

Nonpharmacological management of procedural pain in infants and young children: An abridged Cochrane review

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BACKGROUND: Acute pain and distress during medical procedures are commonplace for young children.

OBJECTIVE: To assess the efficacy of nonpharmacological interventions for acute procedural pain in children up to three years of age.

METHODS: Study inclusion criteria were: participants <3 years of age, involved in a randomized controlled or crossover trial, and use of a 'no-treatment' control group (51 studies; n=3396). Additional studies meeting all criteria except for study design (eg, use of active control group) were qualitatively described (n=20).

RESULTS: For every intervention, data were analyzed separately according to age group (preterm-born, term-born neonate and older infant/young child) and type of pain response (pain reactivity, immediate pain-related regulation). The largest standardized mean differences (SMD) for pain reactivity were as follows: sucking-related interventions (preterm: -0.42 [95% CI -0.68 to -0.15]; neonate -1.45 [CI -2.34 to -0.57]), kangaroo care (preterm -1.12 [95% CI -2.04 to -0.21]), and swaddling/facilitated tucking (preterm -0.97 [95% CI -1.63 to -0.31]). For immediate pain-related regulation, the largest SMDs were: sucking-related interventions (preterm -0.38 [95% CI -0.59 to -0.17]; neonate -0.90 [CI -1.54 to -0.25]), kangaroo care 0.77 (95% CI -1.50 to -0.03]), swaddling/facilitated tucking (preterm -0.75 [95% CI -1.14 to -0.36]), and rocking/holding (neonate -0.75 [95% CI -1.20 to -0.30]). The presence of significant heterogeneity limited confidence in nonsignificant findings for certain other analyses.

CONCLUSIONS: Although a number of nonpharmacological treatments have sufficient evidence supporting their efficacy with preterm infants and healthy neonates, no treatments had sufficient evidence to support efficacy with healthy older infants/young children.

Key Words: *Acute pain; Caregiver; Infant; Pain management*

Initial misinterpretations of common infant pain outcomes, such as the lack of declarative memory for painful experiences during infancy (1), the muted responses of premature infants after a barrage of painful procedures (2), and unacceptable rates of serious adverse events due to poor knowledge of infant responses to analgesics and anesthetics during the 1950s to 1970s (3), perpetuated widespread neglect of infant pain treatment.

Established research supports infants' anatomical and functional capacity to perceive pain (4,5) and respond to tissue insult in a manner interpretable as pain (6). However, despite significant advocacy work, infant acute pain is still undermanaged or unmanaged (7). Comprehensive meta-analytic reviews of nonpharmacological pain management strategies are essential to the ethical and humane treatment of infants and young children during acutely painful procedures.

While several reviews summarize certain acute pain management techniques for painful procedures in infants and young children

La prise en charge non pharmacologique des douleurs causées par des interventions auprès des nourrissons et des jeunes enfants : une analyse Cochrane abrégée

HISTORIQUE : Il est courant que les jeunes enfants ressentent une douleur aiguë et de la détresse pendant des interventions médicales.

OBJECTIF : Évaluer l'efficacité de mesures non pharmacologiques pour soulager une douleur aiguë causée par une intervention chez des enfants de moins de trois ans.

MÉTHODOLOGIE : Les critères d'inclusion dans l'étude s'établissaient comme suit : participants de moins de trois ans faisant partie d'un essai aléatoire et contrôlé ou transversal et utilisation d'un groupe témoin « sans traitement » (51 études; n=3 396). Des études supplémentaires respectant tous les critères sauf la méthodologie (p. ex., recours à un groupe témoin actif) ont fait l'objet d'une description qualitative (n=20).

RÉSULTATS : À chaque intervention, les chercheurs ont analysé les données séparément compte tenu du groupe d'âge (nouveau-né prématuré ou à terme et nourrisson plus âgé ou jeune enfant) et du type de réponse à la douleur (réactivité à la douleur, régulation immédiate liée à la douleur). Les plus grandes différences moyennes standardisées (DMS) de réactivité à la douleur s'établissaient comme suit : interventions liées à la succion (prématuré : -0,42 [95 % IC -0,68 à -0,15]; nouveau-né : -1,45 [IC -2,34 à -0,57]), technique kangourou (prématuré : -1,12 [95 % IC -2,04 à -0,21]) et emmaillotement ou enroulement facilité (prématuré : -0,97 [95 % IC -1,63 à -0,31]). En cas de régulation immédiate liée à la douleur, les plus grandes DMS s'établissaient comme suit : interventions liées à la succion (prématuré : -0,38 [95 % IC -0,59 à -0,17]; nouveau-né : -0,90 [IC -1,54 à -0,25]), technique kangourou : 0,77 (95 % IC -1,50 à -0,03]), emmaillotement ou enroulement facilité (prématuré : -0,75 [95 % IC -1,14 à -0,36]), et fait de bercer ou de prendre dans les bras (nouveau-né : -0,75 [95 % IC -1,20 à -0,30]). Une hétérogénéité importante limitait l'intervalle de confiance des résultats non significatifs de certaines autres analyses.

CONCLUSIONS : Même si les données sont suffisantes pour appuyer l'efficacité d'un certain nombre de traitements chez les prématurés et les nouveau-nés en santé, aucun traitement ne s'associe à des données probantes suffisantes pour en étayer l'efficacité chez les nourrissons plus âgés et les jeunes enfants.

(8-10), no comprehensive meta-analyses were attempted. Moreover, to our knowledge, there have been no meta-analyses conducted on the broad range of nonpharmacological interventions for managing acute pain and distress in young children from zero to three years of age. Given the frequency of acutely painful procedures for healthy children in early childhood (eg, immunizations) and for hospitalized infants (11), this significant gap in the literature deserves a higher priority.

The full review (12) also takes a novel and in-depth look at the nonpharmacological pain management literature by controlling for age and type of pain response. Age was considered crucial due to the steep trajectory of infant development, both psychologically and physiologically. Moreover, given the different physiological and psychological mechanisms subsuming the initial reaction to a painful stimulus (more automatic and/or reflexive reactivity such as initial distress cry) and during the period of recovery from the painful insult (more under voluntary control; such as whimpering cry minutes after a

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painful stimuli), timing of pain response was also considered important to explore (see Hadistavropoulos and Craig [13] for in-depth discussion regarding observational measures of reflexive and voluntary pain reactions during infancy and childhood).

METHODS

Search strategy

Only randomized controlled trials (RCTs) and randomized crossover trials (RCrTs) using a no-treatment control group that involved the nonpharmacological management of acute procedural pain in infants and children zero to three years of age were included. No language restrictions were used during the search. Due to the existence of meta-analyses specifically pertaining to circumcision surgery (14,15), sucrose (16), breastfeeding (17) and music (18), these types of studies were excluded from the review.

A unique search strategy for MEDLINE (1966 to April 2011), PsycINFO (1967 to April 2011), EMBASE (1980 to April 2011), and CINAHL (1982 to April 2011) was created in collaboration with three librarians affiliated with the Cochrane Collaboration (online Appendix 1). Completed unpublished trials were located through Dissertation Abstracts International (1980 to 2010), the Cochrane Central Register of Controlled Trials (CENTRAL; Issue 3 2010) on The Cochrane Library and www.clinicaltrials.gov (2010). Appeals were made to pediatric electronic mailing lists (Pain in Child Health [PICH; pich-l@lists.dal.ca], Pediatric Pain [Pediatric-pain@lists.dal.ca], American Psychological Association Division 54 [Pediatric Psychology; div54-members@lists.apa.org]). Finally, the reference lists of recently published reviews were also consulted.

Study selection

Review authors were not blinded to authors, institutions, journals or results. Using the full-text articles, authors reviewed articles for inclusion (see Acknowledgements). Figure 1 displays the summary of the literature search.

Data extraction

Data extraction was conducted using a form designed for the present review. Each form also included a risk of bias/quality questionnaire (online Appendix 1). Every included article was extracted independently by at least two authors and compared. When two authors disagreed, the original article and/or the lead author was consulted to achieve consensus.

Qualitative, quantitative, and study quality data were compiled in Excel 2007 (Microsoft Corporation, USA), RevMan 5 or SPSS version 19.0 (SPSS Inc, USA), respectively. A random sampling of 25% (RevMan5) to 30% (Excel and SPSS) of all data entered across all three programs was double checked by a subteam of review authors.

Only objectively measured behaviorally-based responses to pain were analyzed (see full review (12) for detailed list of measures included). When studies had more than one unidimensional behavioral pain measure, the most specific measure available was used. For example, pain facial expression was used over cry duration. If multimodal measures were used (ie, measures that provided a total score based on behavioural and physiological measurement or multiple behavioural scales), the total score was used.

Quality and treatment integrity assessment

Every study included in the present review was scored for quality and treatment integrity by at least two review authors. The Yates Quality of Study Design and Methods Scale (19) was used to develop the study quality rating form for this review, as this scale was specifically validated for nonpharmacological treatments.

Three minor modifications were made to the Yates scale (12). The maximum score on the revised Yates scale was 23 points, with higher scores indicating higher quality (Table 3 for risk of bias scores). See online appendix for the modified measure.

While the majority of studies were deemed of satisfactory-marginal quality, five studies were classified as lower/unknown quality due to receiving a score of 13 or less (20-24).

Treatment integrity was also assessed because almost one-half of the analyzed studies were crossover designs. Two raters independently judged the treatment integrity on five dimensions: treatment adherence, treatment exposure, quality of delivery, participant responsiveness, and program differentiation (25) to arrive at an overall judgment. Only one study had lower/unknown treatment integrity (26).

Data synthesis

Overall strategy: Three main principles guided the meta-analysis of the data collected for the present review:

1. Certain types of methods had to be excluded to validly pool results. Accordingly, for a treatment study to be included in the meta-analysis, it had to have at least one trial that was an RCT or RCrT that used a no-treatment control group and included a measure that included a behavioural pain outcome. Trials that studied a relevant nonpharmacological treatment that did not meet these requirements were qualitatively described within the review to further contextualize the findings.
2. Studies within the 13 different treatments (Table 3) were first separated into one of three age groups:
 - Preterm born: infants born at 36 weeks gestation or less.
 - Neonate full-term: infants born at 37 weeks until one month of age.
 - Older infant/young child: infants older than one month to 36 months of age. For brevity, this group will be referred to as 'Older infant'.
3. Studies within each age group were then further divided into one of two pain response types:
 - Pain reactivity: measured within the first 30 s after the painful stimulus was discontinued.
 - Immediate pain-related regulation: measured after the first 30 s post acutely painful stimulus. If multiple measurements were taken after the first 30 s elapsed, the measurement closest to the 30s-time point was used.

Statistical analyses

Primary analyses: The results from individual studies were pooled using the generic inverse method for a random-effects model in RevMan 5. Using this statistical methodology, an index of the variability of the sample (standard error) and sample size was used to determine how influential each study would be to the final meta-analytic statistic (standardized mean difference [SMD]). A 95% CI was also reported, which incorporated the standard error of the pooled treatment effect for the treatment effect (ie, SMD). As RCTs and RCrTs were included, different procedures, obtained from a Cochrane statistical consultant, were used. Details of this procedure are presented elsewhere (12). When data were missing, study authors were contacted or recommended techniques for interpolation/estimation from P values, *t* scores and F scores were used (25).

Secondary analyses: When two or more trials were meta-analyzed in the primary analysis and heterogeneity and/or quality was an issue, secondary sensitivity analyses were conducted. The I^2 statistic (27) determined the impact of heterogeneity. When heterogeneity was an issue due to highly variable SMD(s), analyses were re-run without these studies to examine the impact of the pooled findings. When analyses included a study of lower/unknown quality or treatment integrity, analyses were also re-run without these studies to examine the impact on the pooled findings. Authors' conclusions were based on a synthesis of all three potential analytic steps. Qualitative information from excluded studies were only provided as additional contextual information.

RESULTS

For the final analysis, 51 trials (3396 participants) were included quantitatively (Table 1) (20-24,26,28-72) and 20 trials (Table 2) (73-92) were qualitatively mentioned. Thirty-five separate primary analyses were run among the 13 interventions, three age groups and two pain response types. Table 3 presents the primary meta-analytic results from

this review (SMD, 95% CI and I²) and, when applicable, the secondary statistics re-run with studies removed due to heterogeneity and/or study quality.

Of the 3396 participants, 1581 were in treatment conditions only, 1153 were in control conditions and 662 were in a crossover condition. Of the 51 studies, 21 used a cross-over design and 30 used a between-groups design.

The following painful procedures (determined by respective study authors rather than review authors) were included in this review: 29 studies examined treatments for heelstick, 10 studies examined needle-injection procedures, six studies assessed venipuncture, two examined NICU diaper changes, two studies investigated endotracheal suctioning and two studied a neonatal intensive care unit (NICU) weighing procedure.

DISCUSSION

The summary interpretation of the primary meta-analytic findings, contextualized by secondary heterogeneity and quality/treatment integrity analyses, are presented in Table 4. Based on these results, treatments were assigned a number from 1 to 4, for each age and pain response type. As will be discussed below, the ratings reflect whether, as the literature currently stands, evidence supported the specific treatment for pain management (efficacy) or did not support the specific treatment for pain management (inefficacy). Each treatment's efficacy or inefficacy was further qualified by the level of support (sufficient versus limited).

Treatment efficacy was denoted by either a 1 (sufficient evidence, ie, two or more quality trials supporting efficacy) or 2 (limited evidence, ie, either due to quality, quantity or heterogeneity of trials, supporting efficacy). Treatment inefficacy was denoted by either a 3 (limited evidence [ie, either due to quality, quantity or trial heterogeneity]) or a 4 (sufficient evidence [ie, two or more quality trials supporting inefficacy]). Blank cells indicate no applicable research for that combination of treatment, age and pain response. A discussion of each of the findings follows.

Kangaroo care (also known as skin-to-skin contact)

An infant is placed on their caregiver's bare chest before, during and after a painful procedure.

Preterm infants: Sufficient evidence suggests kangaroo care is efficacious in reducing pain reactivity and improving immediate pain-related regulation. While there was substantial heterogeneity, secondary analyses confirmed this finding.

Four studies that were excluded from the statistical analyses (73-76) also indirectly support kangaroo care as efficacious in improving pain reactivity and immediate pain-related regulation in preterm infants.

Neonates: Limited evidence suggests that kangaroo care is not efficacious as an intervention for pain reactivity or immediate pain-related regulation. However, heterogeneity undermines our confidence in the pooled results. Given the exposure times in the premature infant literature, future research should explore whether using a longer exposure time in kangaroo care for neonates prior to the painful procedure (ie, 10 min or longer akin to preterm techniques), could lead to a significant treatment effect.

Swaddling/facilitated tucking

A swaddled infant is securely wrapped in a blanket to prevent excessive movement. Facilitated tucking is a hand-swaddling technique that holds the infant's extremities flexed and contained.

Preterm infants: There was sufficient evidence to support the use of swaddling/tucking as an efficacious intervention for reducing pain-related distress reactivity and immediate pain-related regulation in preterm infants. Two studies (74,77), that were not included in the analysis due to use of an active control group, suggested that swaddling was as efficacious as containment but not as efficacious as kangaroo care.

Neonates: Limited evidence supports the efficaciousness of swaddling/tucking related interventions for the healthy neonate.

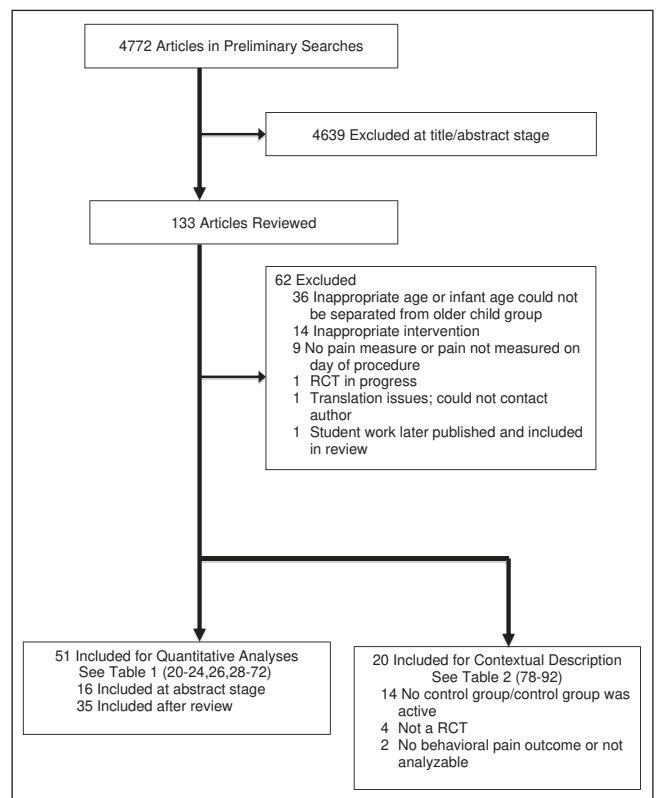


Figure 1) Literature search results. RCT Randomized controlled trial

Non-nutritive sucking-related strategies

An object (eg, pacifier, nonlactating nipple) is placed into an infant's mouth to stimulate orotactile or sucking behaviours during a painful event.

Preterm infants: There is sufficient evidence that sucking is efficacious in reducing pain-related distress reactivity and improving immediate pain-related regulation. Pain relief may be maximized if sucking begins at least 3 min before the painful stimuli. Two studies that were not included in the analyses due to the use of an active control group (85,89) also suggest that sucking helps diminish pain reactivity.

Neonates: The results show sufficient evidence for sucking to reduce pain reactivity and immediate pain-related regulation. Four studies that were not included due to the exclusion criteria (84-86,91), also lend support to the efficacy of sucking to improve immediate pain-related regulation.

Older infants: Limited evidence suggests that sucking may be an efficacious intervention to improve pain reactivity.

Swallowing water

Water is administered for ingestion without inciting extensive sucking (eg, water administered by a dropper).

Preterm infants: There was limited evidence that water is an inefficacious intervention for pain reactivity or immediate pain-related regulation for preterm infants.

Neonates: There was limited evidence that water is an inefficacious intervention for pain reactivity or immediate pain-related regulation.

Older infants: There was limited evidence that water is an inefficacious intervention for immediate pain-related regulation.

The above studies used 'water' as a treatment arm (comparing them to a 'no-treatment' control), while most other studies in the literature used water as the 'no-treatment' control group. Given the more common use of water in the literature and the limited evidence at every age group of its inefficacy, it is not recommended that further research use water as a treatment arm for young child procedural pain studies.

TABLE 1
Quantitative studies Included in analyses

First author (reference)	Year	Between/crossover	Age	Sample size	Intervention	Reactivity findings	Regulation findings	Risk of bias score
de Sousa (28)	2008	Between-groups trial	Preterm	64	Kangaroo care	Supports efficacy	–	19
Akcan (29)	2009	Between-groups trial	Preterm	50	Kangaroo care	–	Supports efficacy	19
Castral (30)	2008	Between-groups trial	Preterm	59	Kangaroo care	Supports efficacy	Does not support efficacy	15
Ferber (31)	2008	Crossover trial	Preterm	29	Kangaroo care	Supports efficacy	Supports efficacy	19
Johnston (32)	2003	Crossover trial	Preterm	74	Kangaroo care	Supports efficacy	Supports efficacy	19
Kostandy (33)	2008	Crossover trial	Preterm	10	Kangaroo care	Supports efficacy	Supports efficacy	16
Kashaninia (34)	2008	Between-groups trial	Neonate	100	Kangaroo care	Supports efficacy	–	16
Gray (35)	2000	Between-groups trial	Neonate	23	Kangaroo care	–	Supports efficacy	18
Chermont (36)	2009	Between-groups trial	Neonate	320	Kangaroo care	Does not support efficacy	Does not support efficacy	20
Belliemi (37)	2001	Crossover trial	Preterm	17	Non-nutritive sucking-related	Supports efficacy	–	15
Liaw (38)	2010	Between-groups trial	Preterm	104	Non-nutritive sucking-related	Does not support efficacy	Supports efficacy	22
Corbo (39)	2000	Crossover trial	Preterm	26	Non-nutritive sucking-related	Supports efficacy	Supports efficacy	15
Bo (40)	2000	Crossover trial	Neonate	27	Non-nutritive sucking-related	–	Supports efficacy	17
Blass (41)	1999	Between-groups trial	Neonate	20	Non-nutritive sucking-related	–	Supports efficacy	14
Greenberg (20)	2002	Between-groups trial	Neonate	42	Non-nutritive sucking-related	–	Does not support efficacy	11
Yilmaz (42)	2010	Between-groups trial	Neonate	60	Non-nutritive sucking-related	Does not support efficacy	Supports efficacy	17
Liu (43)	2010	Between-groups trial	Neonate	70	Non-nutritive sucking-related	Supports efficacy	Supports efficacy	18
Curtis (44)	2007	Between-groups trial	Older infant	41	Non-nutritive sucking-related	–	Supports efficacy	21
Axelin (45)	2009	Crossover trial	Preterm	20	Swaddling or tucking	Supports efficacy	–	21
Comaru (46)	2009	Crossover trial	Preterm	47	Swaddling or tucking	Supports efficacy	–	21
Hill (47)	2005	Crossover trial	Preterm	12	Swaddling or tucking	Supports efficacy	–	21
Ward-Larson (48)	2004	Crossover trial	Preterm	40	Swaddling or tucking	Supports efficacy	–	17
Corff (26)	1995	Crossover trial	Preterm	30	Swaddling or tucking	–	Supports efficacy	14
Fearon (49)	1997	Crossover trial	Preterm	15	Swaddling or tucking	–	Supports efficacy	20
Axelin (50)	2006	Crossover trial	Preterm	20	Swaddling or tucking	Supports efficacy	Does not support efficacy	16
Morrow (51)	2010	Between-groups trial	Neonate	42	Swaddling or tucking	Supports efficacy	–	18
Herrington (52)	2007	Crossover trial	Preterm	11	Touch or massage	–	Does not support efficacy (touch)	20
Jain (53)	2006	Crossover trial	Preterm	23	Touch or massage	–	Supports efficacy (massage)	19
Kozub (54)	2001	Crossover trial	Older Infant	20	Touch or massage	Does not support efficacy	–	22
Sizun (55)	2002	Crossover trial	Preterm	19	Environmental modification	Supports efficacy	–	14
Catelin (56)	2005	Crossover trial	Preterm	45	Environmental modification	Supports efficacy	Supports efficacy	16
Johnston (57)	1997	Between-groups trial	Preterm	44	Simulated rocking	Does not support efficacy	–	16
Johnston (58)	2007	Crossover trial	Preterm	19	Maternal voice	Does not support efficacy	–	17
Carbajal (59)	2003	Between-groups trial	Neonate	90	Rocking and/or holding	Does not support efficacy	–	20
Gormally (60)	2001	Between-groups trial	Neonate	41	Rocking and/or holding	Supports efficacy	Supports efficacy	14
Ipp (61)	2004	Between-groups trial	Older Infant	106	Rocking and/or holding	Does not support efficacy	–	19
Cohen (21)	2002	Between-groups trial	Older Infant	90	Video distraction	Supports efficacy	–	10
Cohen (62)	2006	Between-groups trial	Older Infant	126	Video distraction	–	Supports efficacy	17
Bustos (63)	2008	Between-groups trial	Older Infant	50	Structured parent involvement	Does not support efficacy	–	18
Stevens (64)	1999	Crossover trial	Preterm	122	Non-nutritive sucking-related	Supports efficacy	–	17
Whipple (22)	2004	Between-groups trial	Preterm	60	Swaddling or tucking	Does not support efficacy	Supports efficacy	8
					Non-nutritive sucking-related (pacifier & lullaby)	–		
Elserafy (65)	2009	Crossover trial	Preterm	36	Non-nutritive sucking-related- pacifier	Does not support efficacy	Does not support efficacy	18
					Swallowing water	Does not support efficacy	Does not support efficacy	
					Non-nutritive sucking-related- pacifier with water	Does not support efficacy	Does not support efficacy	
Carbajal (66)	1999	Between-groups trial	Neonate	75	Swallowing water	Does not support efficacy	–	22
Belliemi (67)	2002	Between-groups trial	Neonate	60	Non-nutritive sucking-related	Supports efficacy	–	20
					Non-nutritive sucking-related	Supports efficacy	–	
Campos (23)	1994	Between-groups trial	Neonate	60	Touch or massage	Does not support efficacy	–	13
					Non-nutritive sucking-related	–	Supports efficacy	
					Rocking and/or holding	–	Supports efficacy	

TABLE 1 – CONTINUED

First author (reference)	Year	Between/crossover	Age	Sample size	Intervention	Reactivity findings	Regulation findings	Risk of bias score
Im (68)	2008	Between-groups trial	Neonate	99	Non-nutritive sucking-related Touch or massage	– –	Does not support efficacy Does not support efficacy	13
Allen (24)	1996	Between-groups trial	Neonate Older Infant	34 30	Swallowing water	– –	Supports efficacy Does not support efficacy	7
Cramer-Berness (69)	2005	Between-groups trial	Older Infant	123	Toy distraction Structured parent involvement	Does not support efficacy Supports efficacy	– –	18
Cramer-Berness (70)	2005b	Between-groups trial	Older Infant	117	Toy distraction Structured parent involvement	Does not support efficacy Does not support efficacy	– –	19
Bauchner (71)	1996	Between-groups trial	Older Infant	435	Parent presence Structured parent involvement	– –	Does not support efficacy Does not support efficacy	17
Hillgrove Stuart (72)	2008	Between-groups trial	Older Infant	99	Toy distraction - RA Toy distraction - Parent	Does not support efficacy Does not support efficacy	Does not support efficacy Does not support efficacy	20

*Dash indicates no research performed for that treatment, age and pain response combination. RA Research assistant

Rocking and/or holding

An infant is held and/or gently moved up and down or side-to-side by a caregiver.

Neonates: In terms of pain reactivity, rocking/holding was not efficacious in reducing pain reactivity but substantial heterogeneity reduces our confidence. One study, not included due to lack of randomization (89), suggested a significant difference in pain reactivity between infants who were held and control infants. However, there was sufficient evidence to support the efficaciousness of rocking/holding interventions for immediate pain-related regulation.

Older infants: There was limited evidence suggesting rocking/holding is not an efficacious intervention for pain-related distress reactivity in older infants.

Artificial rocking and water

An infant is placed in a bassinet-type machine that provides a swaying motion. Water is administered via a dropper.

Preterm infants: Limited evidence indicates that simulated rocking and water is not an efficacious intervention for reducing pain-related distress pain reactivity for preterm infants.

Touch/massage/therapeutic touch

An infant's body (i.e. touch, massage) or energy field (therapeutic touch) is 'stroked' or rubbed to provide some type of counter-stimulation to the nociceptive input.

Preterm infants: Current evidence does not support touch/massage-related interventions as efficacious in improving the immediate pain-related regulation but caution is warranted given the presence of substantial heterogeneity. One study not included in the analysis due to exclusion criteria (79) demonstrated that massage was more efficacious at reducing preterm infant's heart rate than light pressure or no massage therapy.

Neonates: Limited evidence suggests touch/massage related interventions are not efficacious to reduce pain reactivity or immediate pain-related regulation. One study that was not included in the analysis due to exclusion criteria (78) provides further support to these findings.

Older infants: Limited evidence suggests that therapeutic touch is not efficacious in reducing pain reactivity in older infants.

Environmental modification

Interventions involved modifying the environment in which an infant experiences painful procedures (ie, low noise and lighting, clustering procedures to avoid over handling, soothing smells).

Preterm infants: While the pooled result from two studies suggest that environmental modification was not efficacious for pain reactivity, this must be interpreted with caution due to substantial heterogeneity. However, there is limited evidence to suggest that environmental modification is efficacious for immediate pain-related regulation.

Toy distraction

Toy distraction is defined as the use of a toy to divert attention from the painful stimulus.

Older infants: Sufficient evidence suggests that toy distraction is not efficacious for reducing pain-related distress reactivity in older infants. Limited evidence suggests that it is also not efficacious for improving immediate pain-related regulation.

Video distraction

An audio-visual screen displaying two-dimensional moving images with coordinated audio is used to divert the infants attention from the painful stimulus

Older infants: Limited evidence suggests that video distraction is efficacious in reducing pain-related reactivity. Limited evidence also supports efficacy for improving immediate pain-related regulation.

Structured parental involvement

Parents are instructed about strategies that are accepted as pain-reducing but are not given any materials to aid them (eg, rocking, holding, shushing, talking, rubbing, tickling, and distracting attention without toy or video).

Older infants: Structured parent involvement was not found to be efficacious for pain reactivity. However, caution should be applied to this finding as post-hoc heterogeneity analyses contradicted this finding when one outlying study was removed. In addition, one excluded study also suggested that structured parental involvement significantly improved time to regulate post-immunization (90).

Simulated maternal voice

An infant is exposed to a reproduction of the mother's voice to help simulate the fetal environment.

Preterm infants: Results from one study indicated that mother's voice was not more efficacious than a no-treatment control for reducing pain-related distress reactivity for preterm infants.

Parent presence

The parent is present during a painful procedure but not interacting extensively with the child in a manner thought to be pain reducing.

Older infants: Limited evidence indicates that parent presence is not efficacious for improving immediate pain-related regulation.

CONCLUSIONS

Implications for practice

For preterm infants, there was sufficient evidence to recommend kangaroo care, sucking-related interventions, and swaddling/facilitated tucking interventions for both pain reactivity and immediate pain-related regulation. For neonates, there was sufficient evidence to

TABLE 2
Studies included for further contextual information

First author (reference)	Year	Age	Intervention	Pain reactivity findings	Pain regulation findings	Reason for exclusion from quantitative analyses
Cong (73)	2009	Preterm	Facilitated tucking vs non-nutritive sucking	Supports efficacy	–	No behavioural pain measure reported
Johnston (74)	2008	Preterm	Kangaroo care	Does not support efficacy	Supports efficacy	Control group was active
Johnston (75)	2009	Preterm	Kangaroo care	No difference between kangaroo care and enhanced kangaroo care	No difference between kangaroo care and enhanced kangaroo care	Control group was active
Ludington-Hoe (76)	2005	Preterm	Kangaroo care	Supports efficacy	Supports efficacy	Control group was active
Huang (77)	2004	Preterm	Kangaroo care	No difference between swaddling and containment	–	Control group was active
Cignacco (78)	2008	Preterm	Kangaroo care	No difference between multisensorial stimulation and facilitated tucking	No difference between multisensorial stimulation and facilitated tucking	Control group was active
Diego (79)	2009	Preterm	Kangaroo care	–	Supports efficacy	Control group was active
Goubet (80)	2003	Preterm	Smell (familiar vs unfamiliar)	No difference between familiar and unfamiliar odour	Familiar odour more efficacious than unfamiliar odour	Control group was active
Grunau (81)	2004	Preterm	Multisensorial stimulation vs facilitated tucking	No difference between prone and supine positioning	–	No control group
Vivancos (82)	2010	Neonate	Non-nutritive sucking	Does not support efficacy	Does not support efficacy	Not an RCT
Okan (83)	2010	Neonate	Non-nutritive sucking	Does not support efficacy	Supports efficacy	No means or SDs reported; could not contact author
Aguirre (84)	2008	Neonate	Non-nutritive sucking vs non-nutritive sucking & swaddling	Non-nutritive sucking more efficacious than facilitated tucking	–	Control group was active
Bueno (85)	2010	Neonate	Pacifier vs swaddling	No difference between non-nutritive sucking and non-nutritive sucking with swaddling	No difference between non-nutritive sucking and non-nutritive sucking with swaddling	Control group was active
Campos (86)	1989	Neonate	Positioning (prone vs supine)	No difference between pacifier and swaddling	Pacifier more efficacious than swaddling	Control group was active
Goubet (87)	2007	Neonate	Rocking and/or holding	–	Familiar odour more efficacious than unfamiliar odour	Control group was active
Rattaz (88)	2005	Neonate	Smell (familiar vs unfamiliar)	No difference between familiar and unfamiliar odour	Familiar odour more efficacious than unfamiliar odour	No control group
Weissman (89)	2009	Neonate	Smell (familiar vs unfamiliar)	Supports efficacy	–	Not an RCT
Felt (90)	2000	Older Infant	Structured parental intervention	–	Supports Efficacy	Not an RCT
Morelius (91)	2009	Older Infant	Swaddling or tucking	–	Does Not Support Efficacy	Not an RCT
Ipp (92)	2009	Older Infant	Swallowing water Vaccination order	Supports injecting DPTAP-Hib vaccine before PCV	–	Does Not Support Efficacy No control group

*Dash indicates no research done for that treatment, age and pain response combination. DPTAP-Hib Diphtheria and tetanus toxoids and acellular pertussis and Haemophilus influenzae type b vaccine; PCV Pneumococcal conjugated vaccine; RCT Randomized controlled trial

recommend sucking-related interventions as an efficacious treatment for pain reactivity and immediate pain-related regulation. Rocking/holding was also found to be efficacious for neonatal immediate pain-related regulation. For older infants, there were no treatments reviewed that demonstrated sufficient evidence. Overall, due to heterogeneity, some analyses that found a lack of treatment effect need to be interpreted with caution. Finally, while more rigorous research is needed to confirm these findings, environmental modification (preterms), sucking (neonates) and video distraction (older infant/child) have limited evidence supporting efficacy.

Implications for research

Significant gaps in the existing treatment literature on non-pharmacological management of acute pain in infancy have been discerned. Based on established patterns of efficacy in other age groups/pain response types, it would seem especially productive to the field of infant pain management to investigate:

- Kangaroo care for older infants' pain reactivity and immediate pain-related regulation (eg, for the two-month immunization)
- Sucking-related interventions for older infants'/young children's pain reactivity
- Swaddling or tucking-related interventions for older infants' pain reactivity and immediate pain-related regulation (eg, two-month immunization)
- Rocking/holding for older infants' immediate pain-related regulation

In addition, preliminary work from other studies (excluded from our overall quantitative analyses for methodological reasons) suggests that more research is needed to explore: exposing an infant to a familiar odor (80,87,88), feeding an infant formula (89) and administering the least painful immunization first (92) as potential non-pharmacological interventions for acute pain.

TABLE 3
Summary of meta-analyses

Treatment	Age group	Pain type	Total, n	Effect size (95% CI)	Heterogeneity analysis (95% CI)	Risk of bias analysis (95% CI)
Kangaroo care	Preterm	Reactivity	177	-1.12 (-2.04 to -0.21) I ² = 89%	-0.38 (-0.65 to -0.12) I ² = 0%	-
Kangaroo care	Preterm	Immediate regulation	163	-0.77 (-1.50 to -0.03) I ² = 82%	-0.45 (-0.69 to -0.20) I ² = 0%	-
Kangaroo care	Neonate	Reactivity	420	-0.89 (-2.89 to 1.10) I ² = 98%	-	-
Kangaroo care	Neonate	Immediate regulation	343	-0.66 (-1.73 to 0.42) I ² = 82%	-	-
Swaddling/tucking	Preterm	Reactivity	261	-0.97 (-1.63 to -0.31) I ² = 88%	-0.90 (-1.22 to -0.59) I ² = 0%	-
Swaddling/tucking	Preterm	Immediate regulation	65	-0.75 (-1.14 to -0.36) I ² = 0%	-	-0.61 (-1.12 to -0.11) I ² = 0%
Swaddling/tucking	Neonate	Reactivity	42	-1.26 (-1.92 to -0.60)	-	-
Non-nutritive sucking	Preterm	Reactivity	305	-0.42 (-0.68 to -0.15) I ² = 48%	-0.32 (-0.05 to -0.15) I ² = 0%	-
Non-nutritive sucking	Preterm	Immediate regulation	226	-0.38 (-0.59 to -0.17) I ² = 0%	-	-0.36 (-0.59 to -0.13) I ² = 0%
Non-nutritive sucking	Neonate	Reactivity	220	-1.45 (-2.34 to -0.57) I ² = 88%	-1.88 (-2.25 to -1.50) I ² = 0%	-
Non-nutritive sucking	Neonate	Immediate regulation	325	-0.90 (-1.54 to -0.25) I ² = 84%	-	-0.51 (-0.91 to -0.29) I ² = 11%
Non-nutritive sucking	Older infants	Immediate regulation	41	-0.89 (-1.53 to -0.25)	-	-
Swallowing water	Preterm	Reactivity	36	-0.24 (-0.71 to 0.23)	-	-
Swallowing water	Preterm	Immediate regulation	36	-0.23 (-0.70 to 0.24)	-	-
Swallowing water	Neonate	Reactivity	50	0.10 (-0.45 to 0.66)	-	-
Swallowing water	Neonate	Immediate regulation	34	-0.53 (-1.21 to 0.16)	-	-
Swallowing water	Older infants	Immediate regulation	30	0.00 (-0.72 to 0.72)	-	-
Rocking/holding	Neonate	Reactivity	131	-0.33 (-1.05 to 0.39) I ² = 73%	-	-
Rocking/holding	Neonate	Immediate regulation	81	-0.75 (-1.20 to -0.30) I ² = 0%	-	-
Rocking/holding	Older infants	Reactivity	106	0.23 (-0.15 to 0.62)	-	-
Simulated rocking + water	Preterm	Reactivity	44	0.00 (-0.59 to 0.59)	-	-
Touch or massage	Preterm	Immediate regulation	34	-0.71 (-2.33 to 0.90) I ² = 86%	-	-
Touch or massage	Neonate	Reactivity	40	-0.30 (-0.92 to 0.32)	-	-
Touch or massage	Neonate	Immediate regulation	66	-0.24 (-0.73 to 0.24)	-	-
Touch or massage	Older infants	Reactivity	20	-0.21 (-0.84 to 0.41)	-	-
Environment modification	Preterm	Reactivity	64	-6.44 (-17.13 to 4.26) I ² = 97%	-	-
Environment modification	Preterm	Immediate regulation	45	-4.01 (-5.26 to -2.77)	-	-
Toy distraction	Older infants	Reactivity	259	-0.10 (-0.35 to 0.14) I ² = 0%	-	-
Toy distraction	Older infants	Immediate regulation	133	-0.08 (-0.50 to 0.33) I ² = 0%	-	-
Video distraction	Older infants	Reactivity	90	-0.70 (-1.13 to -0.27)	-	-
Video distraction	Older infants	Immediate regulation	126	-0.84 (-1.20 to -0.47)	-	-
Structured parent involvement	Older infants	Reactivity	209	-0.26 (-0.70 to 0.17) I ² = 60%	-0.49 (-0.83 to -0.14) I ² = 0%	-
Structured parent involvement	Older infants	Immediate regulation	288	0.02 (-0.21 to 0.25)	-	-
Mother's voice	Preterm	Reactivity	19	-0.29 (-0.94 to 0.35)	-	-
Parent present	Older infants	Immediate regulation	278	0.00 (-0.24 to 0.23)	-	-

*Dash indicates no research performed for that treatment, age and pain response combination

TABLE 4
Summary conclusions

Treatment arm	Preterm infants		Neonates		Older infants	
	Reactivity	Immediate regulation	Reactivity	Immediate regulation	Reactivity	Immediate regulation
Kangaroo care	1	1	3	3	–	–
Non-nutritive sucking-related	1	1	1	1	–	2
Swaddling/tucking-related	1	1	2	–	–	–
Touch or massage-related	–	3	3	3	3	–
Environment modification	3	2	–	–	–	–
Simulated rocking and water	3	–	–	–	–	–
Simulated mother's voice	3	–	–	–	–	–
Swallowing water	3	3	3	3	–	3
Rocking or holding	–	–	3	1	3	–
Toy distraction	–	–	–	–	4	3
Video distraction	–	–	–	–	2	2
Parent present	–	–	–	–	–	3
Structured parent involvement	–	–	–	–	3	3

1 Sufficient evidence supports efficacy for reducing pain-related behaviours (support of two or more trials); 2 Limited evidence suggests efficacy for reducing pain-related behaviours (eg, support of one trial or heterogeneity among trials); 3 Limited evidence suggests inefficacy for reducing pain-related behaviours (eg, support of one trial or heterogeneity among trials); 4 Sufficient evidence supports inefficacy for reducing pain-related behaviours (support of one or more trials). Dash indicates no research performed for that treatment, age and pain response combination

It is also important to note that certain treatments were grouped together based on similar mechanisms of action despite not being the same treatment (eg, swaddling and tucking, non-nutritive sucking related strategies), which was supported by our heterogeneity analyses. However, with more research, future revisions may be able to report SMDs and CIs separately for treatments encompassed within these groups.

Moreover, given the frequency of immunization during the first years of life, it was disheartening that there were no efficacious nonpharmacological treatments for the older infant/young child. Although there is a substantial evidence base for pharmacological strategies such as sucrose and topical anaesthetics (93), from an economic and pragmatic perspective, it would behoove researchers to spend more resources in investigating efficacious nonpharmacological pain management for older infants.

The lack of developmentally-informed work on parent-mediated interventions was also a cause for a concern. Over the first years of life, it has been argued (94) that the caregiver is the most important context for the infant in pain. Currently, studies that have attempted to formally structure parent behaviour have been limited and, thus, shown to be ineffective. More work on improved parent interventions, especially ones that capitalize on an infant's primary need for proximity to the parent during periods of distress (95), is needed. Teaching a parent how to soothe more efficaciously their infant or young child in acute pain is a simple, low-cost intervention that is not being used to its potential in today's acute pain context.

In conclusion, while a number of non pharmacological treatments have a sufficient body of evidence supporting their use with preterm infants and to a lesser extent, healthy neonates, more research is needed to create a sound repertoire of empirically-supported nonpharmacological treatments for procedural pain in older infants/young children.

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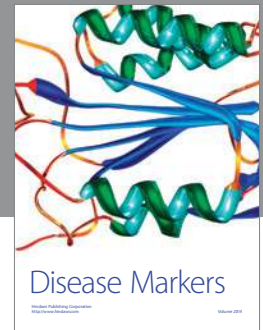
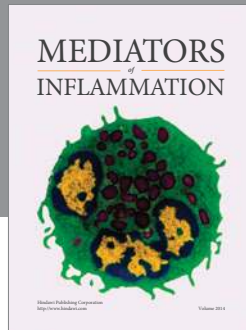
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