Received: 27 December 2022 | Revised: 24 April 2023 | Accepted: 27 April 2023

DOI: 10.1111/apa.16807

ACTA PÆDIATRICA NURTURING THE CHILD WILEY

REVIEW ARTICLE

Systematic review and meta-analysis showed that complementary and alternative medicines were not effective for infantile colic

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Abstract

Aim: Osteopathy and chiropractic techniques are used for babies for different reasons, but it is unclear how effective they are. The aim of this study was to evaluate their effectiveness in reducing crying time and increasing sleeping time in babies with infantile colic.

Methods: A systematic review and meta-analysis was conducted on infantile colic studies that used complementary and alternative medicine techniques as interventions. The outcome measures were hours spent crying and/or sleeping. We used the PubMed, Physiotherapy Evidence Database, Cochrane Library, Embase, Web of Science, Scopus, Osteopathic Medicine Digital Database and Google Scholar databases from inception to 11 November 2022.

Results: The methodological quality of the randomised control trials ranged from fair to high. We focused on five studies with 422 babies. Complementary treatments failed to decrease the crying time (mean difference −1.08, 95% CI: −2.17 to 0.01, $I^2 = 92\%$) and to increase sleeping time (mean difference 1.11, 95% CI: −0.20 to 2.41; I^2: 91%), compared with no intervention. The quality of the evidence was rated as very low for both outcome measures.

Conclusion: Osteopathy and chiropractic treatment failed to reduce the crying time and increase sleeping time in babies with infantile colic, compared with no additional intervention.

KEYWORDS
chiropractic, colic, complementary therapies, infant, osteopathy

Abbreviations: CAM, complementary and alternative medicine; MD, mean difference; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-analysis; WHO, World Health Organisation.

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1 | INTRODUCTION

Infantile colic was first clinically defined by Wessel et al.[1] as a baby crying uncontrollable and inexplicable for more than 3 h/day, for 3 days/week, for 3 weeks. Other symptoms are now included in the clinical diagnosis, such as difficulties in passing gas and constipation.[2] Babies who have infantile colic mainly present with prolonged crying and difficulties sleeping. Crying episodes begin in the first 15 days of life and gradually resolve spontaneously by 3–4 months of age.[3,4] The worldwide prevalence of infantile colic in children under the age of 3 months has been reported to be 20%,[5] making this an important health and socioeconomic problem.

Several treatment techniques have been described for infantile colic, such as pharmacological interventions,[6] probiotics, dietary modifications,[7] physiotherapy[8] or other complementary and alternative medicines (CAMs). Structural osteopathy,[9] cranial osteopathy,[10] visceral osteopathy and chiropractic treatments[11] are the most frequently performed CAM techniques.

Osteopathy and chiropractic treatments are manual therapies that are defined as CAMs by the World Health Organization (WHO). These are covered in two WHO documents: benchmarks for osteopathic education published in 2010,[12] and guidelines on basic training and safety in chiropractic, published in 2005.[13] These documents state that both these CAM treatments use manual palpation to diagnose and treat diverse musculoskeletal disorders and highlight the repercussions of these therapies on the nervous system and general health. Osteopathy and chiropractic both use a holistic approach, which emphasises the relationship between the body, mind and spirit in health and disease.[12,13]

Both therapies are based on the theory that misalignments in bone structure and tensions in soft tissue may have a negative impact on functioning and well-being. That is why the most common techniques used in CAMs are mobilising and manipulating the spine and joints, soft tissues techniques and cranial and visceral techniques.[14,15] The clinical reasoning behind the use of these techniques is based on a number of different beliefs. These include the fact that the birth process can cause extreme pressures in the cranial structure and that poor positioning in the uterus can cause spinal dysfunction.[16]

Some authors have discussed how effective these interventions are in treating infantile colic and other paediatric disorders, but the quality of the published studies has been low. Dobson et al reported unclear results about the use of manipulative therapies for infantile colic[16] and Côté et al.[17] stated that CAMs were not effective for treating non-musculoskeletal disorders. The results of the systematic review and meta-analysis conducted by Posadzki et al were in line with other studies. The authors concluded that the effectiveness of osteopathy for treating different paediatric conditions remained unproven.[18] Studies have disagreed on the effectiveness of using chiropractic treatment. Ernst concluded that chiropractic care was not based on convincing data from rigorous clinical trials,[19] but Alcantara et al, concluded that it could be a promising approach.[20]

Key Notes

- This systematic review and meta-analysis evaluated whether osteopathy and chiropractic treatment reduced crying time and increased sleeping time in babies with infantile colic.
- Five studies on 422 children were analysed and they showed that these complementary and alternative medicines were infective in tackling infantile colic.
- The quality of the evidence was rated as very low for both outcome measures.

It is necessary to clarify how effectively osteopathy and chiropractic approaches can treat or reduce infantile colic, due to the lack of high-quality evidence to support these intervention and the heterogeneity of the results. Moreover, clear conclusions are required, as the number of children seeking manipulative treatment for neuromusculoskeletal disorders is increasing, even though there is no clear evidence to say they are suitable.[15] The aim of this study was to assess the effectiveness of osteopathy and chiropractic treatment in reducing crying time and increasing sleeping time in babies with infantile colic.

2 | METHODS

2.1 | Study design

This study protocol for this systematic review and meta-analysis was registered in the International Prospective Register of Systematic Reviews (CRD42022373815). It has been reported according to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement and the Cochrane recommendations.[21]

2.2 | Search strategy

The literature search was conducted using a number of databases from inception to 11 November 2022: PubMed, the Physiotherapy Evidence Database, the Cochrane Library, Embase, Web of Science, Scopus, Google Scholar and the Osteopathic Medicine Digital Database. The Population, Intervention, Comparison and Outcome framework were used to define the search strategy. The medical subject headings that were used were musculoskeletal manipulation, osteopathic manipulation, chiropractic manipulation and infant. The strategies used to search each database are shown in Appendix S1. The reference lists of all the included studies were searched for grey literature.

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2.3 | Eligibility criteria and study selection

Studies were included in this systematic review and meta-analysis if they focused on babies diagnosed with infantile colic who were treated with any type of CAMs: cranial, visceral or structural osteopathy or chiropractic manipulation or mobilisation. The control groups needed to be selected on the basis of no CAM intervention. Only studies that included outcome measures for crying and/or sleeping with a valid and reliable instrument were included.

Studies were excluded if they included any other paediatric condition or if they did not report any of these measures or used a non-validated instrument. They were also excluded if they were not randomised controlled trials and the papers were not available in English, French or Spanish.

Two reviewers (LC and AC) independently performed the database searches. The references were exported to the Mendeley desktop (Mendeley Ltd, Oxford, UK) and the duplicates were removed. The titles and abstracts were screened to determine whether the papers met the eligibility criteria. Potential full texts were examined by the same reviewers. A third author (SJ) resolved any possible disagreements.

2.3.1 | Data extraction

The same reviewers (LC and AC) independently extracted the data, following the standardised process adapted from the Cochrane Collaboration. These comprised the characteristics of the study population, aspects of the intervention, outcome measures and results. The third author (SJ) resolved any disagreements. Data were analysed using qualitative and quantitative synthesis.

2.4 | Risk of bias and quality of the evidence

The quality of the studies was assessed independently by two authors (LC and AC) using the Physiotherapy Evidence Database scale and the Cochrane Risk of Bias tool. The Physiotherapy Evidence Database scale is an 11-item scale based on the Delphi list developed by Verhagen et al.[22] A score of seven or above was considered high quality, five to six was considered fair quality and four or less was considered poor quality.[22] One item of the Physiotherapy Evidence Database scale, covering eligibility criteria, was related to external validity and was not used to calculate the total score. The Cochrane Risk of Bias tool was used to determine the potential bias and internal validity of the studies and classify them as low, unclear or high risk, based on seven criteria.[23] Both scales have been shown to be reliable for evaluating the quality of studies and assessing the risk of bias.

The certainty of the evidence was assessed using the Grading of Recommendation, Assessment, Development and Evaluation Evidence Profiles classification. This categorises the certainty as high, moderate, low or very low and allows to researchers to evaluate the importance of the results given in the studies. It assesses certainty according to the following domains: study design, risk of bias, inconsistency, indirect evidence, imprecision and other factors.[24] The certainty of the evidence for the meta-analysis was downgraded according to the presence of different indicators. Studies were downgraded according to the risk of bias detected. They were downgraded by one or two levels if more than 25% or 50% of the participants were from studies with poor or fair methodological quality, respectively. In addition, the inconsistency of the results was assessed and studies were downgraded by one level if there was significant heterogeneity in the outcome measurements or intervention or the I^2 value was 50% or more. They were downgraded by two levels if the I^2 was 75% or more.[25,26] The indirectness of the evidence was downgraded by one level if studies included different populations, interventions or comparators. Finally, the imprecision was assessed and studies were downgraded by one level if there were fewer than 100 participants in the comparison group and two levels if the samples comprised 30 individuals or less.[26–28] When it came to the design of the studies, single randomised trials were considered inconsistent and imprecise and regarded as providing low-quality evidence. They could be downgraded further to very low-quality evidence if there was also a high risk of bias.[24,29]

2.5 | Data synthesis and analysis

An independent researcher (SC) used RevMan version 5.4 (Cochrane) to perform the quantitative synthesis of the systematic review and meta-analysis. Data obtained from the included studies were combined when the participants, interventions, comparators and outcomes were appropriate. The quantitative synthesis of the results was carried out according to the outcomes, which were the time spent crying and sleeping.

The meta-analysis was split into two subgroups: osteopathy or chiropractic interventions. Data were combined in the meta-analysis when at least two trials were considered clinically homogeneous. An inverse variance method was performed when studies used different tools to assess the same outcome. RCTs were considered homogeneous if there was a common intervention and outcome. A fixed-effects meta-analysis was performed when each study estimated exactly the same quantity. A random effects meta-analysis was performed when combining the intervention effects was able to incorporate an assumption that the studies were not all estimating the same intervention effect.[30]

Mean and standard deviations (SDs) for the postintervention findings were extracted and so were sample sizes from each group. Mean differences (MDs) and 95% confidence intervals (CIs) were calculated based on the postintervention means and SDs.

Funnel plots and the Eggar's tests were not appropriate, because less than 10 studies were included.

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3 | RESULTS

After the initial screening, 10 studies were considered eligible, but five were excluded after we read the full text, because they did not meet the inclusion criteria. The excluded studies included preterm infants without colic,[31,32] described a secondary analysis of an RCT,[10] did not report the outcomes of interest[33] and used pharmacological interventions as the comparison method.[34] No additional studies were included after we reviewed the reference lists of the included studies and no studies were excluded because of the language they were published in. The selection process for the five studies that we included in our qualitative and quantitative synthesis is shown in the PRISMA flowchart diagram (Figure 1). The kappa agreement between the reviewers was one.

3.1 | Characteristics of the eligible studies

We studied five RCTs with a total of 422 babies with infantile colic. The sample sizes ranged from 28 to 185. The diagnostic criteria for infantile colic in four studies was uncontrollable and inexplicable crying for more than 3 h/day, for 3 days/week, for 3 weeks.[11,35–37] The other study focused on babies that had cried unconsolably for 90 min in each 24-h period on five of the last 7 days.[38] Babies under eight,[11] nine,[36] 12[35,38] and 14[37] weeks of age were recruited. The sociodemographic and clinical characteristics of the babies included in each study are shown in Table 1.

Different complementary interventions, based on manual therapies, were identified in the experimental groups. Two studies used osteopathic techniques based on manipulations and/or mobilisations of the craniosacral complex,[35,38] and three used chiropractic mobilisation or manipulation.[11,36,37] No interventions were applied in the control groups. Table 2 provides detailed descriptions of the interventions.

The duration of the sessions, the number of sessions and the frequency and duration of the intervention varied among the studies. Only two studies defined the duration of the sessions and these ranged from 30 to 40 min.[35,38] The total number of sessions varied from one to four and the duration of the interventions ranged from 1 to 4 weeks.[11,35–38] The frequency ranged from one to three sessions in four studies[35–38] and the other study did not report that data.[11]

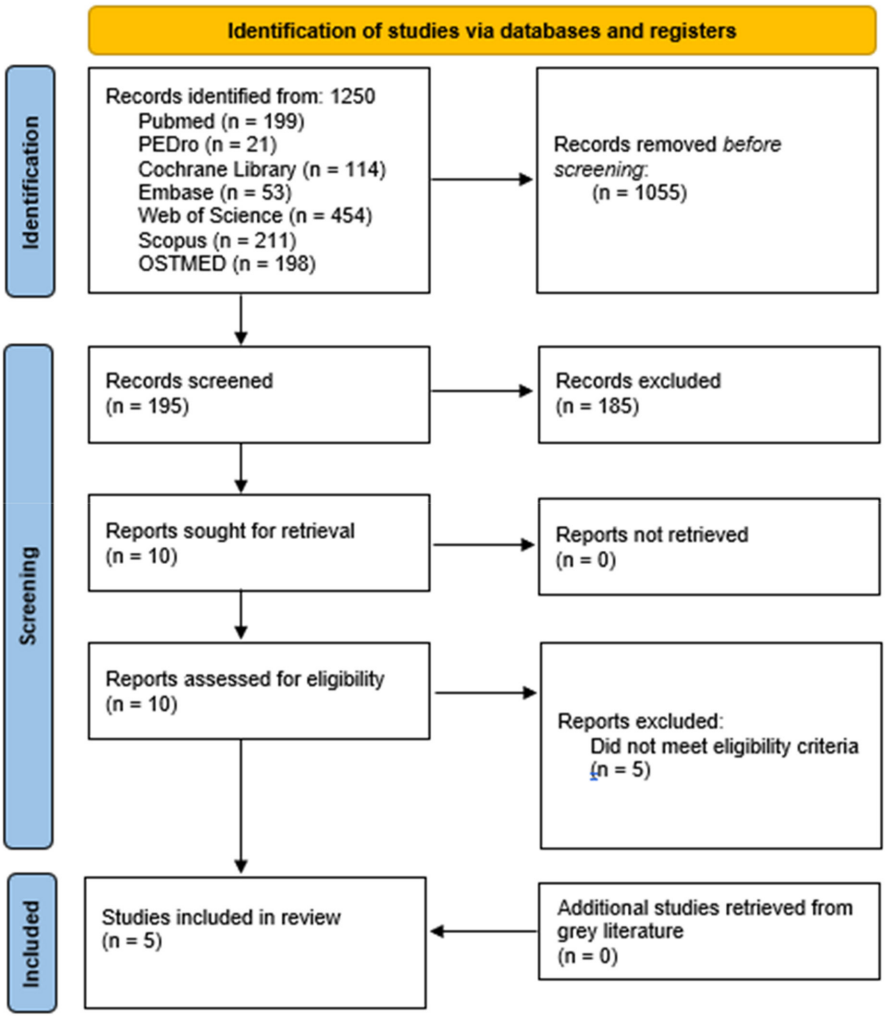

FIGURE 1 PRISMA Flowchart diagram. OSTMED, osteopathic medicine digital database; PEDro, Physiotherapy Evidence Database.

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TABLE 1 Sociodemographic and clinical characteristics of subjects in the included studies.

Author	Number (sex ratio)	Mean age (SD)	Intervention		Outcome (tool)	Main results	Physiotherapy evidence database
			EG	CG			
Castejón-Castejón et al.[35] 2022	58 (29 M/29 F)	EG: 39.14 (20.15) days CG: 33.69 (15.14) days	Osteopathy based on craniosacral therapy	No additional intervention	Crying and sleep diary	Reduced crying and increased sleep in EG vs. CG	6
Hayden et al.[38] 2006	28 (22 M/6 F)	EG:46.4 (5.4) days CG: 44.5 (5.0) days	Osteopathy based on craniosacral therapy	No additional intervention	Crying and sleep diary	Reducing crying in EG vs. CG	5
Holm et al.[37] 2021	185 (90 M/95 F)	EG:6.8 (2.9) weeks CG:6.6 (2.6) weeks	Quiropractic manipulation/mobilisation	No additional intervention	Crying and sleep diary	No differences between groups	8
Miller et al.[11] 2012	69 (35 M/34 F)	EG:4.9 (2.04) weeks CG: 5.25 (1.73) weeks	Quiropractic manipulation/mobilisation	No additional intervention	Crying diary	Reducing crying in EG vs. CG	6
Olafsdottir et al.[36] 2001	86 (47 M/39 F)	No reported	Quiropractic manipulation/mobilisation	No additional intervention	Crying diary	No differences between groups	8

Note: Reductions and increases were statistically significant.

Abbreviations: CG, control group; EG, experimental group; F, female; M, male.

3.2 | Outcome measures

The outcome measures considered by the meta-analysis were assessed at baseline and after the interventions. They were the total number of hours of crying and sleeping during a 24-h period, which was recorded in both crying and sleeping diaries by the parents. No follow-up analyses were performed by any of the five studies.[11,35–38]

3.3 | Study quality and risk of bias

Four studies correctly performed the randomisation process.[11,35–37] Two studies presented a high risk of bias and two reported an unclear risk of bias due to missing outcome data.[11,35,36,38] All the studies appeared to have an unclear risk of bias when it came to selecting the results that were reported.[11,35–38] The results of the assessments carried out using the Cochrane risk-of-bias tool are shown in Figure 2.

The Physiotherapy Evidence Database scale was used to assess the methodological quality of the studies. Three studies were considered to provide fair quality[11,35,38] and two were categorised as a high quality[36,37] (Table 1).

3.4 | Synthesis of the results

The number of hours that an infant spent crying during a 24-h period was measured by all the studies. The meta-analysis showed that osteopathic and chiropractic interventions produced no significant reduction in crying hours compared to no intervention (MD: −1.08, 95% CI: −2.17 to 0.01, I^2 92%; Figure 3).

The amount of time that the infant slept in a 24-h period was measured by three of the studies. The quantitative synthesis showed that osteopathic and chiropractic interventions led to no significant improvement in total sleeping time compared to no intervention (MD 1.11, 95% CI: −0.20 to 2.41, I^2 91%; Figure 3b).

3.5 | Adverse events

We looked at adverse effects in the experimental groups after the interventions. Two studies reported no problems,[11,35] Holm et al.[37] reported that one participant was withdrawn due to increased crying. The other two studies did not assess adverse events during the study period.[36,38]

3.6 | GRADE assessments

The overall certainty of the evidence for both outcome measures was rated as very low, according to GRADE. The certainty assessment found that both outcome variables had a very serious risk of

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TABLE 2 Characteristics of the interventions.

Author	Interventor	Intervention	Control	Duration of sessions	Number of sessions	Sessions per week	Duration of intervention
Castejón-Castejón et al.[35] 2022	Physiotherapists	Balance of the pelvic, thoracic and clavicular diaphragms (transverse planes). Hyoid release, decompression of the sacrum, release of the atlanto-occipital joint, occipital decompression, frontal lift, parietal lift, decompression of the sphenobasilar synchondrosis, decompression of the temporal bone, decompression of the temporomandibular joints and craniosacral balancing.	No additional intervention	EG: 30–40 min	1 to 3	1 per week	3 weeks
Hayden et al.[38] 2006	Osteopaths	Treatment was individualised, according to clinical findings, and involved standard cranial osteopathic techniques until a palpable release of tensions and dysfunction was achieved	No additional intervention	EG: 30 min	4	1 per week	4 weeks
Holm et al.[37] 2021	Quiropractics	Manual therapy could include manipulation or mobilisation of the spine and/or the extremities as indicated by the child's potential biomechanical dysfunctions. Included movement restriction, tenderness or an obvious asymmetry in the muscles or joints. The treatment technique for restricted joint movements in this age group was, in general, very light short-term pressure with fingertips and gentle massage for hypertonic muscles.	No additional intervention	Not reported	4	2 per week	2 weeks
Miller et al.[11] 2012	Quiropractics	Treatment was pragmatic and individualised to examination findings. It consisted of chiropractic manual therapy of the spine. Specifically, this involved low-force tactile pressure to spinal joints and paraspinal muscles if dysfunction was noted on palpation. The manual therapy, estimated at 2 N of force, was given at the area of involvement without rotation of the spine.	No additional intervention	Not reported	Not reported	Not reported	1 to 5 weeks
Olafsdottir et al.[36] 2001	Quiropractics	Dysfunctional articulations were manipulated and mobilised using light fingertip pressure.	No additional intervention	Not reported	3	3 per week	1 week

Abbreviation: EG, experimental group.

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bias and showed inconsistencies and evidence of serious indirectness. The results were uncertain and presented very little confidence in the estimated effect (Table 3).

4 | DISCUSSION

The aim of this study was to assess the effectiveness of osteopathy and chiropractic treatment in reducing crying time and increasing sleeping time in babies with infantile colic. The meta-analysis of the five studies found that CAMs did not reduce the hours spent crying during a 24-h period when they were compared with no additional intervention. Moreover, the meta-analysis of three studies showed that CAMs did not increase sleeping time when it was compared with no intervention. The certainty of the evidence was rated as very low.

The methodological quality of the RCTs we included ranged from fair to high. In general, blinding paediatric participants in RCTs is an issue and so is blinding therapists in studies that provide conservative non-pharmacological interventions. Blinding the parents may increase the quality of such studies. Despite this, only two of the studies in this systematic review and meta-analysis use blinded methodology.[11,37] Authors have previously discussed the need to improve the methodological designs of RCTs on CAMs therapies. None of the studies controlled the effect of the intervention by using sham or placebo groups. In addition, adverse effects should be considered whenever manipulation techniques are performed.[39] Two of the studies did not report any adverse events, while another study withdrew one patient due to increased crying.[37] A patient being withdrawn or dropping out due to a worsened outcome variable could be considered an adverse effect and may lead to a risk of bias when the results are reported.

It is noteworthy that the three studies that demonstrated statistically significant improvements in the experimental groups were classified as having fair quality.[11,35,38] Moreover, the studies with high quality did not demonstrate any statistically significant differences.[36,37]

Another systematic review and meta-analysis that investigated the clinical effectiveness of osteopathy and chiropractic

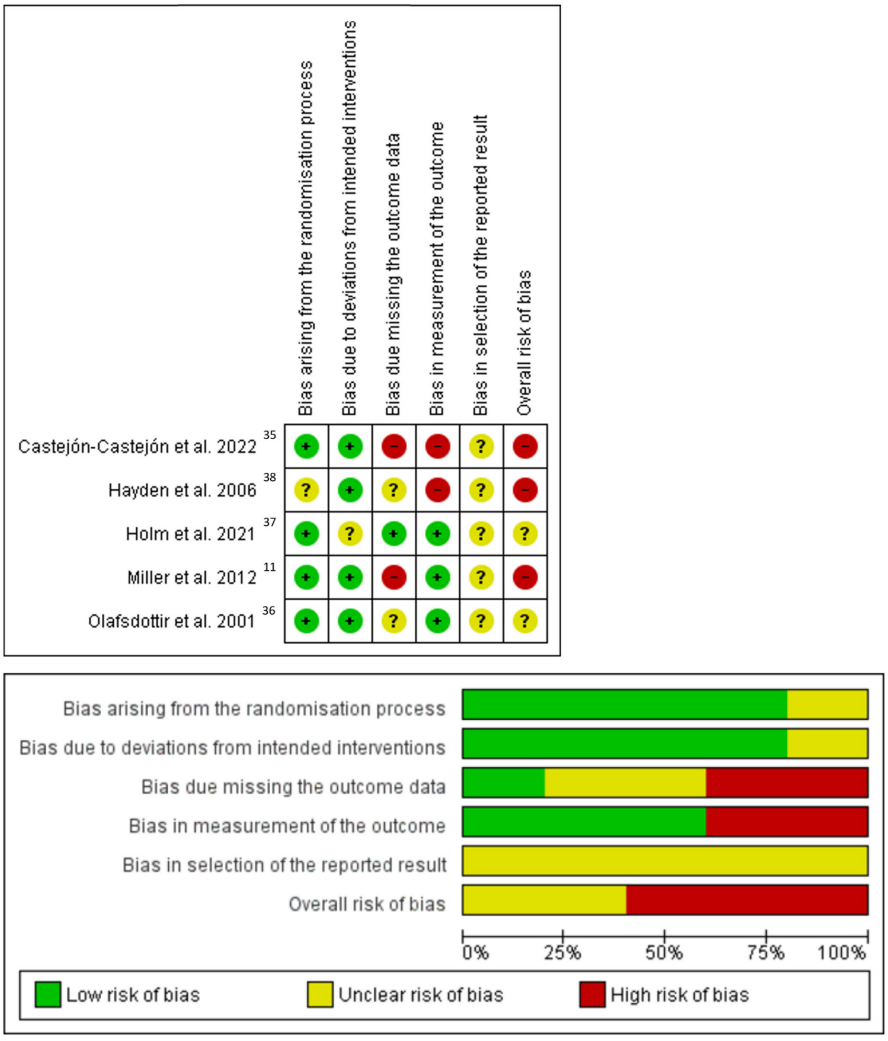

FIGURE 2 Risk of bias Cochrane tool.

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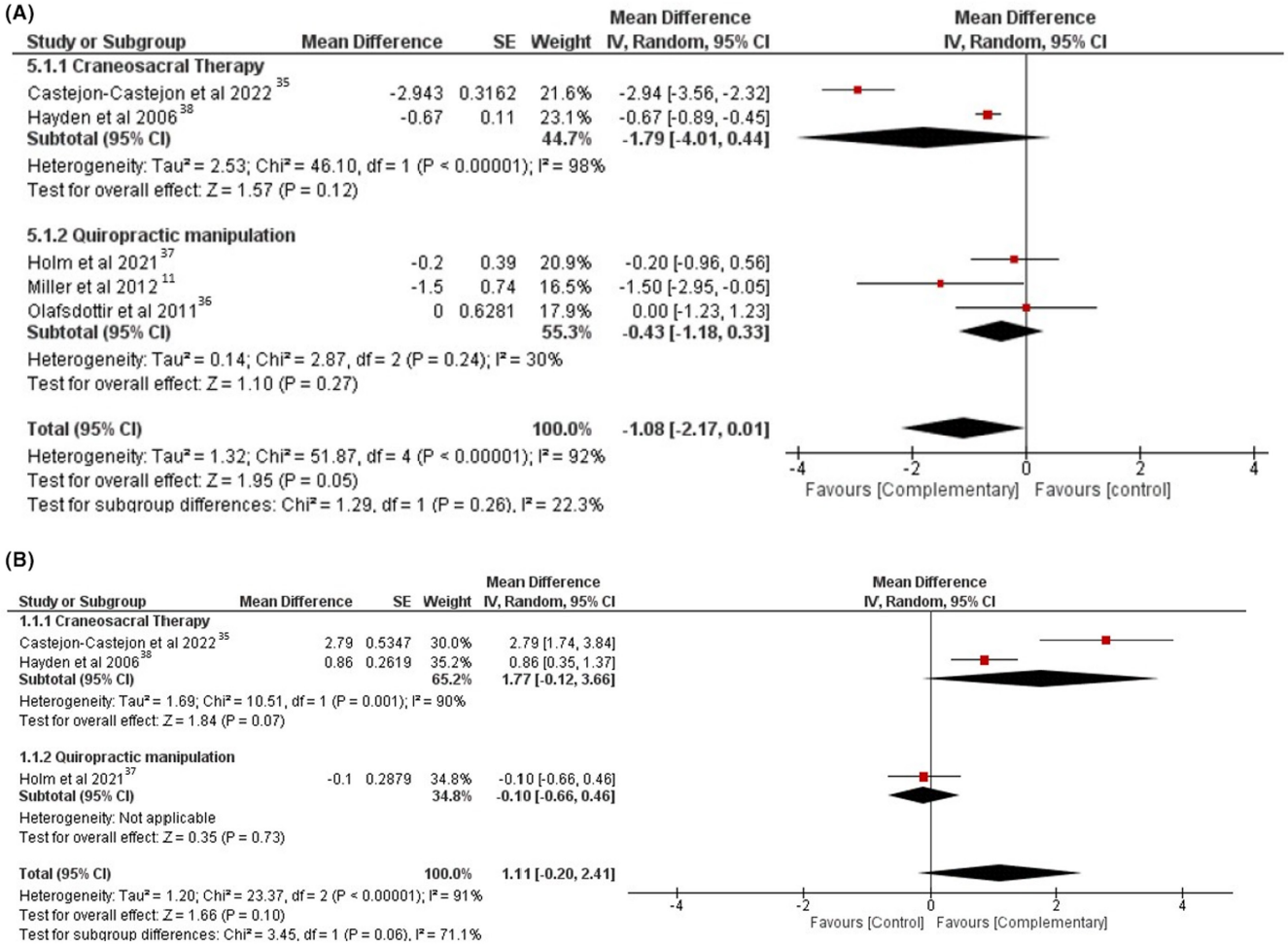

FIGURE 3 (A) Forest plot of total crying time after osteopathic and chiropractic treatment. (B) Forest plot of total sleeping time after osteopathic and chiropractic treatment.

CAMS treatment on crying infants and found some small benefits. However, this systematic review included studies with different infant populations and designs apart from RCTs,[40] which inevitably led to bias. On the contrary, previous studies suggested that osteopathy and chiropractic interventions did not produce positive effects when treating paediatric conditions.[18,19,41] An updated review by Ernst showed that chiropractic spinal manipulation failed to demonstrate its effectiveness for treating infantile colic.[19] Posadzki et al.[18] updated systematic review and meta-analysis showed that osteopathy was not effective for treating children with different disorders, including infantile colic. Meanwhile, Guillaud et al. examined using these techniques and therapeutic strategies for cranial osteopathy. The authors concluded that there was virtually no methodologically strong evidence to demonstrate the clinical efficacy of these approaches.[42] Several authors have questioned the validity, plausibility and use of osteopathic methods.[43,44] Hartman et al.[43] suggested that cranial osteopathy should not be used in academic and clinical settings until outcome studies showed that these techniques produce a positive clinical effect.

The results of this study were in accordance with previous evidence that suggested that CAMs failed to show short-term benefits for infantile colic. The medium-term and long-term effects of these interventions have not been assessed by any study. This is understandable, because infantile colic gradually and spontaneously improves between the third and fourth month of age. However, the interventions have typically lasted from 1 to 4 weeks, so follow-up studies could be performed until the third or fourth month of age.

The Consolidated Standards of Reporting Trials and the Template for Intervention Description and Replication promote the need for information on treatment dosage, so that the results obtained by researchers and/or in the clinical fields can be reproduced. In the studies we reviewed, the intervention was applied after a subjective evaluation performed by an osteopath or a chiropractor.[11,35–38] The evaluation was based on the manual palpation of structures, in order to try and diagnose dysfunctions or impairments. It would be difficult to replicate these in other studies. Treatment was based on the subjective findings during the evaluation. That is why the interventions were very heterogeneous. None of the studies showed anything measurable regarding

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TABLE 3 Certainty of evidence according to GRADE.

Certainty assessment							Number of participants		Effect		Certainty
Number of studies	Study design	Risk of bias	Inconsistency	Evidence of indirectness	Imprecision	Others	Experimental group	Control group	Relative (95% CI)	Absolute (95% CI)	
Crying (Crying diary)											
5	RCTs	Very serious[a]	Very serious[b]	Serious[c]	Not serious	None	220	202	-	SMD **1.08 SD less** (2.17 less to 0.01 higher)	⊕◯◯◯ Very low
Sleep (Sleep diary)											
3	RCTs	Very serious[a]	Very serious[b]	Serious[c]	Not serious	None	139	126	-	SMD **1.11 SD less** (0.2 less to 2.41 higher)	⊕◯◯◯ Very low

Abbreviations: CI, confidence interval; SMD, standarised mean difference.

[a]More than 50% of the participants were from studies with poor or fair methodological quality. These aspects were considered: lack of allocation concealment, random allocation and/or sample size calculation, participant and personnel blinding, blinding of outcome assessors.

[b]Significant heterogeneity regarding outcome measurement or intervention or I^2 value was ≥75%.

[c]The interventions were heterogeneous and not detailed in the studies. High: we are very confident that the true effect was close to the estimate of the effect. Moderate: we are moderately confident in the effect estimate. The true effect was close to the estimate of the effect, but the result could be different. Low: confidence in the effect estimate was limited and the true effect could have been substantially different from the estimate of the effect. Very Low: there was little confidence in the effect estimate and the true effect was likely to be substantially different from the estimate effect.

the evaluation and/or treatment processes,[11,35–38] which contributed to research bias.

Although no high-quality evidence has been produced to support the suitability of these interventions for infantile colic, different surveys have shown that an increasing number of parents are seeking CAMs for their children's non-musculoskeletal disorders.[15,45] We feel that a number of recommendations should be implemented in future studies. These are pre-registration trials, medium-term or long-term follow ups, sham or simulated interventions that provide comparisons, clearer presentations of assessments and interventions and proper statistics. Otherwise, CAMs should not be used or recommended for infantile colic.

From a clinical point of view, the results of this systematic review and meta-analysis were in accordance with previous studies that pointed to the lack of evidence supporting the use of CAMs for babies with infantile colic. Including CAMs in public and/or private healthcare systems would require high-quality evidence. Using CAMs for infantile colic cannot be recommended based on the current evidence.

This study had three main limitations. Firstly, the lack of RCTs may have influenced the results. Secondly, the heterogeneity in the experimental study groups complicated the interpretation of the results. These included the type and the duration of the interventions applied. Thirdly, the lack of medium-term and long-term follow ups may have influenced the results achieved.

5 | CONCLUSION

This systematic review and meta-analysis showed that CAMs failed to reduce crying time and increase sleeping time for babies with infantile colic when they were compared with no additional intervention. The findings specifically relate to osteopathy and chiropractic treatment.

CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to declare.

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How to cite this article: Cabanillas-Barea S, Jiménez-del-Barrio S, Carrasco-Uribarren A, Ortega-Martínez A, Pérez-Guillén S, Ceballos-Laita L. Systematic review and meta-analysis showed that complementary and alternative medicines were not effective for infantile colic. Acta Paediatr. 2023;112:1378–1388. https://doi.org/10.1111/apa.16807

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