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Combined effect of external treatment of herbal medicine and tuina in congenital muscular torticollis

Systematic review and meta-analysis

Eunjin Kim, KMD, PhD[a], Jungyoon Choi, KMD[b], Sang Yeon Min, KMD, PhD[c,*]

Abstract

Background: Congenital muscular torticollis (CMT) is the third most common musculoskeletal disease in children. With no standardized treatment method hence, so it is necessary to find an effective treatment method that can be received comfortably by children. This review assessed the efficacy of an external treatment of herbal medicine (ETHM) with tuina for CMT in children.

Methods: This study searched the English, Chinese, and Korean databases (total of 10) until June 7 2022, without any language restrictions. All included studies were randomized clinical trials (RCTs) of ETHM with tuina as an intervention comparted to the same tuina alone according to the inclusion and exclusion criteria. The mean differences (MD), standardized mean differences (SMD), risk ratio (RR) with the 95% confidence interval (CI), and risk of bias (ROBs) were calculated using Review Manager Version 5.4 software. The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) rating system was used to assess the quality of evidence. The publication bias was evaluated using a funnel plot, the Egger test, the fail-safe N test, and the Duval and Tweedle's trim and fill method using Review Manager Version 5.4 software, the software R Version 4.1.1 and R studio Version 1.4.1106 program.

Results: Nineteen RCTs with 1710 patients were included in the meta-analysis. ETHM plus tuina improved the outcomes of the total effective rate (TER) [RR 1.21, 95% CI:1.15 to 1.26, $P < .001$], sternocleidomastoid (SCM) muscle thickness [MD: −1.82, 95% CI: −2.23 to −1.41, $P < .001$], cervical rotation range [MD: 13.43, 95% CI: 10.41–16.45, $P < .001$] and lateral flexion range [MD: 8.50, 95% CI: 6.15–10.85, $P < .001$], tissue elasticity grade [SMD: −0.46; 95% CI: −0.71 to −0.22, $P = .0002$], muscle elasticity scores [RR: 1.56; 95% CI: 1.04 to 2.34, $P = .03$], and clinical symptom and sign scores [SMD: −0.78; 95% CI: −1.09 to −0.47, $P < .001$].

Conclusions: ETHM plus tuina have a combined effect on CMT children. However, further studies with high-quality clinical trials are needed to obtain more robust clinical evidence.

Abbreviations: CI = confidence interval, CMT = congenital muscular treatment, ETHM = external treatment of herbal medicine, GRADE = Grading of Recommendations Assessment, Development, and Evaluation, MD = mean differences, RCT = randomized controlled trial, RR = risk ratio, SCM = sternocleidomastoid, SMD = standardized mean differences, TER = total effective rate.

Keywords: congenital muscular torticollis, external treatment, herbal medicine, meta-analysis, pediatrics, systematic reviews, tuina

1. Introduction

Congenital muscular torticollis (CMT), synonymous with wryneck[1] and twisted neck,[2] is one of the third most frequent musculoskeletal disorders in neonates. The reported prevalence of CMT ranges from 3.9% to 16%.[3,4]

The sternocleidomastoid (SCM) muscle originates from the manubrium of the sternum and the clavicle and attaches to the mastoid process of the temporal bone. The main function of the muscle is rotating the head to the opposite side and flexing the neck. If there is unilateral tightness or shortening in SCM muscle, the infant's head loses balance, tilts to one side, and

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All data generated or analyzed during this study are included in this published article [and its supplementary information files].

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rotates to the contralateral side with a restriction of the passive and active cervical range of motion.[5] CMT is usually diagnosed by the clinical symptoms. Ultrasonography is the initial imaging method for assessing the severity of muscle fibrosis and comparing the difference in the thickness of the SCM muscle on both sides.[6] Magnetic resonance imaging can determine if there is a non-muscular cause or not.[7] Approximately 50% of CMT cases are confirmed within 2 to 3 weeks to 2 months after birth.[7] Early intervention should be started as soon as possible when asymmetry is noticed to prevent secondary complications, such as positional plagiocephaly, facial deformity, and scoliosis.[8,9]

Because surgical treatment is considered after 12 months,[10] conservative treatments, such as alternative and complementary therapy, are performed first. Usually, traction therapy, kerotherapy, acupuncture, small needle knife, paraffin therapy, and other physical therapy are performed based on tuina.[11] Among the various inventions, the topical application of traditional herbal medicine is one of the treatment methods for musculoskeletal disorders such as wounds, bruises, cramps, and muscle pains.[12] External therapy of herbal medicine (ETHM) plus tuina, which is used widely in Asian countries, can be an improved curative effect. It has the advantages of safety and non-invasiveness, relatively low cost, no age limit, and high acceptance by parents.[13]

Previously, a systematic review and meta-analysis of tuina for CMT reported that tuina has similar effects to stretching therapy and is more effective when combined with ultrashort wave therapy or function training.[14] On the other hand, there are few reports on the efficacy of tuina with ETHM. This review systematically evaluated the enhancing effect when combined ETHM and tuina for CMT.

2. Methods

2.1. Protocol and registration

This systematic review and meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.[15] The protocol of this review was registered with INPLASY (registration number: INPLASY202210017) on January 5, 2022 and published in the Medicine Journal on March 11, 2022.[16]

2.2. Eligibility criteria

2.2.1. Types of studies. Only randomized controlled trial (RCT) of ETHM combined with tuina for treating of CMT were included. Non-RCTs, RCT protocol, animal studies, case reports, surveys, and reviews were excluded.

2.2.2. Types of participants. Children aged zero to two years diagnosed with any type of CMT were included. The exclusion criteria were as follows: patients with torticollis caused by other diseases, such as skeletal torticollis, compensatory torticollis due to atlantoaxial joint subluxation, visual impairment, hearing impairment, and neurotic torticollis due to cervical muscle paralysis; those with severe organ dysfunction and complications, such as heart, liver, and kidney.

2.2.3. Types of interventions. The interventions of the experimental group included tuina therapy plus ETHM: no limitation of the number of herbs, formulation, dosages, duration, and whether to use heat stimulation or steam fumigation.

2.2.4. Types of comparisons. The interventions of controlled groups included only the same tuina methods as the experimental group. There were no restrictions on the type of tuina, and whether to use powders as a tuina medium (e.g., talcum powder), but combined with magnetic therapy or physiotherapy was excluded.

2.2.5. Types of outcome measure. The primary outcomes were the total effective rate, the thickness of the mass in the SCM muscle, and the cervical range of the motion of rotation or lateral flexion of the affected side. The secondary outcomes were symptom scores and grade (e.g., tissue elasticity grade, muscle elasticity scores, clinical symptoms and scores), recurrence rate, and adverse events.

2.3. Information sources

2.3.1. Data sources. The following ten electronic databases were searched, without any language and year restrictions until June 7, 2022: three English databases (PubMed, Excerpta Medica data BASE, and the Cochrane Central Register of Controlled Trials), three Chinese databases (China National Knowledge Infrastructure, Chinese Scientific Journal Database, and Wan Fang Database), and four Korean medical databases (Oriental Medicine Advanced Searching Integrated System, Korean Studies Information Service System, Science On, and Research Information Sharing Service).

2.3.2. Search strategy. The search terms were as follows: ("wry neck" OR "twisted neck" OR "torticollis" OR "cervical dystonia" OR "CMT" OR "congenital muscular torticollis") AND ("herbal medicine" OR "herb" OR "decoction" OR "remedy" OR "Chinese medicine" OR "Korean medicine" OR "Kampo" OR "formula" OR "herbal drug" OR "herbal medicine" OR "plant" OR "Chinese drug" OR "Chinese prescript" OR "Chinese materica" OR "traditional medicine" OR "traditional Chinese medicine" OR "East Asian traditional medicine" OR "external" OR "application"). Slight modifications of the search terms were used for each database using each country's language. In addition, this study excluded the gray literature, unpublished papers, and ongoing clinical trials for more accurate and core results. The total search strategy was attached separately (see Supplement File 1, Supplemental Digital Content, http://links.lww.com/MD/I23, Search strategy for each database).

2.4. Study selection and data extraction

2.4.1. Study selection. Two review authors (E.J.K. and J.Y.C.) searched the literature by retrieving the title and abstracts first, full-text finally. The two reviewers (E.J.K. and J.Y.C.) independently performed the same process and crosschecked according to the selection criteria. Disagreements between the two reviewers (E.J.K. and J.Y.C.) were resolved through consultation, but if there was still a lack of consensus, a third reviewer (S.Y.M.) was involved to reach an agreement.

2.4.2. Data extraction. Two reviewers (E.J.K. and J.Y.C.) independently extracted data from the included studies. In the case of discrepancies in the data extraction results, agreement was reached through discussion among all authors. The data extracted in detail are as follows.

(1) study design: year of publication, first author name, sample size, total treatment periods, and follow-up periods;
(2) patient characteristics: age, gender, and type of CMT;
(3) intervention: ETHM (formulation, administration, treatment duration, composition of herbal medicines, caution), and frequency of herb;
(4) comparators: tuina (target muscles or acupoint, manipulations, tuina massage medium, treatment duration, additional education);
(5) outcome measurement and intergroup differences

Table 1

The Quality of evidence.

Outcomes	Subgroup	No. participants (studies)	Anticipated absolute effects (95% CI)		Relative effect (95% CI)	Heterogeneity (*I2*, *P*)	Quality of evidence (GRADE)	Comments
			Risk with control group*	Risk with intervention group				
Total effective rate	Total	1315 (15 studies)	779 per 1000	943 per 1000 (896–982)	RR 1.21 (1.15–1.26)	I^2 = 33% P = .11	⨁⨁⨁◯MODERATE	Risk of bias (–1)† Publication bias (0)‡
SCM thickness	Total	679 (7 studies)	–	MD 1.82 lower (2.23 lower to 1.41 lower)	–	I^2 = 51% P = .06	⨁⨁⨁⨁High	Inconsistency (0)§
Subgroup 1 (age)	<6 mo	442 (4 studies)	–	MD 1.83 lower (2.12 lower to 1.54 lower)	-	I^2 = 6% P = .37	⨁⨁⨁⨁High	Inconsistency (0)‖
	≥6 mo	237 (3 studies)	–	MD 1.91 lower (3.16 lower to 0.66 lower)	–	I^2 = 77% P = .01	⨁⨁⨁◯MODERATE	Imprecision (–1)¶
Subgroup 2 (formulation)	Decoction	200 (1 studies)	–	MD 1.66 lower (2.13 lower to 1.19 lower)	–	Not applicable	⨁⨁⨁◯MODERATE	Imprecision (–1)#
	Ointment	407 (5 studies)	–	MD 1.75 lower (2.14 lower to 1.36 lower)	–	I^2 = 16% P = .31	⨁⨁⨁◯MODERATE	Imprecision (–1)**
	Fumigation	72 (1 studies)	–	MD 3.08 lower (4.01 lower to 2.15 lower)	–	Not applicable	⨁⨁⨁◯MODERATE	Imprecision (–1)#
Cervical ROM								
Rotation range	Total	200 (1 studies)	–	MD 13.43 higher (10.41 higher to 16.45 higher)	–	Not applicable	⨁⨁⨁◯MODERATE	Imprecision (–1)#
Flexion range	Total	200 (1 studies)	–	MD 8.5 higher (6.15 higher to 10.85 higher)	–	Not applicable	⨁⨁⨁◯MODERATE	Imprecision (–1)#
Recurrence rate	Total	237 (3 studies)	26 per 1000	8 per 1000 (1–79)	RR 0.33 (0.04–3.09)	Not applicable	⨁⨁◯◯ LOW	Imprecision (–2)††††
Symptom scores								
Tissue elasticity grade (1–4)	Total	268 (3 studies)	–	SMD 0.46 lower (0.71 lower to 0.22 lower)	–	I^2 = 0% P = .91	⨁⨁⨁◯MODERATE	Imprecision (–1)¶
The number of muscle elasticity scores relieved after treatment (3–5 points to 1–2 points)	Total	174 (2 studies)	287 per 1000	448 per 1000 (299–672)	RR 1.56 (1.04–2.34)	I^2 = 0% P = .75	⨁⨁⨁◯MODERATE	Imprecision (–1)¶
Clinical symptoms and sign scores	Total	169 (2 studies)	–	SMD 0.78 lower (1.09 lower to 0.47 lower)	–	I^2 = 0% P = .95	⨁⨁⨁◯MODERATE	Imprecision (–1)¶

CI = confidence interval, Grade = Grading of Recommendations Assessment, Development, and Evaluation, MD = mean difference, ROM = range of motion, RR = risk ratio, SCM = sternocleidomastoid muscle, SMD = standardized mean difference.

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

†High risk of bias in blinding of participants and personnel, other bias.

‡Although the funnel plot for publication bias seemed to be asymmetry and the Egger regression test indicated probability for publication bias (P = .0169), False-safe N was 304, and adjusted RR using the trim and fill method was consistent with that of the original analysis.

§Although I^2 = 51%, the quality of evidence was not lowered because studies with the same effect direction and clinically heterogeneous were collected and meta-analyzed.

‖Although I^2 = 77% and P = .01, the quality of evidence was not lowered because studies with the same effect direction and clinically heterogeneous were collected and meta-analyzed.

¶Small number of studies were included, and their small sample size did not meet the OIS criterion.

#Only one study was included, and its small sample size did not meet the OIS criterion.

**The 95% CI included no effect (MD value included 0).

††Only one study was included, and its small sample size did not meet the OIS criterion. and the 95% CI included no effect (RR value included 1).

‡‡Only one study was included, and its small sample size did not meet the OIS criterion. and the 95% CI included no effect (SMD value included 0).

2.5. Assessment of risk of bias

Methodological quality within a study was assessed independently by two review authors (E.J.K. and J.Y.C.) using the Cochrane risk of bias tool[17]: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other biases into three levels (low, unclear, and high). Disagreements were resolved through discussion among the authors (E.J.K., J.Y.C., and S.Y.M.).

2.6. Statistical analysis

Review Manager (Revman) software (version 5.4, the Cochrane Collaboration, London, UK) was used to perform the meta-analysis. The data were summarized using the risk ratio (RR) with 95% confidence intervals (CI) for the dichotomous outcomes and standard mean difference (SMD) or mean difference (MD) with 95% CIs for the continuous outcomes. Descriptive analysis was conducted when the number of reported studies was one or not estimable.

2.6.1. Assessment heterogeneity. The Higgins I^2 index was used to assess the heterogeneity among the included studies. $I^2 \geq 50\%$ was considered potential heterogeneity. Hence, a random effect model was used for pooling data, and $I^2 < 50\%$ indicated low heterogeneity, so a fixed-effect model was used. Subgroup analysis and sensitivity analysis were conducted if the heterogeneity was significant,

2.6.2. Assessment of reporting bias. Potential publication bias was presented using a funnel plot if more than 10 trials were included. The asymmetry of the funnel plot was verified using the Egger regression test[18] by the software R (Version 4.1.1, R Foundation for Statistical Computing, Vienna, Austria) and R studio program (Version 1.4.1106, Integrated Development for R. R Studio, PBC, Boston, MA) using the "meta" package as a default setting. If there is a publication bias, the fail-safe N test,[19] and the Duval and Tweedle's trim and fill method[20] is evaluated additionally using the software R and R studio program. The fail-safe N test estimated the number of additional studies required to lower the effect size under significance and the trim and fill method determined the effect of publication bias on the pooled analysis.

2.6.3. Subgroup analysis and sensitivity analysis. When meta-analysis showed significant heterogeneity, subgroups analysis was performed to identify the source of heterogeneity. Subgroup analysis was conducted based on the age and formulation of ETHM.

The robustness of the meta-analysis results was tested through sensitivity analysis by excluding the studies one by one.

2.7. Quality of evidence

The certainty of evidence was evaluated according to the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) rating standards (http://gradepro.org). The following categories were evaluated: study design, risk of bias, inconsistency, indirectness, imprecision, and reporting bias. Based on the author's assessment, the GRADE system classified the level of evidence as high, moderate, low, or very low (Table 1).

2.8. Ethical approval

The ethical approval and the consent of patients were not necessary, because this study was a systemic review and the meta-analysis did not patient recruitment but literature research.

3. Results

3.1. Study selection

After selecting studies in each database using the prepared search strategy, 1322 records were obtained; 141, 362, and 819 records were retrieved from three English databases, three Chinese databases, and four Korean databases, respectively. After duplicates were removed, 37, 298, and 767 studies remained. Reviewing the titles and abstracts of the remained studies, 1029 were left out of 1102 studies. We screened 73 articles for eligibility by evaluating the full-text articles, and 54 were removed for the following reasons: not CMT (n = 1) , not RCT (n = 41), not ETHM (n = 9), not compared to tuina (n = 1), not same tuina between experimental and control group (n = 2). Finally, 19 RCTs[21–39] were included in a systematic review and meta-analysis (Fig. 1).

3.2. Characteristics of study

The 19 included studies were all RCTs and were conducted in China. The publication year ranged 2008 to 2021, and the sample size varied from 40 to 200. The total treatment duration also varied from 12 days to 6 months. The total periods of treatment were mostly the same experimental and control group. In one study,[26] however, experimental group received treatment for 60 to 90 days, while the control group received treatment for 90 to 150 days. In two studies, other treatments were added to the experimental group.[23,24] There were two studies with a follow-up period after treatment. One[23] was for regularly three months to consolidate the curative effect and prevent a recurrence, and another one[28] was for 6 to 12 months to evaluate the recurrence rate (Table 2).

3.3. Characteristics of the participants

The youngest patients were 5 days, and those up to two years of age were recruited. In the study of Li,[24] 2 out of 20 patients in the experimental group gave up, and there was no dropout in other studies. The referenced diagnostic criteria books were five cases of "Practical Pediatric Surgery,"[40] two cases of "Practical Pediatrics,"[41] two cases of "Tuina,"[42] four cases were not reported, and six were other textbooks and papers. The types of CMT are described: left and right, presence of mass (mass, diffuse, no-mass), mass shape (oval mass, cord-like), other symptoms (dysplasia of the neck muscle and trapezius muscle, tilt, and facial deformities) (Table 2).

3.4. Interventions

3.4.1. Characteristics of tuina. Twelve cases[21,22,27–33] used a medium during tuina, and seven cases[23–26,34,38,39] used only tuina without a medium. In the experimental group, there were four studies in which ETHM was the medium of tuina,[27,32,33,35] and the other eight studies used the same medium as control group.[21,22,28–31,36,37] The medium used in the control group was talcum powder with nine, Johnson & Johnson baby powder with two, and lubricating oil with one. The duration of tuina ranged from 15 to 30 minutes. For additional education during treatment, there was one mention of children's self-exercise[23] and one mention of maintaining correct position[26] (see Supplement File 2, Supplemental Digital Content, http://links.lww.com/MD/I24, Tuina treatment information).

The frequency of the target muscle was as following. The SCM muscle was the most common with 17, trapezius muscle with five, shoulder muscles with five, neck muscles with four, back muscles, splenius capitis muscle origin, the muscles of the spine, and supraspinatus with one each. The frequency of the target acupoints was as following: Gyeonjeong (GB21) was

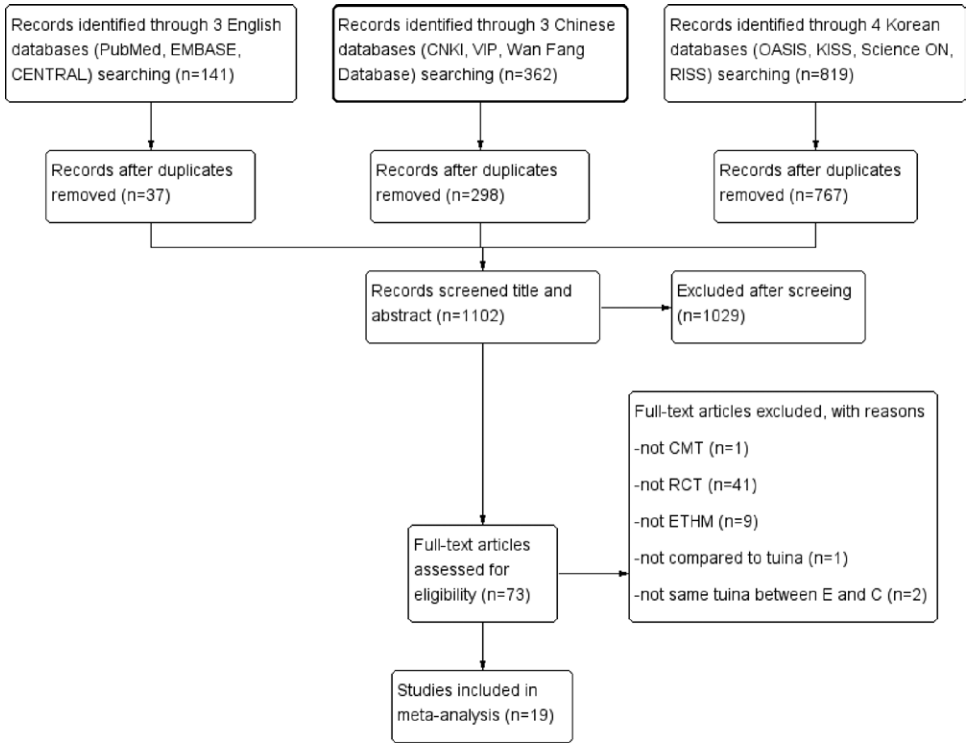

Figure 1. Prisma flow diagram. C = Control intervention, CENTRAL = Cochrane Central Register of Controlled Trials, CMT = congenital muscular treatment, CNKI = China National Knowledge Infrastructure, E = Experimental intervention, EMBASE = Excerpta Medica dataBASE, ETHM = external treatment of herbal medicine, KISS = Korean Studies Information Service System, OASIS = Oriental Medicine Advanced Searching Integrated System, RCT = randomized controlled trial, VIP = Chinese Scientific Journal Database.

the most common with six, Pungji (GB20) with four, Budol (LI18) with three, Inyeong (ST9) and Qiaogong point with two, Sudol (ST10), Yepung (TE17), Cheonjong (SI11), Ashi points, and other related acupoints with one. The other bone rankings were face and mandible region, occipital bone, and neck with 1 each (see Supplement 2, Supplemental Digital Content, http://links.lww.com/MD/I24, Tuina treatment information).

The manipulation techniques during tuina were kneading 18 times, pulling 15 times, pinching 10 times, pressing and rotation 10 times, plucking and flicking nine times, rubbing and grasping eight times, passive stretching seven times, pushing five times (see Supplement File 3, Supplemental Digital Content, http://links.lww.com/MD/I25, Manipulations of tuina).

3.4.2. Characteristics of ETHM. In the 19 included studies, ETHM was used as a medium concurrently with tuina in four cases,[27,32,33,35] and administered separately from tuina in 15 cases.[21–26,28–31,34,36–39] Furthermore, ETHM was used with hot compressed treatment in six cases,[24,31,37,38,41,42] without in 11 cases.[22,25,27,29–33,35–37] The used formulations were ointment nine times, decoction nien times, powder once, patch once, fumigation once, and two types of ETHM used in two studies.[28,34] The duration of ETHM varied from 10 minutes to overnight. The cautions noted were allergic reactions in two studies[31,34] and burns in one study[23] (Table 3).

Fifty three herbs were used. *Carthami Flos* was used 14 times, *Lycopodii Herba* and *Olibanum* 10 times, *Myrrha* eight times, and the rest were used less than five times (see Supplement File 4, Supplemental Digital Content, http://links.lww.com/MD/I26, Frequency of Herb).

3.5. Outcome measures

The most frequently used outcome measurement was the total effective rate (TER) 15 times.[21,22,25–32,35–39] This was followed by the thickness of the mass in SCM muscle seven times,[22,30,31,33–35,38] tissue elasticity grade[30,32,37] and recurrence rate three times,[26,28,37] muscle elasticity score[22,30] and clinical symptom & sign score two times,[33,35] adverse events,[35] cervical range of motion (ROM) for rotation and lateral flexion range once.[34] The tissue elasticity grade was intensified from stage 1 to stage 4, depending on the hardness of the lesion tissue and the color on ultrasound elastography.[43] The muscle elasticity score was pointed one to five as the color of the diseased muscle and surrounding tissues by ultrasound. If the point was three or higher, it was defined as torticollis.[44] The numbers of patients whose muscle elasticity scores improved after treatment from 3 to 5 points (torticollis) to 1 to 2 points (normal) were evaluated (Table 2).

3.6. Quality assessment

Eight studies were evaluated as "low risk" for random sequence generation; four studies used the random number table method[34,35,37,38]; another four studies generated a random sequence according to odd and even numbers,[27] the random lottery method,[29] computer number generator,[31] and the order of visits.[33] The remaining 11 studies[21–26,28,30,32,36,39] were evaluated as "unclear risk." Most studies did not mention allocation, but only one study[31] used a computer to measure the selection bias, which was evaluated as "Low risk".

Because double-blindness made it impossible to apply herbal medicine externally, the performance bias was all evaluated as "high risk." None of the 19 studies mentioned blinding the outcome assessment, and the detection bias was evaluated as "unclear risk." Most of the studies had no missing data, but one study[24] had a "high risk" of incomplete outcome data because two patients in the experimental group were dropouts due to allergies and a change to another hospital.

Table 2

Basic characteristics of the included studies.

First author (year)	Sample size (E/C)	Age (mean)	Gender (M/F)	Type of CMT (cases)	Experimental intervention	Control intervention	Total treatment periods	Outcome measurements and Intergroup differences	F/u periods
Cai (2014)[21]	96 (56/40)	<42 d	54/42	NR	tuina + ETHM	tuina	3–20 wk	(1) TER* (2) The course of treatment required to cure the patient (i) 1–2 courses (ii) 3–4 courses† (iii) 5–6 courses†	NR
Dai (2021)[22]	84 (42/42)	E: (3.20 ± 0.75) mo C: (3.39 ± 0.84) mo	E: 23/19 C: 26/16	NR	tuina + ETHM	tuina	12 wk	(1) TER* (2) Tissue elasticity grade* (3) Muscle elasticity score* (4) SCM mass thickness†	NR
He (2009) [23]	84 (42/42)	10 d–1.11 yr	45/39	(1) mass: 46 (2) dysplasia of the neck muscle and trapezius muscle: 38	tuina + ETHM + Heparin sodium ointment	tuina	3–6 mo	(1) Head tilt* (2) Neck range of motion* (3) Facial deformity* (4) Neck mass*	F/U for regularly 3 mo
Li (2018) [24]	40 (20/20)	E: (61.39 ± 37.32) d C: (74.65 ± 43.78) d	E: 9/9 C: 12/8	NR	tuina + ETHM + wax therapy	tuina	1 mo	(1) Treatment days* (2) Treatment time (i) Day 1 treatment age/d* (ii) SCM mass thickness/mm* (iii) Head tilt < 15° or ≥ 15° (iv) Facial asymmetry (v) Asymmetrical back of head (vi) Gender (vii) MFS score before treatment (3) MFS score	NR
Ren (2008) [25]	122 (62/60)	15 d–6 mo	NR	(1) left mass: 67 (2) right mass: 43 (3) no mass: 12	tuina + ETHM	tuina	2 mo	(1) TER*	NR
Tian (2010) [26]	60 (30/30)	E: 30 d–19 mo C: 28 d–16 mo	E: 19/11 C: 18/12	(1) mass: 55 (2) no mass: 5	tuina + ETHM	tuina	E: 2–3 mo C: 3–5 mo	(1) Recovery rate*, TER (2) Recurrence rate (F/U 6–12 mo)	NR
Wang (2008) [27]	182 (91/91)	C: 2 d–2 yr (0.48 yr) E: 3 d–2 yr (0.4 yr)	E: 48/43 C: 46/45	NR	tuina + ETHM	tuina	12 d	(1) TER	NR
Wang (2011) [28]	83 (43/40)	E: 23 d–18 mo (5.8 ± 3.7 mo) C: 17 d–16.3 mo (5.5 ± 2.9 mo)	E: 25/18 C: 22/18	E: (1) mass: 29 (2) no mass: 14 C: (1) mass: 24 (2) no mass: 16	tuina + ETHM	tuina	2–3 mo	(1) TER* (2) Curative effect (i) Patient's age (ii) Symptom classification (mass/non-mass)* (3) Recurrence rate (F/U 6–12 mo)	F/U for 6–12 mo
Wang (2016) [29]	78 (39/39)	E: 5 d–1 yr (3.2 ± 0.7 mo) C: 6 d–1 yr (3.1 ± 0.3 mo)	E: 24/15 C: 23/16	E: (1) left CMT: 26 (2) right CMT: 13 C: (1) left CMT: 25 (2) right CMT: 14	tuina + ETHM	tuina	2 mo	(1) TER*	NR

(*Continued*)

Table 2

(*Continued*)

First author (year)	Sample size (E/C)	Age (mean)	Gender (M/F)	Type of CMT (cases)	Experimental intervention	Control intervention	Total treatment periods	Outcome measurements and Intergroup differences	F/u periods
Wang (2018) [30]	90 (45/45)	E: (3.18 ± 0.67) mo C: (3.25 ± 0.73) mo	E: 28/17 C: 25/20	E: (1) mass: 32 (2) tilt: 11 (3) abnormal face: 2 C: (1) mass: 31 (2) tilt: 13 (3) abnormal face: 1	tuina + ETHM	tuina	3 mo	(1) TER* (2) Relationship between children's age in months and TER (3) SCM mass thickness* (4) Tissue elasticity rate* (5) Muscle elasticity score*	NR
Wang (2019) [31]	68 (34/34)	E: 1–5 mo (3.20 ± 1.13) mo C: 1–5 mo (3.14 ± 1.20) mo	E: 19/15 C: 18/16	E: (1) mass: 16 (2) diffuse: 18 C: (1) mass: 1 (2) diffuse: 16	tuina + ETHM	tuina	20 d	(1) TER* (2) SCM mass thickness*	NR
Xu (2017) [32]	80 (40/40)	E: (4.2 ± 1.6) mo C: (5.1 ± 0.7) mo	E: 23/17 C: 25/15	NR	tuina + ETHM	tuina	3–6 mo	(1) TCM syndrome score* (2) TER (i) After 3 treatment courses† (ii) After 6 treatment courses†	NR
Xu (2018) [33]	71 (35/36)	E: (118.23 ± 73.12) d C: (112.97 ± 75.84) d	E: 22/13 C: 22/14	NR	tuina + ETHM	tuina	2 mo	(1) SCM thickness (i) Thickness of affected side (ii) Thickness of healthy side (iii) Thickness ratio* (2) Symptoms and body signs scores (i) Head tilt* (ii) Neck muscles† (iii) Head and face deformities* (iv) Neck mass† (v) Neck activity* (vi) Total score† (3) Safety (i) Complexion (ii) Diet (iii) Mental (iv) Degree of skin lesions† (v) Skin irritation* (vi) Pigmentation* (vii) Number of skin lesions	NR
Yi (2020) [34]	200 (100/100)	E: 15 d-11 mo (3.26 ± 1.05) mo C: 10 d–10 mo (3.38 ± 1.02) mo	E: 59/41 C: 57/43	NR	tuina + ETHM	tuina	1 mo	(1) Cervical rotation and lateral flexion range* (2) SCM mass thickness (i) 15 d after treatment* (ii) 30 d after treatment*	NR
Yuan (2021) [35]	98 (49/49)	E: 5–11 mo (6.2 ± 2.8) mo C: 4–11 mo (6.3 ± 2.8) mo	E: 21/28 C: 18/31	E: (1) left CMT: 28 (2) right CMT: 21 C: (1) left CMT: 30 (2) right CMT: 19	tuina + ETHM	tuina	36 d	(1) TER* (2) Changes in the difference in diameter of bilateral SCM* (3) Clinical symptoms and signs scores * (4) Adverse events	NR

(*Continued*)

Table 2

(Continued)

First author (year)	Sample size (E/C)	Age (mean)	Gender (M/F)	Type of CMT (cases)	Experimental intervention	Control intervention	Total treatment periods	Outcome measurements and Intergroup differences	F/u periods
Zhang (2012) [36]	48 (28/20)	5 d–1.1 yr	NR	NR	tuina + ETHM	tuina	1–3 mo	(1) TER*	NR
Zhang (2019) [37]	94 (47/47)	E: 19 d–12.4 mo (6.4 ± 1.8) mo C: 26 d–13.2 mo (6.6 ± 2.1) mo	E: 22/25 C: 21/26	NR	tuina + ETHM	tuina	2 wk	(1) TER* (2) SCM mass thickness* (3) Tissue elasticity rate* (4) Recurrence rate	NR
Zhang (2020) [38]	72 (36/36)	E: 3–9 mo (5.74 ± 1.31) mo C: 2–10 mo (5.78 ± 1.34) mo	E: 19/17 C: 20/16	E: (1) oval mass: 16 (2) cord-like mass: 20 C: (1) oval mass: 15 (2) cord-like mass: 21	tuina + ETHM	tuina	3 mo	(1) TER* (2) SCM mass thickness and hardness scores* (3) Symptom scores (i) Limited neck rotation* (ii) Head and face deformities* (iii) Neck muscle contracture*	NR
Zhao (2016) [39]	60 (30/30)	1–12 mo	27/33	(1) left CMT: 38 (2) right CMT: 22	tuina + ETHM	tuina	30 d	(1) TER*	NR

C = control intervention, CMT = congenital muscular torticollis, E = experimental intervention, ETHM = external treatment of herbal medicine, F = female, F/U = follow up, M = male, MFS = Muscle Function Scale, NR = not reported, SCM = Sternocleidomastoid, TCM = traditional Chinese medicine, TER = total effect ratio.

*Compared with the control group after treatment $P<.05$.

†Compared with the control group after treatment $P<.01$.

Most studies were ranked "low risk" in reporting bias because pre-specified primary outcomes have been reported. Three studies[27,36,39] were not reported, which are accordingly ranked “unclear risk.” In another bias category, two studies[21,25] were evaluated as “unclear risk” due to nothing stated regarding the baseline. Four studies were evaluated as “high risk”; one study[23] performed manipulation by applying Heparin sodium ointment; another one[24] additionally used wax treatment; one study[26] had different treatment period between the treatment and control group,[23] and one study additionally conducted manipulation with applying a relaxative and relievable muscle ointment (Shujin Sanjie ointment).[28] The remaining studies[22,27,29–39] were comparable at baseline (Fig. 2).

3.7. Meta-analysis results

3.7.1. Total effective rate. Fifteen studies evaluated the TER and included 1315 patients.[21,22,25–32,35–39] The intergroup differences in favor of the experimental group were reported as $P < .05$ in 12 studies[21,22,25,28–31,35–39] and $P < .01$ in one study.[32] One study[26] reported no statistically significant difference between the two groups, and one study[27] did not mention about it. The meta-analysis of the total effective rate showed that ETHM plus tuina were more effective than tuina alone (RR: 1.21, 95% CI: 1.15–1.26, $P < .001$) and revealed low heterogeneity ($P = .011$, $I^2 = 33\%$; Fig. 3).

3.7.2. SCM muscle thickness. Seven studies involving 679 patients measured the SCM muscle thickness in the affected side.[22,30,31,33,34,37,38] The intergroup differences in favor of the experimental group were reported as $P < .05$ in 6 studies[30,31,33,34,37,38] and $P < .01$ in one study.[32]

Compared with tuina alone, ETHM plus tuina decreased the SCM muscle thickness significantly (MD: −1.82, 95% CI: −2.23 to −1.41, $P < .001$). The potential heterogeneity was noted in the result ($P = .006$, $I^2 = 51\%$), and subgroup analysis was performed according to the patient's age and the formulation of the ETHM on SCM muscle thickness. In the protocol of this paper,[19] an analysis of the subgroups according to birth history was also planned, but it was not possible because there was insufficient information. With regard to age, ETHM plus tuina can decrease in patients aged over six months (MD: −1.91, 95% CI: −3.16 to −0.66, $P = .003$) than in the under six months age group (MD: −1.83, 95% CI: −2.12 to −1.54, $P < .001$; Fig. 4). Subgroup analysis according to formulation of the ETHM showed more effectiveness in order of fumigation (MD: −3.08, 95% CI: −4.01 to −2.15, $P < .001$), ointment (MD: −1.75, 95% CI: −2.14 to −1.36, $P < .001$), decoction (MD: −1.66, 95% CI: −2.13 to −1.19, $P < .001$; Fig. 5).

3.7.3. Cervical ROM. One study involving 200 patients measured the cervical ROM.[34] The intergroup differences in favor of the experimental group were reported as $P < .05$. The meta-analysis result showed that ETHM plus tuina had a greater effect than tuina alone: rotation range (MD: 13.43, 95% CI: 10.41–16.45, $P < .001$; Fig. 6A) and lateral flexion range (MD: 8.50, 95% CI: 6.15–10.85, $P < .001$; Fig. 6B).

3.7.4. Symptom scores and grade. The intergroup differences in favor of the experimental group were all reported as $P < .05$.

(1) Tissue elasticity grade

Three studies[22,30,37] involving 268 patients indicated that ETHM plus tuina were more effective than tuina alone therapy in CMT (SMD: −0.46, 95% CI: −0.71 to −0.22, $P = .0002$; Fig. 7A).

(2) Number of muscle elasticity scores relieved after treatment (3 to 5 points to 1 to 2 points)

Table 3

External traditional herbal medicine treatment information.

First author (year)	Formulation	Administration	Treatment duration and frequency	Composition of herbal medicines	Caution
Cai (2014)[18]	decoction	External application to the SCM muscle on the affected side + warm compress	30 min/time, 2 times/d	Safflower (*Carthami Flos*) 10 g Sparganium Rhizome (*Sparganii Rhizoma*) 10 g Ostericum Root (*Angelicae Koreanae Radix*) 10 g Aralia Continentalis Root (*Araliae Cordatae Radix*) 10 g Ground beetle (*Eupolyphaga*) 10 g Chinese Starjasmine Stem (*Trachelospermi Caulis*) 15 g Beautiful Sweetgum Fruit (*Liquidambaris Fructus*)15 g Common Clubmoss Herb (*Lycopodii Herba*)20 g Sappan Wood (*Sappan Lignum*) 25 g	Stop application if allergic symptoms appear
Dai (2021)[19]	ointment	External application appropriate amount to the SCM muscle on the affected side and apply gauze	1 time (night)/d	Relaxative and relievable muscle ointment (Shujin Sanjie ointment) Safflower (*Carthami Flos*) 100 g Myrrh (*Myrrha*) 200 g Earthworm (*Pheretimae Corpus*) 100 g Frankincense (*Olibanum*) 200 g Dragon's Blood (*Draconis Sanguis*) 100 g Notoginseng Root (*Notoginseng Radix*) 200 g	NR
He (2009)[20]	decoction	External application to the SCM muscle on the affected side + warm compress	20–30 min/time, 2 times/d	Safflower (*Carthami Flos*) 15 g Angelica Gigas Root (*Angelicae Gigantis Radix*) 15 g Clematis Root (*Clematidis Radix*) 15 g Broadleaf Vetch (*Speranskia tuberculata*) 15 g Common Clubmoss Herb (*Lycopodii Herba*)15 g Hiraute Shiny Bugleweed Herb (*Lycopi Herba*) 15 g Ostericum Root (*Angelicae Koreanae Radix*) 15 g Angelica Dahurica Root (*Angelicae Dahuricae Radix*) 15 g Smooth Greenbrier Rhizome (*Smilacis Glabrae Rhizoma*) 15 g Sappan Wood (*Sappan Lignum*) 15 g Frankincense (*Olibanum*) 10 g Japanese Zanthoxylum Peel (*Zanthoxyli Fructus*) 10 g	Be careful not to burn child's skin
Li (2018)[21]	decoction	After Wax therapy, external application to the SCM muscle on the affected side	20 min/time, 1 time/d, 6 times/wk	Corydalis Tuber (*Corydalis Tuber*) 15 g Clematis Root (*Clematidis Radix*) 20 g Common Clubmoss Herb (*Lycopodii Herba*) 30 g Frankincense (*Olibanum*) 20 g Safflower (*Carthami Flos*) 20 gCinnamon Twig (*Cinnamomi Ramulus*) 15 g Broadleaf Vetch (*Speranskia tuberculata*) 30 gSuberect Spatholobus Stem (*Spatholobi Caulis*) 30 g	NR
Ren (2008)[22]	ointment	External application appropriate amount to the SCM muscle on the affected side and apply gauze	1 time (night)/d	Relaxative and relievable muscle ointment (Shujin Sanjie ointment) Safflower (*Carthami Flos*) 100 g Myrrh (*Myrrha*) 200 g Earthworm (*Pheretimae Corpus*) 100 g Frankincense (*Olibanum*) 200 g Dragon's Blood (*Draconis Sanguis*) 100 g Notoginseng Root (*Notoginseng Radix*) 200 g	NR

(*Continued*)

Table 3

(*Continued*)

First author (year)	Formulation	Administration	Treatment duration and frequency	Composition of herbal medicines	Caution
Tian (2010)[23]	decoction	After soaking gauze in the decoction, external application to the SCM muscle on the affected side + warm compress (the temperature is 38–43℃)	10–15 min/time, 2–3 times/d	Peach Kernel (*Persicae Semen*) 8 g Safflower (*Carthami Flos*) 8 g Cnidium Rhizome (*Cnidii Rhizoma*) 8 g Angelica Gigas Root (*Angelicae Gigantis Radix*) 8 g Red Peony Root (*Paeniae Rubra Radix*) 8 g Myrrh (*Myrrha*) 8 g Frankincense (*Olibanum*) 8 g Corydalis Tuber (*Corydalis Tuber*) 8 g Salvia Miltiorrhiza Root (*Salviae Miltiorrhizae Radix*) 8 g	NR
Wang (2008)[24]	decoction	Using as a medium during tuina	1 time/d	Self-made stretch liquid Safflower (*Carthami Flos*) 5 g Borneol (*Borneolum Syntheticum*) 10g Common Clubmoss Herb (*Lycopodii Herba*) 15 g	NR
Wang (2011)[25]	ointment	External application to the SCM muscle on the affected side and apply gauze conducting manipulation to fully absorbed	NR	Relaxative and relievable muscle ointment (Shujin Sanjie ointment) (no information of composition)	NR
	decoction	After soaking gauze in the decoction, external application to the SCM muscle on the affected side + warm compress	15–20 min/time, 1–2 times/d	Common Clubmoss Herb (*Lycopodii Herba*) 10 g Safflower (*Carthami Flos*) 10 g Mirabilitum (*Natrii Sulfas*) 10 g Costus Root (*Aucklandiae Radix*) 10 g Sappan Wood (*Sappan Lignum*) 15 gChaenomeles Fruit (*Chaenomelis Fructus*) 15 g	NR
Wang (2016)[26]	ointment	External application	1 time (night)/d	Relaxative and relievable muscle ointment (Shujin Sanjie ointment) Safflower (*Carthami Flos*) 100 g Myrrh (*Myrrha*) 200 g Earthworm (*Pheretimae Corpus*) 100 g Frankincense (*Olibanum*) 200 g Dragon's Blood (*Draconis Sanguis*) 100 g Notoginseng Root (*Notoginseng Radix*) 200 g	NR
Wang (2018)[27]	ointment	External application appropriate amount to the SCM muscle on the affected side and apply gauze	1 time (night)/d	Relaxative and relievable muscle ointment (Shujin Sanjie ointment) Safflower (*Carthami Flos*) 100 g Myrrh (*Myrrha*) 200 g Earthworm (*Pheretimae Corpus*) 100 g Frankincense (*Olibanum*) 200 g Dragon's Blood (*Draconis Sanguis*) 100 g Notoginseng Root (*Notoginseng Radix*) 200 g	NR

(*Continued*)

Table 3
(*Continued*)

First author (year)	Formulation	Administration	Treatment duration and frequency	Composition of herbal medicines	Caution
Wang (2019)[28]	patch	After the tuina, external application patch to the center of the SCM muscle mass on the affected side	2 h/time, 2 times/d, 5 d/wk	Common Clubmoss Herb (*Lycopodii Herba*) Chaenomeles Fruit (*Chaenomelis Fructus*) Curcuma Longa Rhizome (*Curcumae Longae Rhizoma*) Myrrh (*Myrrha*) Frankincense (*Olibanum*) Sparganium Rhizome (*Sparganii Rhizoma*) Vineger (no information of ingredients dosage)	NR
Xu (2017)[29]	ointment produced by Tibet Qizheng Tibetan Medicine Factory, lot number: (2012) national drug labeler Z317; standard number: YBZ143220062012Z; national drug registration number: Z20043178;specification: 20 g.	Using as a medium during tuina	20 min/time, 1 time/d, 5 times/wk	Bai Mai ointment Curcuma Longa Rhizome (*Curcumae Longae Rhizoma*) Nutmeg (*Myristicae Semen*) Nardostachyos Rhizoma (*Nardostachyos Radix*) Actinolite (*Tremolitum*) Licorice (*Glycyrrhizae Radix*) Musk (*Moschus*) Ginger (*Zingiberis Rhizoma*) Fennel (*Foeniculi Fructus*) Acorus calamus (*Acori Calami Rhizoma*)Zanthoxylum Peel (*Zanthoxyli Pericarpium*) Halite (*Halitum*)	NR
Xu (2018)[30]	ointment	Using as a medium during tuina	1 time/d, 5 times/wk	Sansesan ointment Vitex Fruit (*Viticis Fructus*) Angelica Gigas Root (*Angelicae Gigantis Radix*) Red Peony Root (*Paeniae Rubra Radix*) Angelica Dahurica Root (*Angelicae Dahuricae Radix*) Salvia Miltiorrhiza Root (*Salviae Miltiorrhizae Radix*) Curcuma Longa Rhizome (*Curcumae Longae Rhizoma*) Aralia Continentalis Root (*Araliae Cordatae Radix*) Gentiana Macrophylla Root (*Gentianae Macrophyllae Radix*) Ostericum Root (*Angelicae Koreanae Radix*) Cnidium Rhizome (*Cnidii Rhizoma*) (no information of ingredients dosage)	NR

(*Continued*)

Table 3
(*Continued*)

First author (year)	Formulation	Administration	Treatment duration and frequency	Composition of herbal medicines	Caution
Yi (2020)[31]	decoction	After soaking gauze in the decoction, external application to the SCM muscle on the affected side	30–60 min/time, 2–3 time/d	self-made torticollis liquid Salvia Miltiorrhiza Root (*Salviae Miltiorrhizae Radix*) Cnidium Rhizome (*Cnidii Rhizoma*) Safflower (*Carthami Flos*) Peach Kernel (*Persicae Semen*) Sparganium Rhizome (*Sparganii Rhizoma*) Zedoary (*Curcumae Rhizoma*) Sargassum (*Sargassum*) Kelp (*Laminariae Thallus*) Red Peony Root (*Paeniae Rubra Radix*) Peony Root (*Paeoniae Radix*) Clematis Root (*Clematidis Radix*) Aurantii Vascular (*citrus reticulate blanco*) Costus Root (*Aucklandiae Radix*) Rhubarb (*Rhei Rhizoma*) (no information of ingredients dosage)	stop application if allergic symptoms appear
	powder	External application forming torticollis powder like a cake (1 cm) and apply gauze	1 time (night)/d	self-made torticollis powder Salvia Miltiorrhiza Root (Salviae Miltiorrhizae Radix) Safflower (Carthami Flos) Peach Kernel (Persicae Semen) Rhus Galls (Galla Rhois) Cowherb Seed (Vaccariae Semen) Rhubarb (Rhei Rhizoma) Costus Root (Aucklandiae Radix) Clematis Root (Clematidis Radix) (no information of ingredients dosage)	
Yuan (2021)[32]	ointment	Using as a medium during tuina	1 time/d, treatment for 10 d and rest 2 d	Three-color powder ointment Vitex Fruit (*Viticis Fructus*) 30 g Angelica Gigas Root (*Angelicae Gigantis Radix*) 10 g Red Peony Root (*Paeniae Rubra Radix*) 10 g Angelica Dahurica Root (*Angelicae Dahuricae Radix*) 10 g Salvia Miltiorrhiza Root (*Salviae Miltiorrhizae Radix*) 10 g Curcuma Longa Rhizome (*Curcumae Longae Rhizoma)* 10 g Aralia Continentalis Root (*Araliae Cordatae Radix*) 10 g Ostericum Root (*Angelicae Koreanae Radix*) 10 g Gentiana Macrophylla Root (*Gentianae Macrophyllae Radix)* 12 g Cnidium Rhizome (*Cnidii Rhizoma*) 12 g	NR
Zhang (2012)[33]	decoction	External application to the SCM muscle on the affected side	1 time (night)/d	Ostericum Root (*Angelicae Koreanae Radix*) 5 g Common Clubmoss Herb (Lycopodii Herba) 3 g Chaenomeles Fruit (*Chaenomelis Fructus*) 3 g Broadleaf Vetch (*Speranskia tuberculata*) 2 g Dragon's Blood (*Draconis Sanguis)* 1 g Borneol (*Borneolum Syntheticum)* 1 g	NR

(*Continued*)

Table 3

(*Continued*)

First author (year)	Formulation	Administration	Treatment duration and frequency	Composition of herbal medicines	Caution
Zhang (2019)[34]	ointment	External application appropriate amount to the SCM muscle on the affected side and apply gauze	1 time (night)/d	Relaxing muscle ointment Notoginseng Root (*Notoginseng Radix*) Safflower (Carthami Flos) Suberect Spatholobus Stem (*Spatholobi Caulis*) Frankincense (*Olibanum*) Myrrh (*Myrrha*) Common Clubmoss Herb (Lycopodii Herba) Earthworm (*Pheretimae Corpus*) (no information of ingredients dosage)	NR
Zhang (2020)[35]	Fumigation HB3000 Traditional Chinese Medicine Fumigation Therapy Device (Beijing Zeao Medical Technology Co., Ltd.)	Fumigating to the SCM muscle on the affected side (the temperature is 38–43℃)	30 min/time, 2 time (morning, evening)/d	Cinnamon Twig (*Cinnamomi Ramulus*) 30 g Angelica Gigas Root (*Angelicae Gigantis Radix*) 30 g Pueraria Root (*Puerariae Radix*) 30 g Cnidium Rhizome (*Cnidii Rhizoma*) 30 g Broadleaf Vetch (*Speranskia tuberculata)* 30 g Beautiful Sweetgum Fruit (*Liquidambaris Fructus*) 25 g Common Clubmoss Herb (Lycopodii Herba) 25 g Frankincense (*Olibanum*) 15 gMyrrh (*Myrrha*) 15 g Red Peony Root (*Paeniae Rubra Radix*) 15 g Suberect Spatholobus Stem (*Spatholobi Caulis*) 15 g Licorice *(Glycyrrhizae Radix*) 15 g	NR
Zhao (2016)[36]	decoction	External application appropriate amount to the SCM muscle on the affected side and apply gauze + warm compress	15–20 min/time, 1–2 times/d	Common Clubmoss Herb (Lycopodii Herba) 10 g Safflower (Carthami Flos) 10 g Mirabilitum (*Natrii Sulfas*) 10 g Costus Root (*Aucklandiae Radix*) 10 g Sappan Wood (*Sappan Lignum*) 15 g Chaenomeles Fruit (*Chaenomelis Fructus*) 15 g	NR

NR = not reported, SCM = sternocleidomastoid.

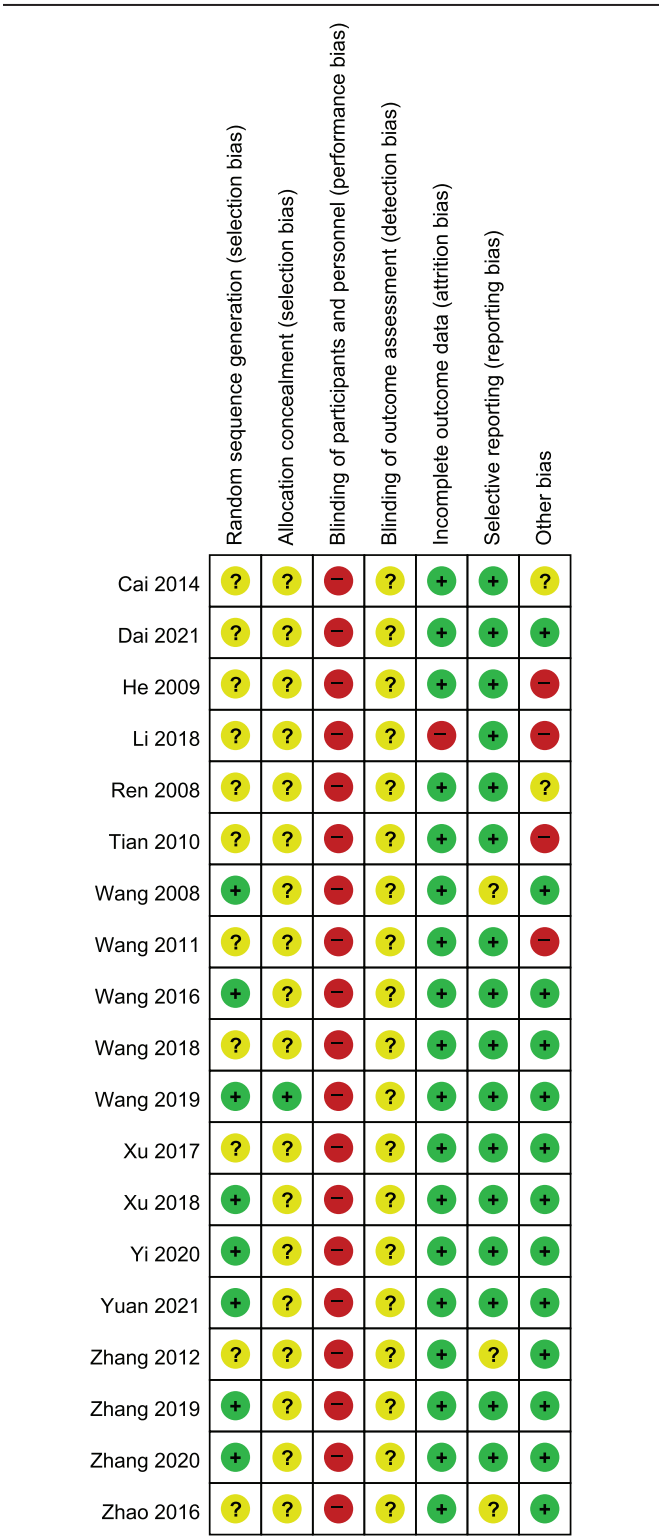

Figure 2. Risk of bias summary.

Two studies[22,30] involving 174 patients reported that ETHM plus tuina was more effective than tuina alone therapy in CMT (RR: 1.56, 95% CI: 1.04–2.34, $P = .03$; Fig. 7B).

(3) Clinical symptoms and sign scores

Two studies[33,35] involving 169 patients indicated that ETHM plus tuina was more effective than tuina alone therapy in CMT (SMD: −0.78, 95% CI: −1.09 to −0.47, $P < .001$; Fig. 7C).

3.7.5. Recurrence rate and adverse events. Three studies involving 237 patients measured the recurrence rate. Two studies[26,28] reported no relapse. Only one study[37] reported recurrence, but there was no statistically significant difference between the experimental and control groups (RR: 0.33, 95% CI: 004–3.09, $P = .33$; Fig. 8). One study involving 98 patients measured the adverse events,[35] but the experimental and control groups reported no adverse events.

3.8. Assessment of reporting bias

The funnel plot of the total effective rate seemed possibly asymmetry (Fig. 9), and the Egger regression test provided possible evidence of publication bias ($t = 2.74$, $P = .0169$) (see Supplement Figure 1, Supplemental Digital Content, http://links.lww.com/MD/I29, Egger regression test for TER). However, the fail-safe N test results were 309, which is higher than the recommended cutoff of 85 (5 k + 10, k = the number of studies included in the meta-analysis). Furthermore using the trim and fill method, four artificial studies were included into the meta-analysis to adjust for funnel plot asymmetry. The adjusted fixed-effects (RR: 1.13, 95% CI: 1.08–1.17, $P < .001$) evaluated using the trim and fill method was consistent with original analysis (RR:1.16, 95% CI: 1.12, $P < .001$) (see Supplement Figure 2A,B, Supplemental Digital Content, http://links.lww.com/MD/I30, Funnel plots of TER original version and the trim and fill method version).

3.9. Sensitivity analysis

Sensitivity analysis was performed using the "leave one out" method and indicated that the meta-analysis is reliable and robust. The sensitivity analysis of the TER was conducted because there was a possibility of reporting bias in the funnel plot and Egger test results (see Supplement File 5, Supplemental Digital Content, http://links.lww.com/MD/I27, sensitivity analysis on TER), and the sensitivity analysis of the SCM thickness was performed because heterogeneity was detected as a result of the meta-analysis ($I^2 > 50\%$) (see Supplement File 6, Supplemental Digital Content, http://links.lww.com/MD/I28, sensitivity analysis on SCM muscle thickness).

3.10. GRADE certainty of evidence

The overall quality of the evidence was presented using the GRADE system. Most results were rated as low to high, because of the high risk of performance bias and other bias, small sample sizes, failure to meet the optimal information size criterion, and the 95% CI including lines with no effect. The quality of evidence was high for the thickness of the SCM muscle (participants' age: under six months subgroup) and the thickness in the SCM muscle (total) because studies with the same effect direction and clinically heterogeneous were collected and meta-analyzed (Table 1).

4. Discussion

According to a previous study, approximately 93% of patients were first diagnosed with CMT when they were under one year. The duration of physiotherapy was 6 months on average, and if there was no improvement, surgery was performed within a year in 51% of patients[45] . Therefore, it is important that patients aged zero to 2 years, who have a possibility of recovery, be treated with complementary and alternative medicine.

All the major English, Chinese, and Korean databases were searched to find RCT using tuina with ETHM versus the same tuina for invention. This meta-analysis was conducted for 19 RCTs including 1710 patients. This is the first review comparing tuina with concomitant treatment.

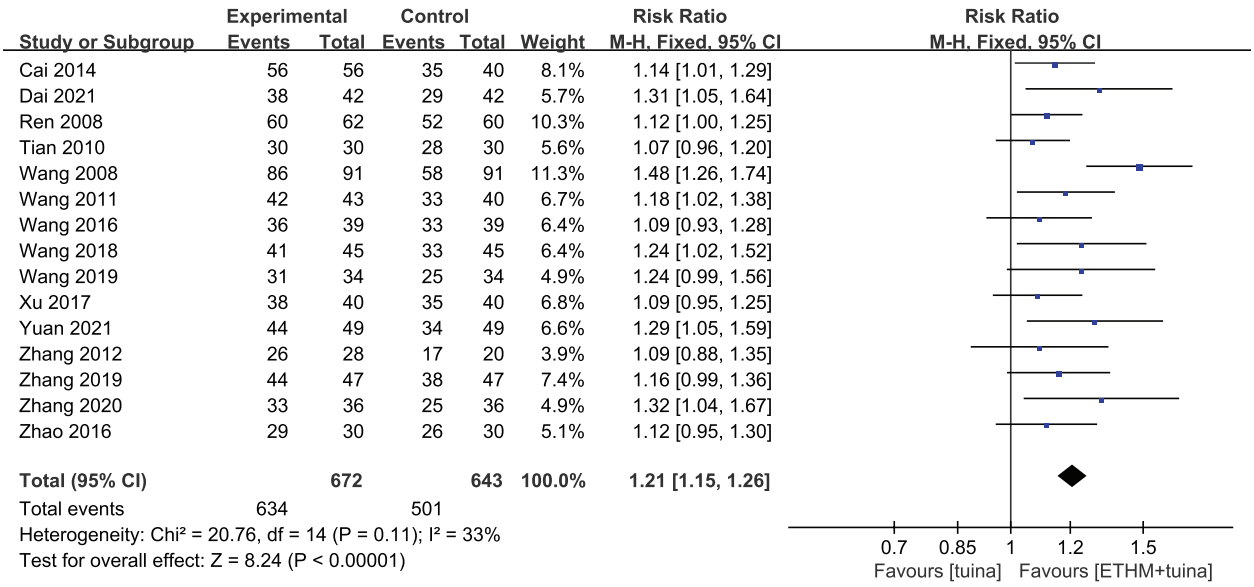

Figure 3. Forest plot of the total effective rate. CI = confidence interval, ETHM = external treatment of herbal medicine.

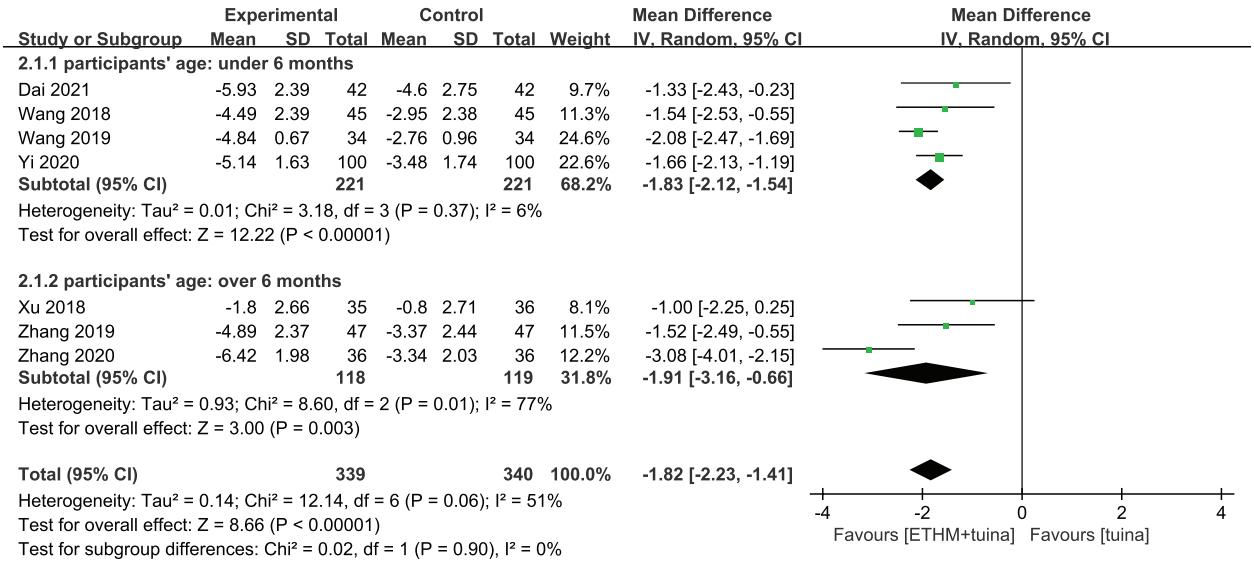

Figure 4. Forest plot of the SCM muscle thickness according to participants' age. CI = confidence interval, ETHM = external treatment of herbal medicine, SCM = sternocleidomastoid muscle.

4.1. Summary of this review

This review showed that tuina combined with the ETHM group was more effective than tuina alone, and the difference was statistically significant for CMT than the tuina group on TER, SCM muscle thickness, cervical ROM and symptom scores and grade (tissue elasticity grade, muscle elasticity scores, and clinical symptoms and sign scores). Subgroup analysis was performed according to patients' age (under 6 months or over 6 months) and formulation of ETHM (ointment, decoction, or fumigation) to explain the heterogeneity of the included study on SCM muscle thickness. The SCM muscle thickness was decreased significantly regardless of age. A significant effect on the recovery of the SCM muscle was noted in patients younger than two years of age. The heterogeneity in these two subgroups decreased ($P = .090$, $I^2 = 0\%$), suggesting that patients' age may be a potential reason for the heterogeneity. Furthermore, the SCM muscle thickness was improved in the order of fumigation, ointment, and decoction. The ETHM absorption may differ depending on the formation. On the other hand, only a few studies are included in each subgroup, which is insufficient to use as evidence. There were no adverse effects, and the recurrence rates were not statistically significant. We performed the fail-safe N test and the trim-and-fill method because of the potential publication bias. The results were relatively robust and the publication bias did not influence the significance of our results. This review is the first paper to analyze the effect of the combination of tuina with ETHM, which is commonly used in the treatment of pediatric torticollis, can provide meaningful information to clinicians.

4.2. Clinical implication

The manipulations of tuina for CMT in the included studies are pushing and kneading, rubbing and pressing, grasping and pinching, flicking and plucking, and stretching and rotary pulling. Tuina manipulations can be divided into two categories: relaxation techniques and stretching and rotary pulling techniques. Relaxation techniques relax tendons and massage

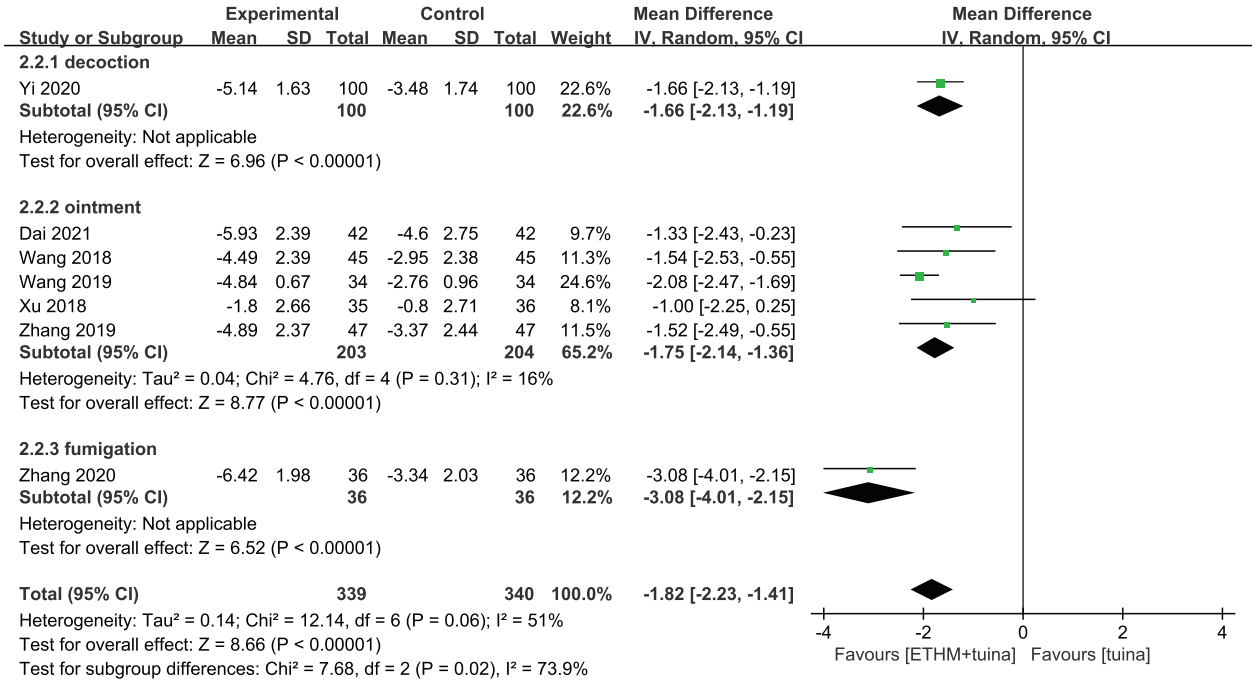

Figure 5. Forest plot of the SCM thickness according to formulation of ETHM. CI = confidence interval, ETHM = external treatment of herbal medicine, SCM = sternocleidomastoid muscle.

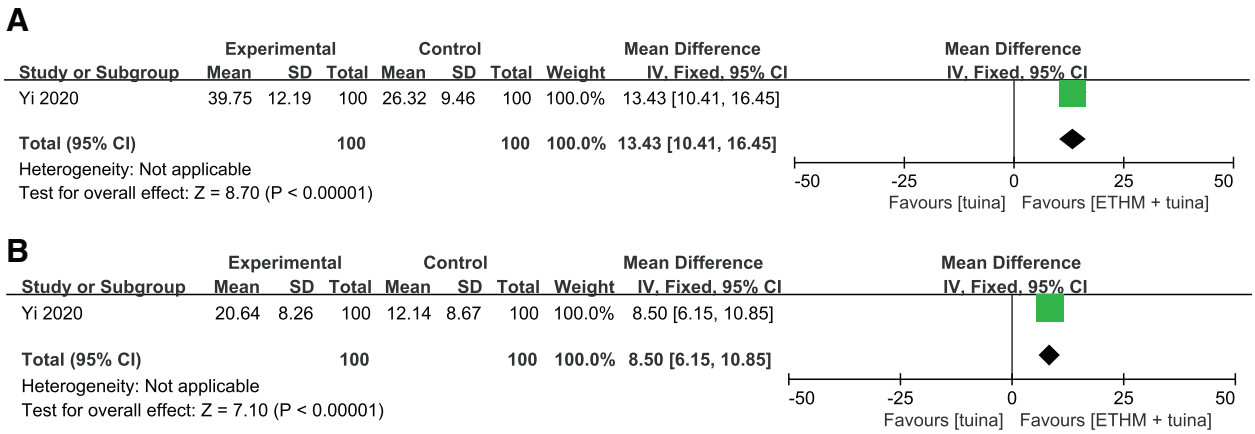

Figure 6. A, B. Forest plot of cervical range of motion (A: rotation, B: flexion). CI = confidence interval, ETHM = external treatment of herbal medicine.

tissue, promoting blood circulation and relieving muscle tension. Stretching and the rotary pulling techniques lengthen the muscle and loosen the hardened mass tissue, so it returns to the average original muscle elasticity and mobility.[46] According to the two studies[28,34] divided according to the presence of a mass or not, additional techniques, such as flicking or plucking, were used in the mass group.

Gyeonjeong (GB21) and Pungji (GB20) were the most frequently used acupoints. GB21 is one of the acupoints of the gall bladder meridian located between the tip of the acromion and the spinous process of C7.[47] It is used clinically to treat shoulder pain, and back pain by relaxing the shoulder muscles.[48] GB20 is located in the posterior region of the neck, below the occipital bone, in the depression between the origins of the SCM muscle and trapezius muscle.[49] It expels the exterior and interior wind and fever, so it is used for headaches, dizziness, and neck pain.[47]

Traditional herbal medicine can regulate qi, promote blood circulation to eliminate stasis, loosen stiff muscles, and relieve pain, so it is often used to produce powders, ointments, and decoctions for external application. Children's soft tissue has a thin cuticle, and the drug is easier to absorb through the skin, with satisfactory compliance for parents.[50]

The most frequently used herbal medicine in this review was Safflower (*Carthami Flos*), Common Clubmoss Herb (*Lycopodii Herba*), Frankincense (*Olibanum*), and Myrrh (*Myrrha*). All these herbs have anti-inflammatory, anti-oxidant effects,[51,52] and de-contracting muscle effect due to the activation of blood flow and removal of blood stasis.[53] Pharmacologically, the main active components of *Carthami Flos* are Safflomin A and B, which reduce blood pressure and facilitate blood circulation.[51] *Lycopodii Herba* is used for joint pain and bruises,[54] because of the antipyretic action of Lycopodin, an alkaloid component.[55] *Olibanum* can inhibit the production and release of various cytokines, particularly the secretion of IL-2 and IFN-γ[56] and *Myrrha* also has anti-inflammatory effects from 1β,6α-dihydroxyeudesm4 (15)-ene.[57] In addition, Quercetin the major component of *Olibanum* and *Myrrha* has the functions of soft tissue recovery such as muscle pain, ligament rupture, local edema, and so on.[58]

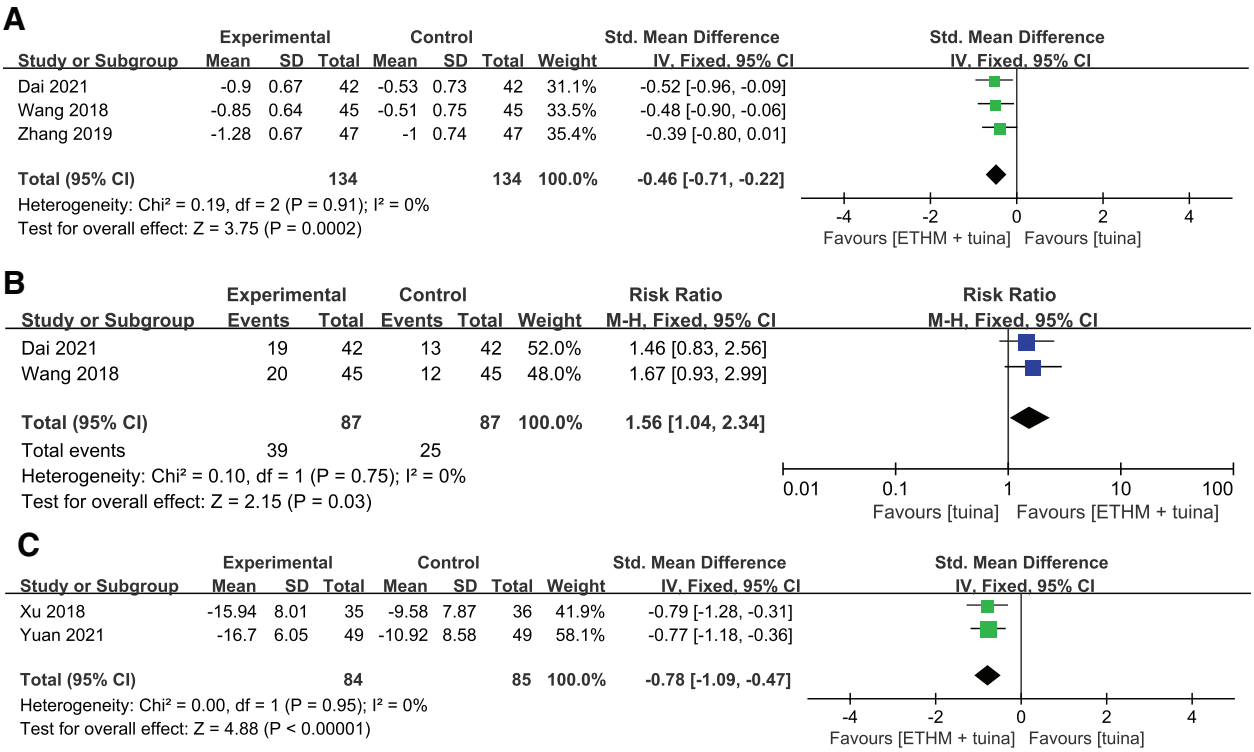

Figure 7. A,B,C. Forest plot of the symptom scores and grade (A: tissue elasticity grade, B: muscle elasticity score, C: clinical symptoms and sign score). CI = confidence interval, ETHM = external treatment of herbal medicine.

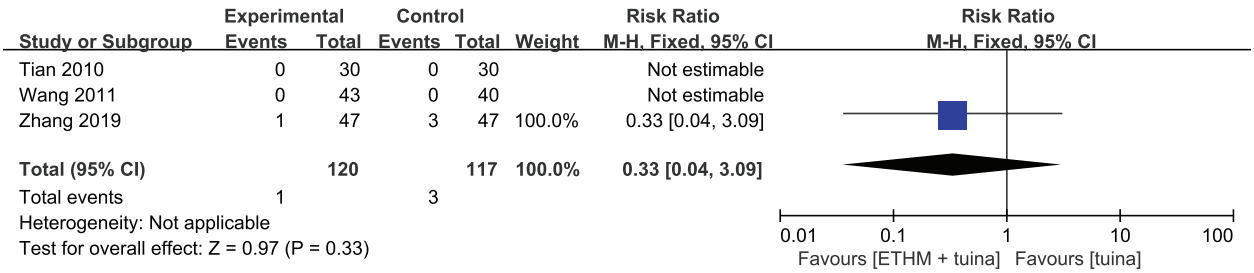

Figure 8. Forest plot of the recurrence rate. CI = confidence interval, ETHM = external treatment of herbal medicine.

Clinically, acupoint herbal patching is used widely for treatment, continuous stimulation of the acupoint, and absorption of drugs.[59] Nevertheless, further research will be needed on the formulation attached to the center of the SCM muscle or the acupoint (GB20, GB21) that is convenient and effective for children.

4.3. Limitations and suggestions for further studies

This review had several limitations. First, few studies mentioned adverse effects and recurrence rates. Because children's skin is soft and tender, more sufficient data on side effects such as allergies or burns, are needed. Moreover, it will be necessary to check for recurrence or musculoskeletal development through a long-term follow-up. Second, the overall methodological quality of included studies varied from low to high, and the incorrect methodological design of individual studies has unavoidable difficulty to blind the participants and therapists with ETHM formulation. More robust clinical evidence will be obtained if the designed type of CMT (muscular torticollis, postural torticollis, and the SCM mass torticollis) and severity (muscle tightness degree) can be assessed. Third, the SCM muscle thickness in the affected side was used as an outcome measurement in seven studies.[22,30,31,33,34,37,38] The result may vary depending on the posture, because the SCM muscle can contract or relax depending on the posture. Only three studies[22,30,38] specified that the measurement posture was described as a supine position, and the remaining studies did not mention it. More objective outcome measurements will be needed to quantitatively the SCM muscle flexibility, like the difference between the muscle thickness changes during contraction and relaxation on bilateral SCM muscle using high-frequency ultrasound.[60]

5. Conclusion

For CMT patients aged zero to 2 years, the treatment is more effective than when ETHM is combined with tuina. Comprehensive standardized practical guidelines for CMT have not been developed, which will have significant meaning in analyzing the integrated effects of ETHM treatment with tuina. ETHM is effective and easily acceptable for children without invasive and pain. This study can provide integrated treatment evidence to clinicians.

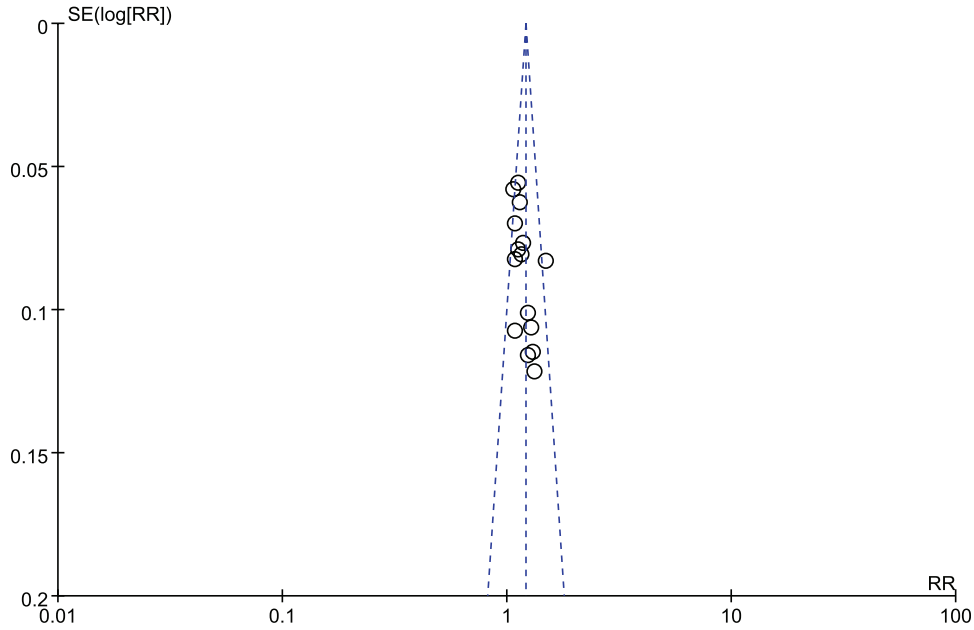

Figure 9. Funnel plot of the total effective rate. RR = risk ratio.

Author contributions

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Investigation: Eunjin Kim, Jungyoon Choi, Sang Yeon Min.
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