% CI[-9.81, -2.59], and p = 0.0008; Fig. 4). The forest plot results show that SMT has a positive effect on the disability in individuals with ANP.

Adverse event In a study by McReynolds et al. [18], only one patient in the SMT group reported a mild adverse reaction: an unusual arm sensation after manipulation. This sensation was transient and self-limiting, resolving without the need for intervention. No serious complications occurred, and her muscle strength, sensation, and deep tendon reflexes remained normal. Based on the short duration, lack of progression, and absence of neurological deficits, this event was classified as mild. Subsequently, no

Certainty Assessment	sment						No. of Participants	icipants	Effect		
No. of Studies	Study Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	SMT	Control	MD [95%Cl]	Certainty	Direction
Pain intensity											
7	RCT	Not serious	Serious ^a	Not serious	Not serious ^c	Not serious	414/821 (50%)	407/821 (50%)	- 1.53 [- 2.22, - 0.83]	$ \bigoplus_{low} \bigoplus_{i \in \mathcal{N}} \bigoplus_{i \in \mathcal{N}} $	In favor of SMT
Cervical range of motion	motion										
3	RCT	Not serious	Not serious	Serious ^b	Serious ^{c,d}	Not serious	137/271 (51%)	134/271 (49%)	11.01 [9.01.12.93]	⊕⊖⊖⊖ Verv low	In favor of SMT
Outcome: Extension	ion										
£	RCT	Not serious	Not serious	Serious ^b	Serious ^{c,d}	Not serious	137/271 (51%)	134/271 (49%)	10.23 [7.77,12.69]	⊕⊖⊖⊖ Very low	In favor of SMT
Outcome: Left lateral Flexion	teral Flexion										
£	RCT	Not serious	Serious ^a	Serious ^b	Serious ^{c,d}	Not serious	137/271 (51%)	134/271 (49%)	7.31 [3.08,11.54]	⊕⊖⊖⊖ Very low	In favor of SMT
Outcome: Right lateral Flexion	^l ateral Flexion										
m	RCT	Not serious	Serious ^a	Serious ^b	Serious ^{c,d}	Not serious	137/271 (51%)	134/271 (49%)	8.14 [6.34.9.95]	$\oplus \ominus \ominus \Theta$	In favor of SMT
Outcome: Left rotation	tation										
Μ	RCT	Not serious	Serious ^a	Serious ^b	Serious ^{c, d}	Not serious	137/271 (51%)	134/271 (49%)	8.34 [4.56,12.12]	⊕⊖⊖⊖ Very low	In favor of SMT
Outcome: Right rotation	rotation										
m	RCT	Not serious	Seriousa	Serious ^b	Serious ^{c,d}	Not serious	137/271 (51%)	134/271 (49%)	8.95 [4.33,13.56]	⊕⊖⊖⊖ Very low	In favor of SMT
Disability											
4	RCT	Not serious	Serious ^a	Serious ^b	Serious ^{c,d}	Not serious	151/295 (51%)	144/295 (49%)	– 6.20 [– 9.81,– 2.59]	⊕ ⊖ ⊖ ⊖ Very low	In favor of SMT
<i>Cl</i> confidence inter	rval, <i>MD</i> mean differe	nce, <i>RCT</i> randomiz	Cl confidence interval, MD mean difference, RCT randomized controlled trials, SMT spinal manipulative therapy, CROM cervical range of motion	MT spinal manipula	tive therapy, CROM	1 cervical range of	notion				

Table 2 Grading of Recommendations Assessment. Development, and Evaluation (GRADE) guality of evidence

n n ĥ $^{\rm a}$ Substantial heterogeneity was observed across the included studies (2 > 50%)

 $^{
m b}$ The sample size was considered small (n < 400), which may limit the robustness of the findings

^c Evidence was derived from populations or interventions that were not directly aligned with the target research question

^d Wide confidence intervals were reported, resulting in reduced precision of the pooled estimates

Study	Design	Design Interventions	Sample size	Female (<i>n</i>)	Age $(\overline{\chi} \pm s)$	Symptom duration Inclusion criteria	Inclusion criteria	Sessions (Duration of program)	Outcome	Main results
Fernández-de-las- Peñas et al. (2004a) [16]	RCT	EG: Thoracic SMT plus exercises, electrotherapy, ultrasound therapy and manual therapy, CG: Exercises, electrotherapy, ultrasound therapy and manual therapy	8	48	31.2	3 weeks to 3 months	The duration of this complaint ranged from 3 weeks to 3 months	Fifteen sessions	VAS	The experimental group had a greater reduction of the VAS compared with control group
Fernández-de-las- Peñas et al. (2004b) [19]	RCT	EG: SMT CG: Exercises, electrotherapy, ultrasound therapy and diathermy	190	30	26.9 ±7.4 27.5 ±6.9	less than 3 months	Less than 3 months duration, and clas- sified in grades II and III according to the QTF	Four weeks	VAS CROM	SMT group had more benefits than the physiother- apy group in the VAS and CROM
McReynolds et al. (2005) [18]	RCT	EG: Cervical SMT CG: Ketorolac	29	18	29 ± 8 30 ± 9	less than three weeks duration	Acute musculo- skeletal neck pain of less than three weeks duration; Patient aged between 18 and 50 years;	Less than 5 min	PRS- 5	SMT is a reasonable alternative to par- enteral nonsteroidal anti-inflammatory medication for patients with ANP
Gonzá lez- Iglesias et al. (2009a) [17]	RCT	EG: Thoracic SMT, electrotherapy/ thermal CG:Electrotherapy/ thermal	22 23	25	34 ±5 34 ±6	18 ± 6 d 17 ± 5 d	Neck or shoulder pain with mechani- cal characteris- tics (including symptoms provoked by neck postures, neck movement, or palpation of the cervical mus- culature) of fess than 1 month in duration	Six sessions, 3 con- secutive weeks	NPRS CROM CROM	SMT into an elec- trotherapy/thermal program was effective in reducing neck pain and disability
Gonzá lez-Iglesias et al. (2009b) [22]	RCT	EG:Thoraacic plus TENS and infra- red lamp CG: TENS and infra- red lamp	23	11 01	34 ± 4 35 ± 6	19.5 ±4.5 d 18.7 ±3.9 d	Patientswith mechanical neck pain of less than 1 month in duration; Mechanical neck pain was defined asgeneralized neck and/or shoulder pain	Three consecutive mondays	VAS NPQ CROM	SMT results in superior clinical benefits that persist beyond the 1-month follow-up period for patients with ANP

 Table 3
 Characteristics of the included studies

Study	Design	Design Interventions	Sample size	Female (<i>n</i>)	Age $(\overline{\chi} \pm 5)$	Symptom duration Inclusion criteria	Inclusion criteria	Sessions (Duration of program)	Outcome	Outcome Main results
Puentedura et al. (2011) [23]	RCT	EG: Cervical SMT and ROM exercise	14	10	34.1 ±7.0	less than 30 days	18 and 60 years of age, have a pri-	Two sessions	NPRS NDI	Patients who received cervical SMT dem-
		CG: Thoracic SMT and ROM exercise	10	Ó	33.1 ± 5.8		mary report of neck pain with or without unilateral upper extremity symp- toms; NDI score of 10/50 points or greater		GROC	onstrated greater improvements in NDI and NPRS scores
Bronfort et al. (2012) [21]	RCT	EG: Cervical SMT CG1: Medication CG2: Home exercise with advice	6 6 6	No reported	48.3 ± 15.2 46.8 ± 12.2 48.6 ± 12.5	7 ± 3.2 week 7.4 ± 3 week 6.8 ± 3.2 week	Age 18 to 65 years; primary symptom of mechanical, non- specific neck pain equivalent to grades I or II; current neck pain of 2 to 12 weeks duration; and a neck pain score of 3 or greater on a scale of 0 to 10	Twelve weeks	NRS, NDI SF- 36 SF- 36	SMT was more effective than medi- cation in both the short and long term
Peña-Salinas et al. (2017) [20]	RCT	EG: First rib SMT CG: Sham placebo intervention	27 26	16	32.11 ± 9.1 37.38 ± 11.9	less than 3 months	Age between 18–50 years; Subjects with neck and/or cervi- cobrachial pain following cervical whiplash	Six consecutive days	РРТ	No significant dif- ferences in mecha- nosensitivity values were observed after intervention in the between- groups comparison
Abbreviations: ANP Acut Pain Rating Scale, NDI N VAS Visual Analogue Scc	e Neck Pail leck Disabil ile, <i>SMT</i> Sp.	<i>Abbreviations: ANP</i> Acute Neck Pain, <i>CROM</i> Cervical Range of Motio Pain Rating Scale, <i>NDI</i> Neck Disability Index, <i>GROC</i> Global Rating of <i>VAS</i> Visual Analogue Scale, <i>SMT</i> Spinal Manipulative Therapy	of Motion, <i>CG</i> Co lating of Change 'y	ntrol Group, EG I Score, NRS Num	Experimental G erical Rating Sc	iroup, <i>FABQ</i> Fear Avoidan :ale, <i>SF- 36</i> 36-item Short.	Abbreviations: ANP Acute Neck Pain, CROM Cervical Range of Motion, CG Control Group, EG Experimental Group, FABQ Fear Avoidance Beliefs Questionnaire, NPQ Northwick Park Neck Pain Questionnaire, NPRS Numerical Pain Rating Scale, NDI Neck Disability Index, GROC Global Rating of Change Score, NRS Numerical Rating Scale, SF- 36 36-item Short-Form, PRS- 5 5 Points Relief Scale, QTF Quebec Task Force, PPT Pressure Pain Threshold, VAS Visual Analogue Scale, SMT Spinal Manipulative Therapy	NPQ Northwick Park Necl ief Scale, QTF Quebec Tası	<pre>< Pain Questi k Force, PPT F</pre>	onnaire, <i>NPR</i> S Numerical Pressure Pain Threshold,

Table 3 (continued)

	Expe	erimen	tal	С	ontrol			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV. Random, 95% CI
Bronfort 2012	-3.67	1.55	91	-2.79	1.7	90	15.4%	-0.88 [-1.35, -0.41]	
Fernández-de-las-Peñas 2004a	-2.27	0.87	44	-1.66	0.91	44	15.8%	-0.61 [-0.98, -0.24]	-
Fernández-de-las-Peñas 2004b	-5.8	0.35	190	-3.7	0.85	190	16.4%	-2.10 [-2.23, -1.97]	•
Gonzá lez-Iglesias 2009a	-3.3	0.95	23	-1.07	0.72	22	15.3%	-2.23 [-2.72, -1.74]	
Gonzá lez-Iglesias 2009b	-3.45	0.8	23	-0.8	0.55	22	15.7%	-2.65 [-3.05, -2.25]	+
McReynolds 2005	-1.7	2.56	29	-2.8	1.8	29	11.4%	1.10 [-0.04, 2.24]	
Puentedura 2011	-4.5	2.15	14	-1.3	1.28	10	10.0%	-3.20 [-4.58, -1.82]	
Total (95% CI)			414			407	100.0%	-1.53 [-2.22, -0.83]	◆
Heterogeneity: Tau ² = 0.76; Chi ²	= 118.06	, df = 6	6 (P < 0	.00001)	; I ² = 9	5%		-	
Test for overall effect: Z = 4.32 (P	< 0.000	1)							-4 -2 0 2 4 Favours [experimental] Favours [control]

Fig. 2 Forest plot of pooled studies comparing spinal manipulative therapy alone or or in combination with other intervention to a placebo or in addition to another intervention for change in pain intensity

other adverse effects were seen in this patient. In a study by Puentedura et al. [23] no patient reported any adverse events during treatment or the 6-month follow-up. Similarly, no patient reported adverse effects in the other six included studies [16, 17, 19–22].

Discussion

Summary of main results

The results of this systematic review and meta-analysis, which are based on eight RCTs [16–23], indicate that SMT is effective in reducing pain and disability and improving CROM in patients with ANP. Additionally, the occurrence of minor adverse effects associated with SMT was rare.

Efficacies of different types of SMT for ANP

The use of cervical spine manipulation, thoracic manipulation, and first rib manipulation has been observed in clinical research on ANP [21-24]. SMT has been reported as a widely applicable treatment for various types of neck pain, regardless of the stage (acute, subacute, or chronic) [3, 5, 16, 19]. Among the different classifications of neck pain, the duration of pain may be the most accurate predictor of the patient's outcome [5]. The mechanisms underlying the effects of thoracic manipulation on cervical pain remain unknown. However, in theory, such treatment can restore structural integrity in dysfunctional regions of the spine, alleviate pain, and initiate the body's natural healing process [33]. The results of the systematic review and meta-analysis indicate that overall, SMT has positive effects in terms of reducing pain and disability and improving CROM in patients with ANP. In a study by Lohman et al. [34] the direct effects of cervical spine SMT on serum concentrations of biochemical markers related to sensory injury were investigated. The study found that cervical SMT intervention led to immediate increases in the serum concentrations of oxytocin, neurotensin, and orexin A (but not cortisol) in female patients with ANP. This suggests that mechanical stimulation through SMT may have altered the expression of these neuropeptides. Experimental evidence suggests that SMT can affect primary afferent neurons, the motor control system, and pain perception originating from the erector spinae muscle [35]. SMT-induced biomechanical changes are thought to impact the central nervous system's ability to process sensory information. Additionally, SMT may also affect the reflex nerve output in muscles and internal organs.

Abundant evidence suggests that SMT can trigger the erector spinae muscle reflex and modulate the excitability of motor neurons [35]. Clinical practice guidelines recommend the use of thoracic SMT, CROM exercise programs, and scapulothoracic and upper limb strengthening exercises to improve compliance (Grade B). Additionally, cervical SMT and/or mobilization are recommended for patients with ANP with impaired mobility (Grade C) [3]. In clinical settings, the management of ANP often involves more than just SMT intervention. The reduction in pain observed in patients may be attributed to a combination of factors, including muscle relaxation and strengthening in the neck and shoulder regions [36–40]. In a study by Puentedura et al. [22] patients who received cervical SMT in conjunction with exercise demonstrated statistically significant decreases in pain and disability compared to those who received thoracic SMT combined with exercise. This suggests that for patients with neck pain lasting less than 30 days, cervical SMT may be more beneficial than thoracic SMT. Furthermore, combining neck SMT with exercise appears to yield better outcomes than SMT alone.

Safety of different types SMT on ANP

Numerous studies have demonstrated that SMT is a safe treatment option for chronic neck pain [41–45]. However, when considering its application for ANP, healthcare professionals should take into account the relative lack of studies specifically focusing on this population. The systematic review and meta-analysis included only _

(A)

	Exp	erimen	tal	c	Control			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV. Fixed, 95% CI
Bronfort 2012	10.62	17.63	91	2.09	17.55	90	14.0%	8.53 [3.40, 13.66]	
Gonzá lez-Iglesias 2009a	11.6	5.21	23	0.9	5.35	22	38.5%	10.70 [7.61, 13.79]	
Gonzá lez-Iglesias 2009b	12.4	4.81	23	0.4	4.71	22	47.5%	12.00 [9.22, 14.78]	
Total (95% CI)			137			134	100.0%	11.01 [9.10, 12.93]	•
Heterogeneity: Chi ² = 1.42,)%					-20 -10 0 10 20
Test for overall effect: Z = 1	1.26 (P	< 0.000	01)						Favours [control] Favours [experimental]

(B)

	Exp	erimen	tal	c	ontrol			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl
Bronfort 2012	10.62	17.63	91	2.09	17.55	90	23.1%	8.53 [3.40, 13.66]	
Gonzá lez-Iglesias 2009a	11.2	8.4	23	1.3	5.25	22	36.6%	9.90 [5.83, 13.97]	
Gonzá lez-Iglesias 2009b	11.7	7.79	23	0.2	5.3	22	40.3%	11.50 [7.62, 15.38]	
Total (95% CI)			137			134	100.0%	10.23 [7.77, 12.69]	•
Heterogeneity: Tau ² = 0.00;	au ² = 0.00; Chi ² = 0.86, df = 2 (P = 0.65); l ² = 0%								-20 -10 0 10 20
Test for overall effect: Z = 8	.14 (P <	0.0000	1)						Favours [control] Favours [experimental]

(C)

Experimental Mean Difference Mean Difference Control Mean SD Total Mean SD Total Weight IV. Random, 95% CI IV. Random. 95% CI Study or Subgroup Bronfort 2012 6.73 15.73 91 4.53 14.43 90 28.7% 2.20 [-2.20, 6.60] Gonzá lez-Iglesias 2009a 1.4 4.45 -0.8 4.22 8.00 [5.20, 10.80] 10.70 [8.12, 13.28] 9.4 5.11 23 22 35.2% Gonzá lez-Iglesias 2009b 9.9 23 22 4.6 36.1% Total (95% CI) 137 7.31 [3.08, 11.54] 134 100.0% Heterogeneity: Tau² = 11.20; Chi² = 10.77, df = 2 (P = 0.005); l² = 81% -20 -10 Ó 10 20 Test for overall effect: Z = 3.39 (P = 0.0007) Favours [control] Favours [experimental]

							(E))	
	Exp	erimen	tal	C	ontrol			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% Cl
Bronfort 2012	6.73	15.73	91	4.53	14.43	90	16.8%	2.20 [-2.20, 6.60]	
Gonzá lez-Iglesias 2009a	11	5.37	23	1.6	4.6	22	38.2%	9.40 [6.48, 12.32]	
Gonzá lez-Iglesias 2009b	9.8	4.97	23	0.5	4.22	22	45.0%	9.30 [6.61, 11.99]	
Total (95% CI)			137			134	100.0%	8.14 [6.34, 9.95]	•
Heterogeneity: Chi ² = 8.44,				6%					-20 -10 0 10 20
Test for overall effect: Z = 8	.85 (P <	0.0000	1)						Favours [control] Favours [experimental]

(E)

	Exp	erimen	tal	C	ontrol			Mean Difference		Mean D	ifference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV. Random. 95% CI		IV. Rande	om. 95% C	í	
Bronfort 2012	7.06	18.48	91	3.26	18.44	90	25.3%	3.80 [-1.58, 9.18]			-		
Gonzá lez-Iglesias 2009a	9	6.35	23	0.6	5.26	22	36.6%	8.40 [5.00, 11.80]					
Gonzá lez-Iglesias 2009b	10.9	5.89	23	-0.4	4.94	22	38.1%	11.30 [8.13, 14.47]			-		
Total (95% CI)			137			134	100.0%	8.34 [4.56, 12.12]			•		
Heterogeneity: Tau ² = 7.13;	Chi ² = 5	5.73, df	= 2 (P :	= 0.06);	l ² = 65%	16			-50	-25	1	25	50
Test for overall effect: Z = 4	.33 (P <	0.0001)						-50	Favours [control]	Favours [

(F)

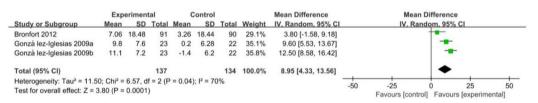


Fig. 3 Forest plot of pooled studies comparing spinal manipulative therapy alone or or in combination with other intervention to a placebo or in addition to another intervention for change in *CROM*: flexion (**A**), extension (**B**), left lateral flexion (**C**), right lateral flexion (**D**), left rotation (**E**) and right rotation (**F**)

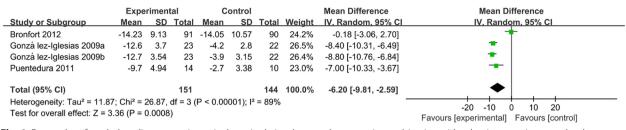


Fig. 4 Forest plot of pooled studies comparing spinal manipulative therapy alone or or in combination with other intervention to a placebo or in addition to another intervention for change in disability

three studies that reported minor discomfort following SMT in ANP patients [18, 21, 23]. It is crucial for healthcare professionals to provide accurate information to patients about SMT as a passive therapy, empowering them to take control of their condition and prevent inappropriate behaviors. In a study by Bronfort et al. [21], 40% of ANP participants receiving SMT reported mild adverse events, mainly musculoskeletal pain, while rare adverse events such as paresthesia, stiffness, or headaches were experienced but were generally not serious. Overall, although specific evidence for the safety of SMT in ANP is limited, it can still be considered as a therapeutic option. A recent systematic review [42] found uncommon severe adverse events associated with SMT for neck pain. However, clinicians or therapists should thoroughly inform patients about potential risks of SMT prior to treatment, allowing patients to make informed decisions about their care.

Factors that might affect the quality of evidence

The high heterogeneity observed in this study may be influenced by various factors that impact the quality of the evidence. These include variability in SMT techniques (cervical, thoracic, and first rib manipulation), differences in intervention intensity and frequency, variations in concurrent treatments, and lack of consistency in treatment parameters. Each of these factors makes it challenging to draw definitive conclusions, establish consistent effects, and determine the optimal treatment course. Hence, caution is required when interpreting the study findings. Future research with standardized protocols and larger sample sizes is needed to address these limitations and reduce heterogeneity in the evidence. Considering these factors, it is important to interpret the results of the study with caution and recognize the potential limitations in generalizing the findings. Future studies with standardized treatment protocols and larger sample sizes may help to better understand the effects of SMT and reduce heterogeneity in the evidence.

Practical and clinical application

In practical and clinical applications, SMT can be considered as an effective treatment option for ANP. Clinical guidelines recommend the use of SMT in conjunction with other approaches, such as exercise therapy (e.g., CROM exercises) or other manipulations (e.g., mobilization), to manage ANP with mobility disorders [3]. However, to draw more definitive conclusions about the efficacy of SMT, there is a need for RCTs with high methodological quality and larger sample sizes. These studies would provide more robust evidence regarding the efficacy of SMT as a standalone treatment or in combination with other forms of physical therapy. Overall, while SMT can be a valuable treatment option for ANP, further research is still needed to establish its specific efficacy and optimal application in clinical practice. Conducting high-quality RCTs with standardized protocols will contribute to a better understanding of the benefits and limitations of SMT for ANP management.

Strengths and limitations of the review

This systematic review has several strengths that contribute to its validity. The review includes a comprehensive search across five significant databases, ensuring a thorough examination of the existing literature. The use of well-tested and verified standards such as PEDro and GRADE enhances the rigor of the review process. The inclusion of both quantitative and qualitative analyses allows for a more comprehensive evaluation of the efficacy of SMT for the treatment of ANP. The review considers eight RCTs [16–23], which provide a range of information on different types of interventions, control groups, outcome measures, and follow-up durations. The current study has limitations regarding the unknown long-term effects of interventions due to varying assessment times and short follow-up durations reported in the included RCTs. This limits the comprehensive understanding of sustained benefits or potential harms of SMT for ANP. Additionally, the lack of blinding in many of the included RCTs raises questions about intervention efficacy, potentially introducing bias and impacting the validity of reported treatment effects. Despite the

strengths of comprehensive search, adherence to standards, and inclusion of various RCTs, caution is necessary when interpreting the findings. To improve the understanding of SMT for ANP treatment, further research with larger sample sizes, consistent study designs, longer follow-up periods, and blinded assessments is needed.

Conclusions

This systematic review and meta-analysis suggest that SMT is effective for reducing pain intensity and disability and improving CROM in patients with ANP. Future studies with better standardization of interventions and comparators are necessary to draw more definitive conclusions about the efficacy of SMT for ANP.

Abbreviations

ANP	Acute neck pain
SMT	Spinal manipulative therapy
GRADE	Grading of recommendations assessment, development, and
	Evaluation
PRISMA	Preferred reporting items for systematic review and meta-analyses
PROSPERO	International prospective register of systematic reviews

Supplementary Information

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Additional file 1: PRISMA Checklist.

Additional file 2: Search strategies.

Additional file 3: Articles excluded.

Authors' contributions

L.R.L., Y.X.D., and J.X.P. contributed to the conception and design of the project. Y.X.D., J.M.C., and J.H.P. drafted the manuscript, while M.X.L. and H.L. reviewed the statistical sections. Y.F.L. revised the manuscript. All authors have read and approved the final version of the manuscript.

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Data availability

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors have no competing interests to declare.

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