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Review

Effects of massage on newborn infants with jaundice: A meta-analysis

Mengjie Lei, Tingting Liu, Yufeng Li, Yaqian Liu, Lina Meng, Changde Jin*

Department of Nursing, School of Tianjin University of Traditional Chinese Medicine, Tianjin, China

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ABSTRACT

Objective: This meta-analysis aims to systematically evaluate the effects of massage on infants with jaundice.

Methods: Multiple electronic databases, including Cochrane Library, PubMed, EMBASE, Web of Science, China Biology Medicine (CBM), Wan Fang Data, VIP Database for Chinese Technical Periodicals and China National Knowledge Infrastructure (CNKI), were used to search for studies on the effects of massage on infants with jaundice. Data were analysed by Rev Man 5.3.

Results: A total of 14 randomised controlled trials with 1889 patients were included. Statistically significant difference in percutaneous bilirubin [$MD = -1.21$, 95% CI (-1.90, -0.52), $P < 0.05$; $MD = -2.00$, 95% CI (-2.68, -1.32), $P < 0.05$; $MD = -2.00$, 95% CI (2.56, -1.44), $P < 0.05$; $MD = -1.93$, 95% CI (-2.44, -1.43), $P < 0.05$] was found between two groups at 48, 72, 96 and 168 h. Studies on the serum total bilirubin level were divided into two subgroups according to sample size, and the results of subgroup analysis showed that the serum total bilirubin level in the intervention group was significantly lower than that in the control group [$MD = -52.06$, 95% CI (-57.76, -46.36), $P < 0.05$ and $MD = -10.65$, 95% CI (-14.66, -6.63), $P < 0.05$]. Statistically significant difference in defecation frequency was observed between the two groups at 48 h after birth[$SMD = 0.44$, 95%CI (0.02, 0.87), $P < 0.05$].

Conclusion: Massage can decrease serum total bilirubin and percutaneous bilirubin levels and increasing defecation frequency. However, due to heterogeneity among studies, numerous multi-centre, large-sample and high-quality randomised controlled trials are needed to verify the effects of massage.

1. Introduction

Neonatal jaundice is a phenomenon of yellow-dyed skin, sclera and other organs in the neonatal period caused by blood bilirubin accumulation, which is a relatively prevalent disease in neonates. More than half of newborns [1,2] and 80% of preterm children [3] develop clinical symptoms of jaundice. The cause of neonatal jaundice is complex. Neonatal jaundice can be divided into physiological jaundice and pathological jaundice. Pathological jaundice can lead to severe bilirubin encephalopathy. Some children can develop neurological sequelae (including cerebral palsy, hearing loss and kernicterus) [4] and even die. In addition, a previous study showed that hyperbilirubinemia is the main cause of neonatal readmission [5]. Neonatal jaundice also increases the risk of suffering from type 1 diabetes in childhood [6]. At present, the treatment and nursing measures of neonatal jaundice mainly include phototherapy, infusion of plasma or albumin and liver protection. In recent years, numerous methods, including herbal oral administration [7], external application of traditional Chinese medicine [8], Chinese massage [9], acupuncture, massage and swimming [10], have been used by researchers to treat and care for neonates with jaundice. Massage is regarded as a new care method for neonates with a positive effect on neonatal disease treatment and health care. Massage on newborns offer numerous advantages. Massage can not only promote physical and intellectual development, immunity, digestion and absorption and emotional communication between mothers and children but also treat several neonatal diseases, such as hypoxic–ischemic encephalopathy, jaundice and bilirubin encephalopathy [11]. At present, the effects of massage on neonatal growth and health care are well verified. However, the effect of massaging on neonatal jaundice is unclear at present, no related systematic review and meta-analysis are found. Therefore, this study systematically evaluates the relevant literature and performs a meta-analysis to evaluate the effect of massaging on neonatal jaundice and provide strong evidence for clinical care.

* Corresponding author.
E-mail address: jcd1886@sina.cn (C. Jin).
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2. Methods

2.1. Search strategy

Chinese and English electronic databases were searched to avoid language bias. The English electronic databases included Cochrane Library, PubMed, EMBASE and Web of Science, whereas the Chinese electronic databases were Chinese Biomedical Literature (CBM) database, Wan Fang database (Wan Fang), VIP Database for Chinese Technical Periodicals (VIP) and China National Knowledge Infrastructure (CNKI). Chinese and English electronic databases were searched from their establishment up to May 2017.

Related research was retrieved after pre-searching. We combined the MeSH terms and text words to determine the search term. Minor adjustments were executed according to specific databases. In addition, other sources, such as the relevant conference papers, academic reports and academic dissertation, were used as supplemental studies to reduce publication bias. Search strategy: Chinese search strategy: ('baby' OR 'newborn' OR 'pediatric' OR 'premature') * AND ('jaundice' OR 'hyperbilirubinemia' OR 'bilirubin' OR 'yellow dye' OR 'serum bilirubin concentration') AND ('touch' OR 'massage' OR 'therapeutic touch' OR 'friction' OR 'trigger'). English search strategy: ('neonatal' OR 'prematurity' OR 'premature infant*' OR 'preterm infant*' OR 'neonate*' OR ' pediatric*' OR ' pediatric*' OR 'newborn' OR 'baby' OR 'birth' OR ' infant*') *AND ('jaundice' OR 'icterus' OR 'hyperbilirubinemia' OR 'serum bilirubin concentration' OR 'TSB') AND ('massag*' OR 'knead*' OR 'oil massage' OR 'therapeutic touch' OR 'manual therapy' OR 'massotherap*' OR 'tactile-kinesthetic stimulation' OR 'friction' OR 'trager').

2.2. Inclusion criteria

Studies selected and analysed in this study should meet the following eligibility criteria: (1) randomised controlled trial (RCT) and controlled clinical trial (CCT); (2) studies were published in either English or Chinese; (3) the subjects were neonates with jaundice within 28 days of birth; (4) control neonates underwent routine comprehensive treatment (such as phototherapy and immunoglobulin supportive treatment); (5) neonates of the intervention group received identical routine comprehensive treatment plus massage; (6) outcome indicators include percutaneous bilirubin levels, serum bilirubin levels, jaundice duration and defecation frequency.

2.3. Exclusion criteria

Studies were excluded if they met any of the following: (1) newborns with jaundice suffering from other serious illnesses, such as severe neonatal respiratory distress syndrome and severe congenital heart disease; (2) neonates of intervention group who were subjected meridian massage and acupressure and local massage; (3) neonates of intervention group who underwent other interventions, such as swimming, Chinese medicine bathing and Chinese acupuncture, in combination with massage.

2.4. Data extraction

First, duplicate studies were removed. Two reviewers blinded to the study independently performed selection according to eligibility criteria and then carried out cross checking. Disagreements between the two reviewers were resolved by consulting the third reviewer.

Two researchers independently completed data extraction, quality evaluation and then cross-checking. If views between the two reviewers were inconsistent, the third researcher was consulted to resolve disagreements. The following information was extracted from the literature: basic information, inclusion and exclusion criteria, type of study, sample size, intervention and outcome of the measurement. The quality evaluation of the literature was carried out independently according to the Cochrane Systematic Review Handbook (version 5.1.0) [12]. The following six components form the literature were assessed: (1) random sequence generation; (2) allocation concealment; (3) blinding; (4) incomplete outcome data and selective reporting; (5) comparability of baseline data; and (6) intentional treatment.

2.5. Data analysis

In this study, meta-analysis was conducted using the RevMan 5.3 software. Data were described and expressed as mean difference (*MD*) or standard mean difference (*SMD*) with 95% confidence interval (*CI*). Heterogeneity was assessed by *I*-squared test (I^2). If significant heterogeneity did not exist among studies ($I^2 \leq 50\%$, $P \geq 0.1$), a fixed effect model was established in the meta-analysis. If significant heterogeneity existed among studies ($I^2 > 50\%$, $P < 0.1$), the source of the heterogeneity was analysed. If only statistical heterogeneity was observed among the studies, without clinical heterogeneity, a randomised effect model was constructed. Descriptive analysis was conducted if the heterogeneity was too obvious and the source could be not determined.

3. Results

3.1. Characteristics of the included studies

A total of 2445 studies in the literature were obtained from Chinese and English electronic databases. Eight studies were obtained by manually retrieving conference papers, academic reports and academic dissertation. The search results of the electronic database are as follows: Cochrane Library 12, PubMed 20, EMBASE 318, Web of Science 20, CBM 363, Wan Fang 751, VIP 366 and CNKI 595. Duplicate studies were excluded by NoteExpress, and 1092 papers remained. Then, 217 studies were retained by reading the title and abstract in the literature. Finally, 14 studies were retained by reading the full text [13–26]. Literature retrieval and screening were conducted in accordance with the principles of the Preferred Reporting Items for Systematic Reviews and Meta-Analysis. The specific process is shown in Fig. 1. A total of 14 randomised controlled trials with 1889 patients were included. Detailed description of the general data for 14 studies is shown in Table 1.

3.2. Methodological quality of included trials

According to the Cochrane risk of bias estimation, generation of allocation sequence in every trial was mentioned. Among all trials, three and three studies were under groups A and B, respectively. The methodological evaluation of all trials is shown in Table 2, and the methodological quality assessment for risk of bias is shown in Fig. 6.

3.3. Percutaneous bilirubin

Given that the development of neonatal jaundice and the different durations of interventions may affect percutaneous bilirubin level, subgroup analysis was conducted in this study according to the time of measuring percutaneous bilirubin (days 1, 2, 3, 4 and 7 after birth). Significant heterogeneity among the study after the subgroup analysis was observed. A randomised effect model was conducted (Fig. 2). Results of the subgroup analysis

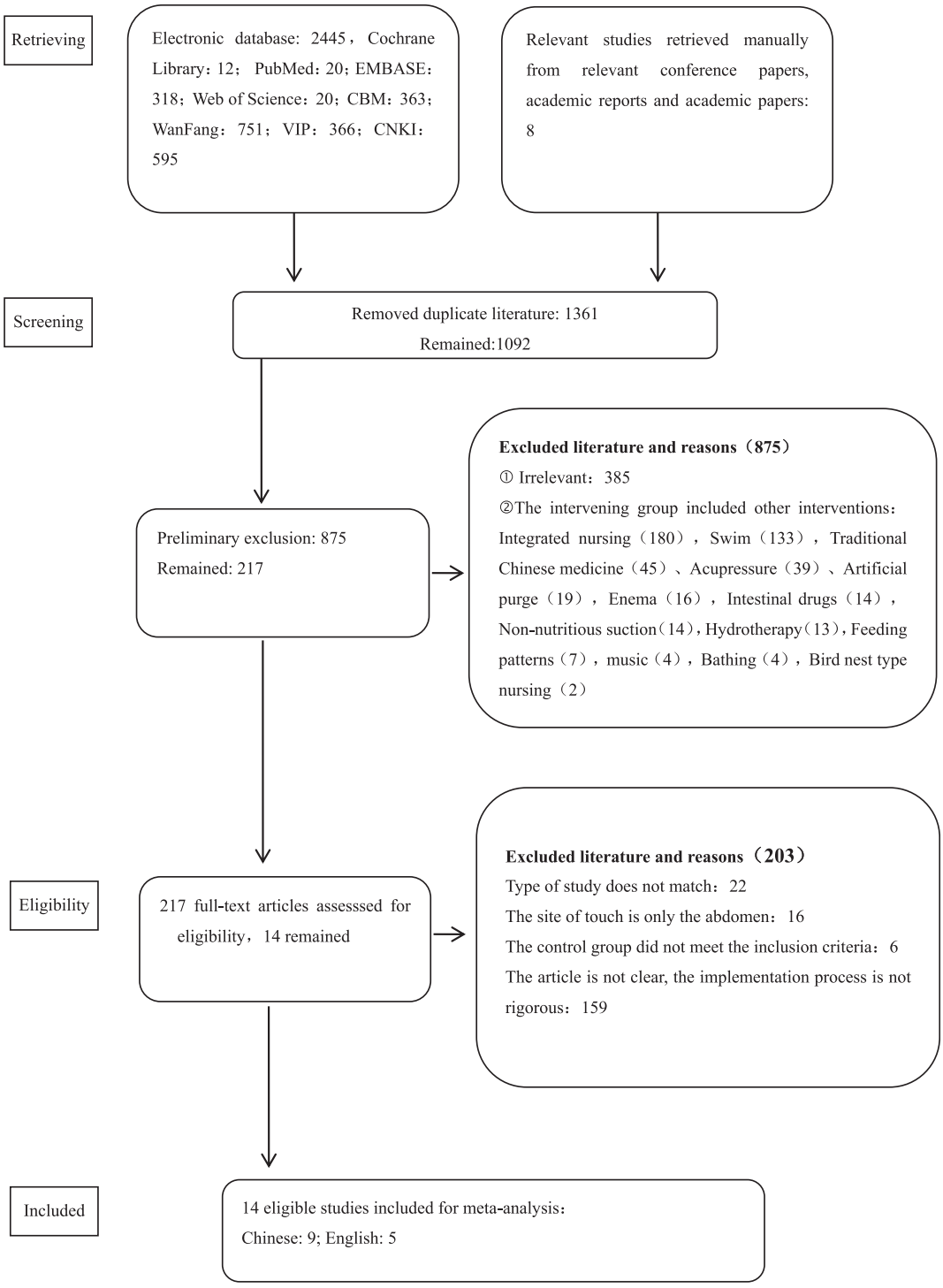

Fig. 1. Flow chart of the study selection procedure.
Abbreviations: CBM: China Biology Medicine; CNKI: China National Knowledge Infrastructure; VIP: VIP Database for Chinese Technical Periodicals; RCT: randomized controlled trial.

suggested that different days of birth is the source of heterogeneity. Percutaneous bilirubin level on days 1, 2, 3, 4 or 7 of birth in Fig. 2 represents percutaneous bilirubin level as measured when neonates are on the first/second/third/fourth and seventh days of birth.

(1) Percutaneous bilirubin level on day 1 of birth. Three studies with 182 children were included [21,25,26]. The result of meta-analysis showed no significant difference in the percutaneous bilirubin level between control and intervention groups [$MD = -0.04$, 95% CI (−0.39, 0.30), $P > 0.05$].
(2) Percutaneous bilirubin level on day 2 of birth. Three studies with 182 children were included [21,25,26]. The result of meta-analysis demonstrated a significant difference in percutaneous bilirubin level between control and intervention groups [$MD = -1.21$, 95% CI (−1.90, −0.52), $P < 0.05$].

Table 1
Characteristics of included studies.

First author, y	Inclusion and exclusion criteria	Type of study	Sample size(I/C)	Interventions	Outcome
Sun Yunhai et al., 2004	Inclusion and exclusion criteria are not reported	RCT	105/105	Massage(once/d, every 15 min, until the 42nd days of birth)	①; ②; ⑤
Wei Lin'an et al., 2007	inclusion criteria: a1,b,c1,d,f,g; exclusion criteria: s;	RCT	34/34	massage(2 times/d, every 15 min)	②; ④; ⑤
Cheng Shuang et al., 2015	inclusion criteria: a1,d,k,l,n; exclusion criteria: s,t;	RCT	I1/I2/I3/C = 73/72/71/70	massage(2 times/d, every 20 min)	⑤; ⑥; ⑦; ⑧
Liu Shanshan et al., 2013	inclusion criteria: a1,c2,o,p; exclusion criteria: s,w;	RCT	40/40	massage(2 times/d, every 10–15 min)	②; ⑤; ⑦
Lai Shuying et al., 2017	inclusion criteria: a1,c2,o,p; exclusion criteria: s,w;	RCT	285/285	massage(2 times/d, every 15–20 min, until the 7th days of birth)	③; ⑤
Zhang Ying et al., 2012	inclusion criteria: c2,d; exclusion criteria: s;	RCT	90/90	massage(2 times/d, every 15 min)	①; ②; ④; ⑤; ⑦; ⑧
Wu Jing,2013	inclusion criteria: a1,q,r,h,l; exclusion criteria: c6,s,t,u,w,x;	RCT	50/50	massage(2 times/d, every 15–20 min, until the 5th days of birth)	①; ②; ⑤; ⑦; ⑧; ⑨
Ye Liying et al., 2015	inclusion criteria: d,n,i; exclusion criteria: s;	RCT	58/58	massage(once/d, every 15–20 min)	②; ⑤; ⑦
Lai Ai-ru et al., 2016	inclusion criteria: l; exclusion criteria: s,t,v;	RCT	50/50	massage(2 times/d, every 30 min, until the 4th days of birth)	⑤; ⑦
Hosein Dalili et al., 2015	inclusion criteria: a1,c3,d,l; exclusion criteria: s,x;	RCT	25/25	massage(3 times/d, every 15–20 min, until the 4th days of birth)	⑤; ⑦
Lin, Chien-Heng et al., 2015	inclusion criteria: a1,c4,d,x; exclusion criteria: t;	RCT	27/29	massage(2 times/d, every 15–20 min, until the 3th days of birth)	①; ⑤; ⑦; ⑧; ⑩
Alehe Seyyedrasooli et al., 2014	inclusion criteria: j,l; exclusion criteria: x,z,ab;	RCT	26/28	massage(3 times/d, every 15 min, until the 4th days of birth)	⑤; ⑦
Jun Chen et al., 2011	inclusion criteria: a1,c3,d; exclusion criteria: s,x;	RCT	20/22	massage(2 times/d, every 15–20 min, until the 5th days of birth)	⑤; ⑦
Mahdi BasiriMoghadam et al., 2015	inclusion criteria: a2,c5,d,l,p; exclusion criteria: s,y,ac;	RCT	20/20	massage(2 times/d, every 20 min, until the 4th days of birth)	⑤; ⑦

a1:term infan; **a2**:infant at 34–36 weeks of gestational; **b**:infant of 1–28 days of birth; **c1**:birth weight:2.5–3.5 kg; **c2**:birth weight:2.5–4.0 kg; **c3**:birth weight:2.8–3.6 kg; **c4**:birth weight:2.5–3.6 kg; **c5**:low birth weight; **c6**:extremely low birth weight; **d**:Apgar score ≥8; **f**: hyperbilirubinemia; **g**:serum bilirubin levels:256μmol/L~336.8umol/L; **h**:blood total bilirubin>205.2umol/L; **i**:It was mainly indirect bilirubin when bilirubin increased; **j**: percutaneous bilirubin on first day<5 mg/dl; **k**:rooming-in care; **l**:breastfeeding; **m**:There is a simple breast milk contraindications in the newborns; **n**:There are yellow dye symptoms in the newborns; **o**:single pregnancy; **p**:Families agree to participate in the study; **q**:Meet the diagnostic criteria for neonatal jaundice; **r**:meet the standard of light therapy; **s**:Neonatal suffer from congenital diseases and complications (such as neonatal asphyxia, hemolytic symptoms, patent ductus arteriosus (PDA), respiratory distress syndrome (RDS) and sepsis, amniotic fluid inhalation syndrome, birth defects; birth trauma, Asphyxia and infection, etc.); **t**:Other causes of jaundice (Hepatitis, hemolytic disease, congenital diseases, familial and perinatal factors, infection, uterine bleeding, glucose-6-phosphate dehydrogenation Enzyme deficiency, gastrointestinal obstruction and biliary atresia); **u**:Pregnant women without diabetes and liver and gall diseases; **v**:Pregnant women without pregnancy complications; **w**:Neonatal of needing oxygen supply and respiratory support; **x**:infants of needing light therapy for jaundice; **y**:The newborns are at the beginning of the phototherapy; **z**:Use the drugs of reducing bilirubin; **ab**:There are the relevant factors of restricting massage in infants(eg: edema, tissue damage, skin infections and rash); **ac**:Infants had discharged before the study was finished.
I/C:sample size of intervention group/sample size of control group.
①weight; ②sleep condition; ③neonatal neurobehavioral determination; ④crying; ⑤Bilirubin levels and duration; ⑥hepatic function; ⑦Defecation; ⑧breastfeeding condition; ⑨The incidence of adverse reactions; ⑩the time of stopping light therapy and discharging.

(3) Percutaneous bilirubin level on day 3 of birth. Four studies with 390 children were included [13,21,25,26]. Statistical results illustrated a significant difference in percutaneous bilirubin levels between control and intervention groups [$MD = -2.00$, 95% CI (−2.68, −1.32), $P < 0.05$].
(4) Percutaneous bilirubin level on day 4 of birth. Three studies with 192 children were included [21,22,25]. The results showed a significant difference in percutaneous bilirubin level between control and intervention groups [$MD = -2.00$, 95% CI (−2.56, −1.44), $P < 0.05$].
(5) Percutaneous bilirubin level on day 7 of birth. Two studies with 290 children were included [13,16]. Results demonstrated significant difference in percutaneous bilirubin level between control and intervention groups [$MD = -1.93$, 95% CI (−2.44, −1.43), $P < 0.05$].

3.4. Serum bilirubin level

3.4.1. Serum total bilirubin level

Five studies containing serum total bilirubin level were included [18–21,25]. The neonates were divided into A, B and C groups according to the severity of jaundice in Zhang Ying [18]. Each group comprised 60 neonates. Then, each group was divided into the massage subgroup and control subgroup, with 30 neonates in each subgroup. Subgroup analysis was conducted in this study according to sample size. Significant heterogeneity among studies was found, and a randomised effect model was established (Fig. 3). The results of subgroup analysis suggested that sample size is the source of heterogeneity. '"Serum total bilirubin level (sample size ≥ 100) ' in Fig. 3 represents serum total bilirubin level of neonates in studies of sample size ≥ 100. 'Serum total bilirubin level (sample size < 100)' in Fig. 3 represents serum total bilirubin level of neonates in studies with sample size < 100.

(1) Serum total bilirubin level (sample size ≥ 100). Three studies with 316 children were included [19–21]. Results demonstrated a significant difference in the serum total bilirubin level between control and intervention groups [$MD = -49.67$, 95% CI (−59.00, −40.34), $P < 0.05$].
(2) Serum total bilirubin level (sample size < 100). Two studies with 222 children were included [18,25]. The results of meta-analysis showed a significant difference in the serum total bilirubin level between control group and intervention group [$MD = -11.95$, 95% CI (−17.84, −6.05), $P < 0.05$].

Table 2
Methodological quality for each included study.

Study	Sequence generation	Allocation concealment	Blinding	Withdraw	Baseline	ITT	Score
Sun Haiyun et al.	unclear	high risk	high risk	low risk	low risk	low risk	B
Wei Lln'an et al.	unclear	unclear	unclear	low risk	low risk	low risk	A
Cheng Shuang et al.	low risk	high risk	high risk	low risk	low risk	low risk	B
Liu Shanshan et al.	unclear	high risk	high risk	low risk	low risk	low risk	B
Lai Shuying et al.	low risk	high risk	high risk	low risk	low risk	low risk	B
Zhang Ying et al.	low risk	high risk	high risk	low risk	low risk	low risk	B
Wu Jing	low risk	high risk	high risk	low risk	low risk	low risk	B
Ye Liying et al.	low risk	high risk	high risk	low risk	low risk	low risk	B
Lai Ai-ru et al.	low risk	high risk	high risk	low risk	low risk	low risk	B
Hosein Dalili et al.	unclear	high risk	high risk	low risk	low risk	low risk	B
Lin, Chien-Heng et al.	unclear	high risk	high risk	low risk	low risk	low risk	B
Alehe Seyyedrasooli et al.	low risk	low risk	high risk	low risk	low risk	low risk	A
Jun Chen et al.	unclear	high risk	high risk	high risk	low risk	high risk	B
Mahdi BasiriMoghadam et al.	low risk	low risk	low risk	low risk	low risk	low risk	A

Blinding: whether patients, care providers and outcome assessors were blinded. Intention-to-treat (ITT): whether trial authors performed analyses to take into account all patients who began the intervention regardless of protocol violations, drop-outs or loss of follow-up.
Sequence generation:low risk[Specific random method was reported]; unclear[Random was mentioned, but the specific random method was not reported]; high risk[Random was not mentioned].
Allocation concealment:low risk[Specific method of allocation concealment was reported]; unclear[Allocation concealment was mentioned, but the specific method of allocation concealment was not reported]; high risk[Allocation concealment was not mentioned].
Blinding:low risk[Specific blinding method was reported]; unclear[Blinding was mentioned, but the specific blinding method was not reported]; high risk[Blinding was not mentioned].
Withdraw:low risk[There was no withdraw, or withdraw was properly handled]; unclear[The method of handling withdraw was not clearly reported]; high risk[Withdraw was not handled].
Baseline:low risk[All factors at baseline were comparable]; unclear[Partly factors at baseline were comparable]; high risk[All factors at baseline were not comparable].
ITT:low risk[There was no need for intentional analysis, or appropriate intentional analysis was carried out]; unclear[Intentional analysis is unclear]; high risk[Appropriate intentional analysis was not carried out].

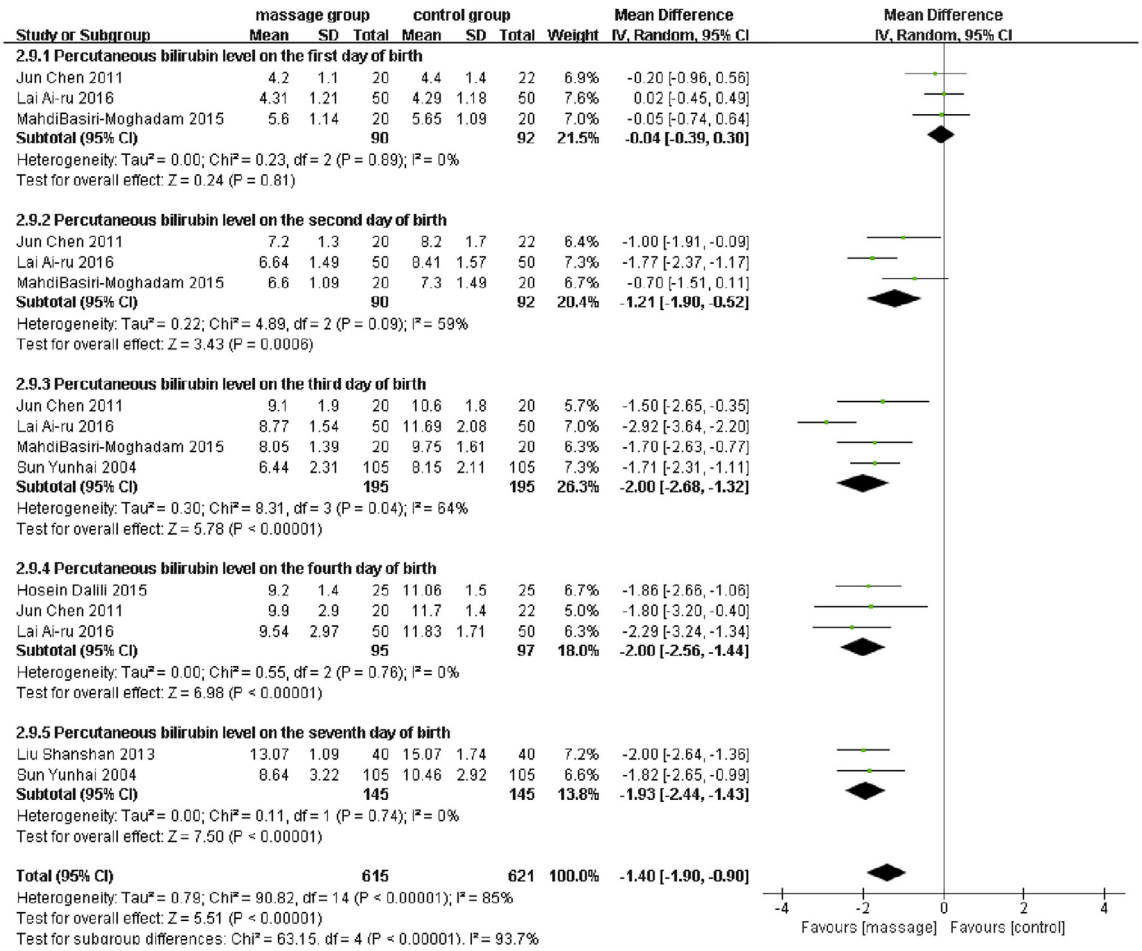

Fig. 2. Forest plot of percutaneous bilirubin level.
"Percutaneous bilirubin level on the first/second/third/fourth/seventh day of birth" in Fig. 2 represents percutaneous bilirubin level of being measured when neonatals are on the first/second/third/fourth/seventh day of birth.

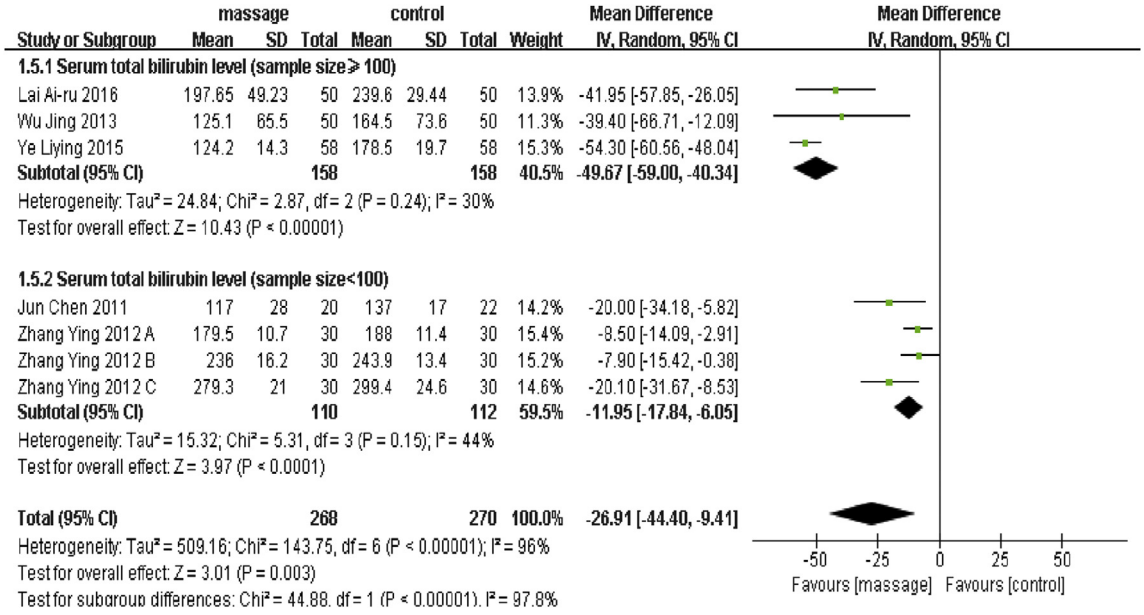

Fig. 3. Forest plot of serum total bilirubin level.
"Serum total bilirubin level (sample size≥100)"in Fig. 3 represents Serum total bilirubin level of neonatal in studies of sample size ≥ 100."Serum total bilirubin level (sample size<100)"in Fig. 3 represents serum total bilirubin level of neonatal in studies of sample size<100.

3.4.2. *Serum indirect bilirubin level*

Three studies involving serum indirect bilirubin level were included [14,19,25]. A total of 210 children were included in these studies. Large heterogeneity was observed among the three studies ($P = 0.006$, $I^2 = 80\%$); however clinical and methodological heterogeneities were not found. Therefore, only descriptive analysis was conducted. Two studies [14,19] showed lower indirect bilirubin level in the intervention group in comparison with the control group. One study [25] indicated no significant difference in indirect bilirubin level between intervention and control groups.

3.5. *The duration of jaundice*

Two studies with 244 children were included [15,19]. Large heterogeneity was observed between the two studies ($P = 0.0001$, $I^2 = 93\%$); thus, only descriptive analysis was conducted. One study [19] illustrated that the duration of jaundice in the intervention group was shorter than that in the control group. One study [15] showed no statistically significant difference in jaundice duration between intervention and control groups.

3.6. *Defecation frequency*

A total of six studies [21–26] were included. One study was described by median with quartile range; hence, this study was not integrated with other studies [24]. Furthermore, a subgroup analysis was performed according to the time of measuring defecation frequency (first, second, third, fourth days of birth). The results showed large heterogeneity among studies (Fig. 4). However, heterogeneity among studies significantly decreased when the largest weight study [21] was removed (Fig. 5). Randomised effect model was established. 'Defecation frequency on the first/second/third/fourth days of birth' in Figs. 4 and 5 represents defecation frequency of being measured when neonates are on the first/second/third/fourth days of birth.

(1) Defecation frequency on the first day of birth. Six studies with 331 children were included [21–26]. The results demonstrated no significant difference in defecation frequency between intervention group and control group ($P > 0.05$) after the study with the largest weight [21] was removed [$SMD = 0.33$, 95% CI (−0.40, 1.05), $P > 0.05$].
(2) Defecation frequency on the second day of birth. Six studies with 331 children were included [21–26]. Defecation frequency in the intervention group was significantly higher than that in the control group [$SMD = 0.44$, 95% CI (0.02, 0.87), $P < 0.05$].
(3) Defecation frequency on the third day of birth. Six studies with 331 children were included [21–26]. No significant difference in defecation frequency between intervention group and control group ($P > 0.05$) after a largest weight study [21] was removed [$SMD = 0.38$, 95% CI (−0.03, 0.79), $P > 0.05$].
(4) Defecation frequency on the fourth day of birth. Five studies with 275 children were included [21,22,24–26]. No significant difference in defecation frequency was observed between intervention group and control group ($P > .05$) after the study with the largest weight [21] was removed [$SMD = 0.18$, 95% CI (−0.51, 0.87), $P > 0.05$].

4. Discussion

4.1. *Analysis on publication bias of the included studies*

A total of 14 studies were included in this study. However, for each outcome indicator, the number of studies included is ≤ 6. According to the Cochrane Handbook, Funnel chart tests should be used only when the number of studies included ≥10 for each outcome indicator. With an extremely low number of studies included, test efficiency is too low to distinguish between opportunity and true asymmetry. Given the limited number of the included studies, the funnel map was not performed. However, two retrieval methods were conducted in this study to reduce publication bias. In addition, the Chinese and English language-based electronic databases were searched to avoid language bias. Repeatedly published works were excluded to avoid the use of the same data.

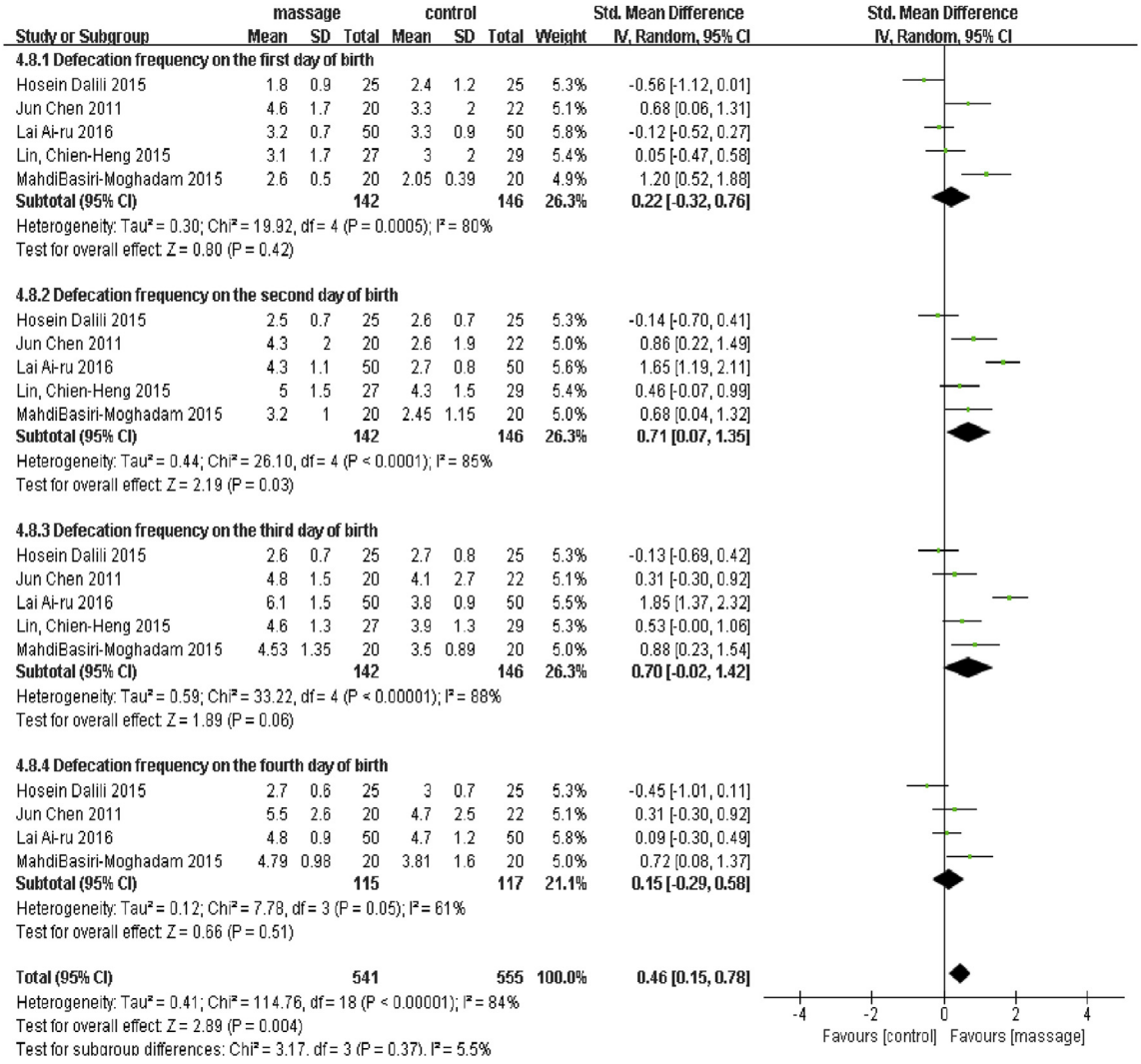

Fig. 4. Forest plot of defecation frequency.
Defecation frequency on the first/second/third/fourth day of birth"in Fig. 4 represents defecation frequency of being measured when neonatals are on the first/second/third/fourth day of birth.

4.2. Methodological analysis of included studies

In this study, 14 randomised controlled studies were included. According to risk of bias estimation, random methods were mentioned in all studies. However, only eight studies referred to the specific method of random, and three studies conducted allocation concealment. Moreover, blinding to participants and personnel was difficult to conduct when the neonatal intervention was massage; therefore, blinding of outcome data was mainly underlined in this study. Blindness was only mentioned in two works. Given that the outcomes of this study were mainly objective indicators, blindness exerted a weak effect on the results of this study. Only one out of the 14 studies involved newborns dropping out. However, no difference in baseline data between intervention group and the control groups was found before the intervention. In addition, given that authors did not distinguish between physiological jaundice and pathological jaundice in the included studies, analysis of this topic was not conducted in this study, which may result in increased risk of bias. Therefore, researchers should pay attention to the distinction of effect of massaging between physiological jaundice and pathological jaundice in the future.

4.3. Effects of massaging on bilirubin levels in neonates with jaundice

Studies showed that high bilirubin levels exist in the meconium. If the meconium accumulates in the intestine and cannot be timely discharged, bilirubin is reabsorbed into the blood. Frequent defecation can reduce bilirubin enterohaepatic circulation and increase bilirubin excretion [27]. In addition, massage can increase the excitability of the vagus nerve by stimulating the skin. Massaging can also promote insulin and gastrin secretion to accelerate the digestion and absorption of food and defecation [28]. The results of this study showed no statistically significant difference in percutaneous bilirubin on day 1 between intervention and control groups, which may be related to the intervention time limit. Statistically significant difference in percutaneous bilirubin on days 2, 3, 4 and 7 was observed between intervention and control groups. The current study focused on the short-term effect of massaging. The studies of long-term effects and follow-up studies were less. Children's serum total bilirubin levels in the intervention group were lower than those in the control group. In addition, the effects of massaging on serum indirect bilirubin levels and jaundice

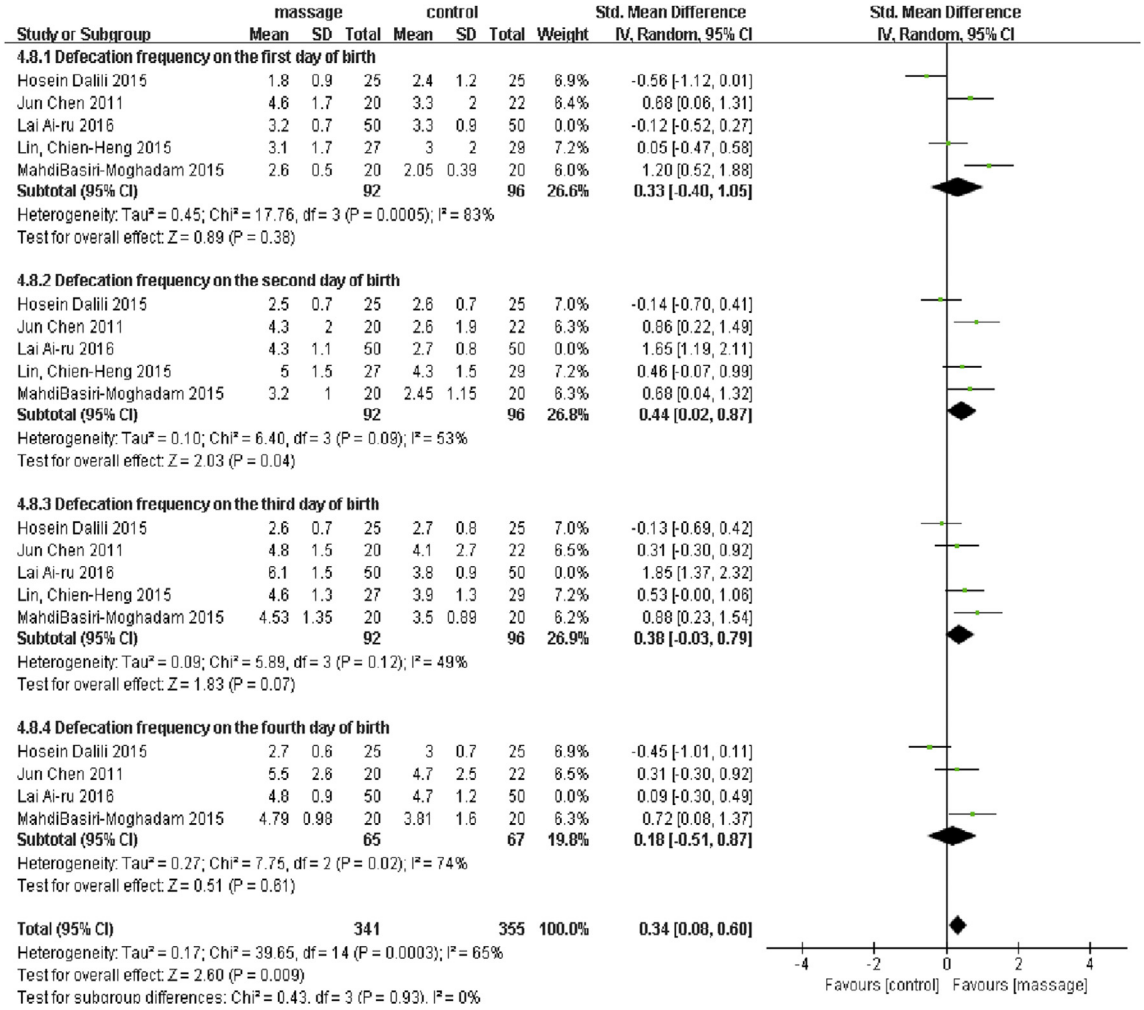

Fig. 5. Forest plot of defecation frequency.
Defecation frequency on the first/second/third/fourth day of birth"in Fig. 5 represents defecation frequency of being measured when neonatals are on the first/second/third/fourth day of birth.

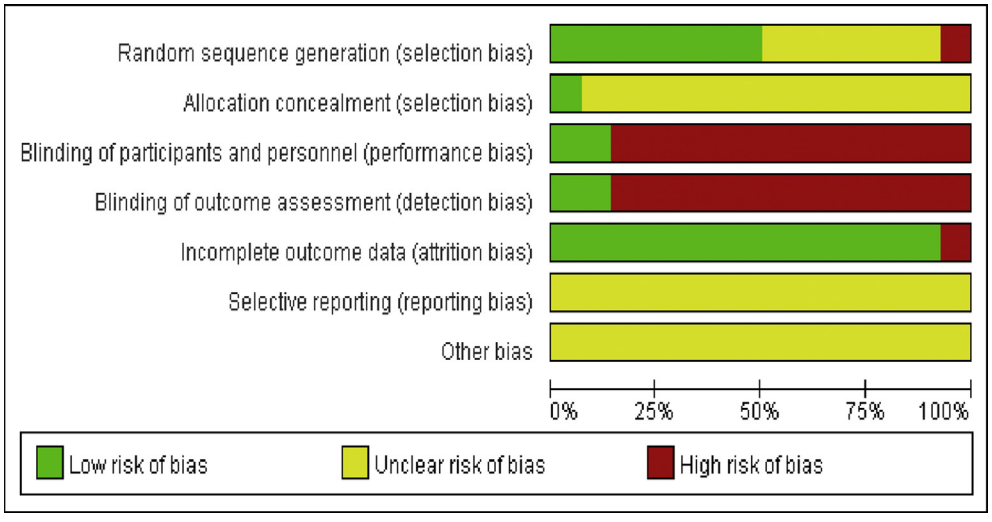

Fig. 6. Methodological quality assessment for risk of bias for each included study.

duration were unclear. Furthermore, large heterogeneity was observed among the studies and may be related to the small number of studies. In the future, researchers should conduct more studies of high quality and large sample size.

4.4. Effects of massaging on defecation frequency in neonates with jaundice

A study showed that bilirubin in the meconium is five to ten times the bilirubin produced daily. Meconium accumulation increases bilirubin reabsorption. Defecation can reduce bilirubin enterohepatic circulation and serum bilirubin levels [29]. Therefore, defecation situation was analysed in this study. Subgroup analysis was performed based on the time of measuring defecation frequency (days 1, 2, 3 and 4 of birth). However, heterogeneity among studies remained large. Heterogeneity was significantly reduced after the study with the largest weight was removed [21]. This finding indicated that individual studies exerted a relatively large impact on the study results. Therefore, touch care for children with jaundice in the number of bowel movements needs to be included in high-quality research to confirm the effects of massaging. In addition, the defecation situation not only included defecation frequency but also the volume of defecation and shape of meconium. However, this meta-analysis included a small number of studies that focused on the volume of defecation and the shape of meconium.

4.5. Potential impact of the ongoing trials

An ongoing study is focused on the effect of mothers' massage on premature newborns [30]. The hypotheses being tested include the following: growth of infant, mood of mother and infant attachment. The study will demonstrate the effect of massaging by mothers on their presumed infants. In the future, researchers should conduct more studies on massage as performed by different intervention implementers to further prove the factors that influence the effect of massage and control related factors to promote the development of massaging. In addition, research on the effect of massaging on newborns of different types of newborns, such as neonates with physiological jaundice, newborns with pathological jaundice, preterm infants or newborns with critical illness, should be conducted.

5. Conclusions

This meta-analysis indicates that massage therapy is an effective intervention for neonatal jaundice. However, given the quality of included studies and the limitations of samples, further long-term and high-quality research studies be conducted to confirm long-term efficacy and safety of this approach.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.ijnss.2018.01.004.

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