ClinicalEvidence

Colic in infants

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ABSTRACT

INTRODUCTION: Colic in infants causes one in six families (17%) with children to consult a health professional. One systematic review of 15 community-based studies found a wide variation in prevalence, which depended on study design and method of recording. METHODS AND OUTCOMES: We conducted a systematic review and aimed to answer the following clinical question: What are the effects of treatments for colic in infants? We searched: Medline, Embase, The Cochrane Library, and other important databases up to September 2009 (Clinical Evidence reviews are updated periodically, please check our website for the most up-to-date version of this review). We included harms alerts from relevant organisations such as the US Food and Drug Administration (FDA) and the UK Medicines and Healthcare products Regulatory Agency (MHRA). RESULTS: We found 27 systematic reviews, RCTs, or observational studies that met our inclusion criteria. We performed a GRADE evaluation of the quality of evidence for interventions. CONCLUSIONS: In this systematic review we present information relating to the effectiveness and safety of the following interventions: advice to increase carrying, advice to reduce stimulation, casein hydrolysate milk, cranial osteopathy, crib vibrator device, focused counselling, gripe water, infant massage, low-lactose milk, simethicone, soya-based infant feeds, spinal manipulation, and whey hydrolysate milk.

QUESTIONS

INTERVENTIONS

Key points

- Colic in infants is defined as excessive crying in an otherwise healthy and thriving baby. The crying typically starts in the first few weeks of life and ends by age 4 to 5 months.

  It causes one in six families with children to consult a health professional.

- We found insufficient RCT evidence to judge whether replacing cows' milk or breast milk with casein hydrolysate milk, low-lactose milk, soya-based infant feeds, or whey hydrolysate formula is effective in reducing crying time.

  Breastfeeding mothers should generally be encouraged to continue breastfeeding.

  Soya milk is associated with possible long-term harmful effects on reproductive health.

- The RCTs examining the effects of reducing stimulation (by not patting, lifting, or jiggling the baby, or by reducing auditory stimulation), crib vibration, infant massage, focused counselling, or spinal manipulation were too small for us to draw reliable conclusions.

- We found no good RCT evidence assessing cranial osteopathy or gripe water for treating colic in infants.

  Despite a lack of evidence from well-conducted trials, gripe water is commonly used by parents for their colicky infants.

- Increasing the time spent carrying the infant (by at least 3 hours) does not seem to reduce the time spent crying, and may increase anxiety and stress in the parents.

- RCTs identified assessing the effects of simethicone are of insufficient quality to draw reliable conclusions on the effectiveness of simethicone in treating colic.

DEFINITION

Colic in infants is defined as excessive crying in an otherwise healthy and thriving baby. The crying typically starts in the first few weeks of life and ends by age 4 to 5 months. Excessive crying is defined as crying that lasts at least 3 hours a day, for 3 days a week, for at least 3 weeks. [1] Be-

cause of the natural course of infant colic, it can be difficult to interpret trials that do not include a placebo or have no treatment group for comparison.

INCIDENCE/ PREVALENCE

Infant colic causes one in six families (17%) with children to consult a health professional. One systematic review of 15 community-based studies found a wide variation in prevalence, which depended on study design and method of recording. [2] Two prospective studies identified by the review yielded prevalence rates of 5% and 19%. [2] One prospective study (89 breast- and formula-fed infants) found that, at 2 weeks of age, the prevalence of crying over 3 hours a day was 43% among formula-fed infants and 16% among breastfed infants. The prevalence at 6 weeks was 12% among formula-fed infants and 31% among breastfed infants. [3] A national survey of 3345 infants found that maternal smoking was potentially associated with colic (OR 1.34, 95% CI 0.88 to 2.04). [4]

AETIOLOGY/ RISK FACTORS

The cause is unclear and, despite its name, infant colic may not have an abdominal cause. It may reflect part of the normal distribution of infantile crying. Other possible explanations are painful intestinal contractions, lactose intolerance, wind, or parental misinterpretation of normal crying. [1]

PROGNOSIS

Infant colic improves with time. One self-reporting parent questionnaire on crying patterns found that 29% of infants aged 1 to 3 months cried for more than 3 hours a day, but that by 4 to 6 months of age the prevalence had fallen to 7% to 11%. [5]

AIMS OF INTERVENTION

To reduce infant crying and distress, and the anxiety of the family, with minimal adverse effects of treatment.

OUTCOMES

Presence and duration of colic, as determined by frequency and duration of crying, measured on dichotomous, ordinal, or continuous scales or by parents' perceptions of severity and duration of colic recorded in a diary.

METHODS

Clinical Evidence search and appraisal September 2009. The following databases were used to identify studies for this systematic review: Medline 1966 to September 2009, Embase 1980 to September 2009, and The Cochrane Library (all databases) Issue 3, 2009. Additional searches were carried out using these websites: NHS Centre for Reviews and Dissemination (CRD) (all databases), Turning Research into Practice (TRIP), and National Institute for Health and Clinical Excellence (NICE). Abstracts of the studies retrieved from the initial search were assessed by an information specialist. Selected studies were then sent to the author for additional assessment, using predetermined criteria to identify relevant studies. Study design criteria for inclusion in this review were: published systematic reviews and RCTs in any language, and containing at least 20 individuals of whom more than 80% were followed up. There was no minimum length of follow-up required to include studies. We excluded all studies described as "open", "open-label", or not blinded unless blinding was impossible. We searched for all comparisons for included interventions, including comparisons against placebo or between included interventions, and reported any RCTs of sufficient quality that we found. We excluded RCTs in infants with normal crying patterns, infants older than 6 months, in interventions lasting less than 3 days, trials with no control groups, or trials with low scores on the Jadad scale. [6] In addition, we use a regular surveillance protocol to capture harms alerts from organisations such as the US Food and Drug Administration (FDA) and the UK Medicines and Healthcare products Regulatory Agency (MHRA), which are added to the reviews as required. To aid readability of the numerical data in our reviews, we round many percentages to the nearest whole number. Readers should be aware of this when relating percentages to summary statistics such as relative risks (RRs) and odds ratios (ORs). We have performed a GRADE evaluation of the quality of evidence for interventions included in this review (see table, p 11). The categorisation of the quality of the evidence (high, moderate, low, or very low) reflects the quality of evidence available for our chosen outcomes in our defined populations of interest. These categorisations are not necessarily a reflection of the overall methodological quality of any individual study, because the *Clinical Evidence* population and outcome of choice may represent only a small subset of the total outcomes reported, and population included, in any individual trial. For further details of how we perform the GRADE evaluation and the scoring system we use, please see our website (www.clinicalevidence.com).

QUESTION What are the effects of treatments for colic in infants?

OPTION ADVICE TO INCREASE CARRYING

Duration of crying

Compared with general advice Advice to increase carrying the baby may be no more effective than general advice at reducing the duration of crying (low-quality evidence).

For GRADE evaluation of interventions for colic in infants, see table, p 11 .

Benefits:

Advice to increase carrying versus general advice:
We found two systematic reviews (search dates 1996 [1] and 1999), [7] which identified the same single RCT. [8] The RCT (66 infants) included in the reviews compared advising mothers of babies with colic to increase supplemental carrying of their infant (defined as carrying in additional to while feeding or in response to crying) for at least 3 hours a day versus general advice (to carry, check baby's nappy, feed, offer pacifier, place baby near mother, or use background stimulation such as music). [8] Women in the "advice to increase carrying" group increased supplemental carrying by 4.5 hours daily compared with 2.6 hours daily in the general-advice group, with overall mean carrying time of 6.1 hours daily in the "advice to increase carrying" group compared with 3.9 hours daily in the general-advice group. The RCT found no significant difference in daily crying time at any time point up to 6 weeks (mean difference in crying time at 6 weeks: +3 minutes, 95% CI −37 minutes to +32 minutes; P value not reported; reported as not significant). [8]

Harms:

Advice to increase carrying versus general advice:
The RCT gave no information on harms. [8]

Comment:

Clinical guide:
Although not harmful in itself, carrying babies for more than 4 hours a day may increase anxiety and stress in the parents.

OPTION ADVICE TO REDUCE STIMULATION

Duration of crying
Compared with no advice Advising mothers to reduce stimulation of the baby may be more effective than no advice at reducing the duration of crying after 7 days in babies under 12 weeks (low-quality evidence).

For GRADE evaluation of interventions for colic in infants, see table, p 11 .

Benefits:

Advice to reduce stimulation versus no advice:
We found two systematic reviews (search dates 1996 [1] and 1999), [7] both of which identified the same single RCT. [9] The RCT (42 infants, median age 10 weeks) included in the reviews compared advising mothers to reduce stimulation (by not patting, lifting, or jiggling the baby, or reducing auditory stimulation) versus empathetic interview giving no advice. [9] For infants under 12 weeks, advice to reduce stimulation significantly improved a change-rating scale for proportionately more infants compared with no advice (after 7 days: 14/15 [93%] improved with advice *v* 6/12 [50%] with control; ARI 43%, 95% CI 8% to 49%; RR 1.9, 95% CI 1.2 to 2.0; NNT 2, 95% CI 2 to 13). [9] Improvement in the change-rating scale was defined as a score of +2 or better on a scale from –5 to +5 that indicated a perceived change in crying since the start of the trial. It is unclear whether this scale has been validated (see comment below).

Harms:

Advice to reduce stimulation versus no advice:
The RCT gave no information on adverse effects. [9]

Comment:

Mothers given advice to reduce stimulation were also given permission to leave their infants alone to cry if they felt that they could no longer tolerate the crying. It is unclear whether the improved change score represents a true change in the hours that the baby cried, or altered maternal perception.

OPTION CASEIN HYDROLYSATE MILK

Duration of crying
Compared with focused counselling Eliminating cows' milk or soya milk may be less effective at reducing the duration of crying (low-quality evidence).

Casein hydrolysate milk or hypoallergenic diet for breastfeeding mother compared with cows' milk or control diet for mother Giving casein hydrolysate milk to bottle-fed babies, or a hypoallergenic diet for breastfeeding mothers, may be more effective at reducing the duration of crying compared with giving bottle-fed babies cows' milk-based formulae or a control diet for breastfeeding mothers (very low-quality evidence).

Note
We found no clinically important results from RCTs about the effects of casein hydrolysate milk compared with cows' milk.

For GRADE evaluation of interventions for colic in infants, see table, p 11 .

Benefits: We found two systematic reviews (search dates 1996 [1] and 1999), [7] which identified the same two RCTs. [10] [11]

Casein hydrolysate milk versus cows' milk:
The reviews included one RCT, [10] which was too small to meet our inclusion criteria and has been excluded from this *Clinical Evidence* review.

Casein hydrolysate milk versus counselling:
See benefits of focused counselling, p 5 .

Casein hydrolysate milk or hypoallergenic diet for breastfeeding mother versus cows' milk or control diet for breastfeeding mother:
The reviews included one RCT (122 infants, 115 [94%] followed up) comparing active diet (infants bottle fed casein hydrolysate milk or breast fed by mothers on a hypoallergenic diet) versus control diet (infants bottle fed cows' milk formula or breast fed with mothers on a control diet). In breastfed infants, maternal diet was free of artificial colourings, preservatives, and additives, with a low intake of common allergens (e.g., milk, egg, wheat, and nuts) in the hypoallergenic group compared with a normal intake in the control group. [11] A total of 38 (33%) infants were bottle fed and 77 (67%) were breast fed, but the RCT did not specify what proportions of the 54 infants receiving the active diet were bottle or breast fed. The RCT pooled the results of breast- and bottle-fed babies and found that the active diet significantly reduced infant distress compared with control diet (distress reduction from baseline [measured by parents on a validated chart]: 39% with active diet *v* 16% with control diet; P = 0.012). [11] However, the number of bottle-fed infants was too small to establish or exclude important effects in infants bottle fed casein hydrolysate milk compared with cows' milk.

Harms: **Casein hydrolysate milk versus cows' milk:**
The RCT gave no information about harms. [10]

Casein hydrolysate milk versus counselling:
See harms of focused counselling, p 5 .

Casein hydrolysate milk or hypoallergenic diet for breastfeeding mother versus cows' milk or control diet for breastfeeding mother:
The RCT gave no information about harms. [11]

Comment: The large number of withdrawals in one RCT, and the pooling of the results of bottle- and breastfed infants in another, make it difficult to draw definite conclusions about the effects of replacing cows' milk with casein hydrolysate milk.

Clinical guide:
There is insufficient evidence of a difference in effect of different formulas of bottle milk on colic in infants. If a baby is thriving on standard formula milk, the consensus is that there is no need to change milks. An exception to this general rule is that infants with colic in atopic families might benefit from a change to a hypoallergenic formula. Breastfeeding mothers should generally be advised to continue breastfeeding.

OPTION CRANIAL OSTEOPATHY

We found no direct information from RCTs about the effects of cranial osteopathy in infants with colic.

For GRADE evaluation of interventions for colic in infants, see table, p 11 .

Benefits: We found no systematic review and no RCTs on the effects of cranial osteopathy in infants with colic.

Harms: We found no RCTs.

Comment: **Clinical guide:**
We found no evidence of benefit from cranial osteopathy in infants with colic.

OPTION CRIB VIBRATOR DEVICE/CAR RIDE SIMULATION

Duration of crying
Crib vibrator plus reassurance compared with reassurance alone Use of a crib vibrator device may be no more effective at reducing the duration of crying after 2 weeks (very low-quality evidence).

Crib vibrator plus reassurance compared with counselling plus reassurance We don't know how a crib vibrator plus reassurance and focused counselling on specific management techniques (responding to crying with gentle soothing motion, avoiding over-stimulation, using a pacifier, and prophylactic carrying) plus reassurance compare in reducing the duration of crying at 2 weeks (very low-quality evidence).

Compared with infant massage We don't know how a crib vibrator device and infant massage compare at reducing duration of crying (low-quality evidence).

For GRADE evaluation of interventions for colic in infants,
see table , p 11

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Benefits:

Crib vibrator plus reassurance versus counselling plus reassurance versus reassurance alone:
See benefits of focused counselling, p 5 .

Crib vibrator versus infant massage:
See benefits of infant massage, p 6 .

Harms:

Crib vibrator plus reassurance versus counselling plus reassurance versus reassurance alone:
See harms of focused counselling, p 5 .

Crib vibrator versus infant massage:
See harms of infant massage, p 6 .

Comment: None.

OPTION FOCUSED COUNSELLING OF MOTHERS ABOUT BEHAVIOURAL MODIFICATION TECHNIQUES

Duration of crying

Counselling plus reassurance compared with reassurance alone We don't know whether focused counselling on specific management techniques (responding to crying with gentle soothing motion, avoiding over-stimulation, using a pacifier, and prophylactic carrying) plus reassurance is more effective than reassurance alone at reducing the duration of crying after 2 weeks (very low-quality evidence).

Counselling plus reassurance compared with crib vibrator plus reassurance We don't know how focused counselling on specific management techniques (responding to crying with gentle soothing motion, avoiding over-stimulation, using a pacifier, and prophylactic carrying) plus reassurance and a crib vibrator plus reassurance compare in reducing the duration of crying at 2 weeks (very low-quality evidence).

Compared with casein hydrolysate milk Focused counselling may be more effective than replacing cows' milk or soya milk with casein hydrolysate at reducing duration of crying (low-quality evidence).

For GRADE evaluation of interventions for colic in infants, see table, p 11 .

Benefits:

Counselling plus reassurance versus crib vibrator device plus reassurance versus reassurance alone:
We found two systematic reviews (search dates 1996 [1] and 1999, [7] which identified the same single RCT). [12] The RCT (38 infants) assessed maternal anxiety and the hours of crying each day by questionnaire. [12] The RCT compared three interventions: counselling mothers about specific management techniques (responding to crying with gentle soothing motion, avoiding over-stimulation, using a pacifier, and prophylactic carrying) plus giving the mother reassurance and support; crib vibrator device plus giving the mother reassurance and support; and giving the mother reassurance and support alone. It found no significant difference among groups for hours of infant crying over 2 weeks (mean hours of crying: results presented graphically; reported as not significant; mean maternal anxiety score: results presented graphically; reported as not significant). [12]

Counselling versus elimination of cows' milk or soya milk protein by substitution with casein hydrolysate:
We found two systematic reviews (search dates 1996 [1] and 1999), [7] which identified the same single RCT. [13] The RCT (20 infants) found that counselling parents to respond to their babies' cries by feeding, holding, offering a pacifier, stimulating, or putting the baby down to sleep decreased the duration of crying compared with substitution of soya or cows' milk with casein hydrolysate

formula, but this difference was not significant (mean decrease in crying, recorded by parent diary; 2.1 hours/day with counselling *v* 1.2 hours/day with dietary change; P = 0.05). [13] The RCT may have been too small to detect a significant difference in effect.

Harms:

Counselling plus reassurance versus crib vibrator device plus reassurance versus reassurance alone:
The RCT gave no information about harms. [12]

Counselling versus elimination of cows' milk or soya milk protein by substitution with casein hydrolysate:
The RCT gave no information about harms. [13]

Comment:

Clinical guide:
Despite a lack of evidence of any effect on the amount of time the baby cried, most clinicians would consider it good practice to offer reassurance and support to mothers of colicky infants.

OPTION GRIPE WATER

We found no direct information from RCTs about the effects of gripe water in infants with colic.

For GRADE evaluation of interventions for colic in infants, see table, p 11 .

Benefits: We found no systematic review or RCTs on the effects of gripe water in infants with colic.

Harms: We found no RCTs.

Comment:

Clinical guide:
Despite the lack of evidence from well-conducted trials, gripe water is commonly used by parents for infants with colic.

OPTION INFANT MASSAGE

Duration of crying
Compared with crib vibrator device We don't know how infant massage and a crib vibrator device compare at reducing duration of crying (low-quality evidence).

For GRADE evaluation of interventions for colic in infants, see table, p 11 .

Benefits:

Infant massage versus usual care:
We found no systematic review or RCTs.

Infant massage versus crib vibrator device:
We found no systematic review. We found one RCT (58 infants, 47% with colic; see comment below) comparing massage versus a crib vibrator device over a 4-week period. [14] Infant massage (performed 3 times/day) included gentle stroking of the skin over different parts of the head, body, and limbs, using olive oil and maintaining eye contact. The crib vibrator device was used for 25-minute periods at least three times daily. Colic symptom ratings were obtained from parental diaries of crying. The RCT found no significant difference between massage and crib vibrator device for colic-related crying or parental rating of symptoms (AR for less colicky crying: 64% with massage *v* 52% with crib vibrator device; P = 0.24). [14] Only 47% of infants in the RCT had colic, so the results may not apply specifically to infants with colic. [14] The RCT stated that "use of a crib vibrator device was considered a control intervention based on an earlier study [12] in which a similar device was as effective as parental education or reassurance and support and was chosen instead of nothing to improve parental compliance". It is unclear whether reduced crying in this RCT reflects the natural course of colic in infants or the specific effect of interventions. [14] The RCT may have lacked power to detect clinically important effects.

Harms:

Infant massage versus crib vibrator device:
The RCT gave no information about harms. [14]

Comment:

Clinical guide:
We found no evidence of benefit from infant massage. Although parents are possibly inclined to massage, it may actually unsettle and over-stimulate colicky infants.

OPTION LOW LACTOSE MILK

Duration of crying

Compared with untreated formula/breast milk We don't know whether low lactose milk is more effective than untreated formula/breast milk at reducing duration of crying (very low quality evidence).

For GRADE evaluation of interventions for colic in infants, see table, p 11 .

Benefits:

Bottle-fed pooled breast milk versus low-lactose breast milk versus cows' milk versus low-lactose cows' milk:
We found two systematic reviews (search dates 1996 [1] and 1999, [7] 2 RCTs) and two additional RCTs. [15] [16] The two RCTs [17] [18] included in the reviews and the first additional RCT [15] were too small to meet our inclusion criteria (see methods) and have been excluded from this *Clinical Evidence* review. The second additional RCT (crossover, 53 infants) found that low-lactose formula/breast milk reduced crying time after crossover at 25 days compared with untreated formula/breast milk, but the difference was not significant (median: 11.0 hours with lactase *v* 14.1 hours with no lactase; median difference in crying time 23%; P = 0.09). [16]

Harms:

The RCT gave no information about harms. [16]

Comment:

It is difficult to draw firm conclusions from this RCT. [16] The babies were not selected on the basis of confirmed lactose intolerance. The crossover design of the included RCT limits its validity and clinical utility; because colic in infants has a naturally variable course. [16]

Clinical guide:
We found no evidence of benefit with low-lactose milk in the treatment of colic in infants and, consequently, no reason to use this milk in daily practice.

OPTION SIMETHICONE (ACTIVATED DIMETICONE [DIMETHICONE])

Duration of crying
Compared with placebo We don't know whether simethicone is more effective than placebo at reducing the duration of colic (very low-quality evidence).

Compared with spinal manipulation Simethicone may be less effective at reducing duration of crying after 2 weeks (low-quality evidence).

For GRADE evaluation of interventions for colic in infants, see table, p 11 .

Benefits:

Simethicone versus placebo:
We found three systematic reviews comparing the effects of simethicone versus placebo on duration of crying or presence of colic in infants. [1] [7] [19] The two earlier reviews [1] [7] have been superseded by the most recent review [19] and are therefore not discussed further here.

The review (search date 2007) did not pool data, so the three included RCTs (136 infants) that met *Clinical Evidence* quality criteria for inclusion are reported separately. The review included three open-label RCTs that did not meet *Clinical Evidence* inclusion criteria for this review, and are therefore not discussed further. [19]

The first RCT identified by the review (double-blind, crossover, 83 infants aged 2–8 weeks) compared 0.3 mL of simethicone versus placebo (duration of treatment, average of 1 week) before feeds. [20] It found no significant difference in colic (using the standard colic definition), when rated by carers, between simethicone and placebo (28% improved with simethicone *v* 37% with placebo *v* 20% with simethicone plus placebo; effect size for simethicone *v* placebo –0.10, 95% CI –0.27 to +0.08). [20]

The second RCT identified by the review (double-blind, crossover trial, 27 infants aged 2–8 weeks) found no significant difference between simethicone and placebo (10 drops before meals, duration of treatment 24 hours) in improvement as rated by parental interview, 24-hour diary, or behavioural observation (effect size +0.06, 95% CI –0.17 to +0.28; see comment below). [21]

The third, poor-quality, RCT identified by the reviews (double-blind, crossover trial, 26 infants aged 1–12 weeks) reported no details on how cases of colic were defined. [22] It found that simethicone significantly reduced the number of crying attacks on days 4 to 7 of treatment compared with placebo (effect size 0.54, 95% CI 0.21 to 0.87). [22]

Simethicone versus spinal manipulation:
See benefits of spinal manipulation, p 8 .

Harms:

Simethicone versus placebo:
The first two RCTs gave no information about adverse effects. [20] [21] The third RCT reported that no infants treated with simethicone experienced adverse effects. [22]

Simethicone versus spinal manipulation:
See harms of spinal manipulation, p 8 .

Comment:

The crossover design of two of the RCTs limits their validity, as they did not report results before crossover, and colic in infants has a naturally variable course; therefore the effects of simethicone may have continued even after a washout period. [20] [21]

Clinical guide:
Although we found no good-quality trials to show benefit, simethicone is widely used for colic in infants in some countries. Further trials are not considered of clinical importance and are unlikely to be undertaken. According to the available evidence, there is no reason to use simethicone in the treatment of colic in infants.

OPTION SOYA-BASED INFANT FEEDS

We found no direct information from RCTs about the effects of soya-based infant feeds in infants with colic.

For GRADE evaluation of interventions for colic in infants, see table, p 11 .

Benefits:

Soya-based infant feeds versus cows' milk formula:
We found two systematic reviews (search dates 1996 [1] and 1999), [7] which between them identified two RCTs comparing soya-based infant feeds versus cows' milk formula. The first RCT [23] identified by the reviews was too small to meet our inclusion criteria (see methods) and has been excluded from this *Clinical Evidence* review. The second RCT identified by the reviews provided insufficient evidence, as it considered infants admitted to hospital for colic and used weak methods (Jadad scale 1 [6]). [24]

Harms:

Soya-based infant feeds versus cows' milk formula:
The RCTs gave no information about harms. [23] [24] The Chief Medical Officer for the UK reported that soya infant feeds should not be recommended as preferred treatment in healthy babies as they have a high phyto-oestrogen content and may affect long-term reproductive health. [25]

Comment:

Clinical guide:
We found no evidence of sufficient quality to determine the benefit of soya milk in the treatment of colic in infants. Soya milk should be avoided because of its possible long-term harmful effects on reproductive health. There is insufficient evidence for the effect of different formulas of bottle milk on colic in infants to warrant changing milks in a baby who is thriving on a standard formula milk. An exception to this general rule is that infants with colic in atopic families might benefit from a change to a hypoallergenic formula. Breastfeeding mothers should generally be encouraged to continue breastfeeding.

OPTION SPINAL MANIPULATION

Duration of crying
Compared with simethicone Spinal manipulation may be more effective at reducing duration of crying after 2 weeks (low-quality evidence).

Compared with holding Spinal palpation by a chiropractor seems no more effective than the baby being held by a nurse at reducing the duration of crying after 8 days (moderate-quality evidence).

For GRADE evaluation of interventions for colic in infants, see table, p 11 .

Benefits:

We found one systematic review (search date 2005) of reviews. [26] It identified one systematic review (search date not reported). [27] We also found one subsequent review (search date 2007). [19]

Spinal manipulation versus simethicone (activated dimeticone [dimethicone]):
The first [27] and second [19] reviews identified the same single RCT. [28] The RCT (41 infants) compared 2 weeks of spinal manipulation versus 2 weeks of daily treatment with simethicone. Parents were not blinded to treatment allocation, and they recorded length of crying in a colic diary. [28] The RCT found that spinal manipulation significantly reduced crying compared with simethicone (mean reduction in crying for days 4 to 7: 2.4 hours with spinal manipulation *v* 1.0 hours with simethicone; P = 0.04). [28]

Spinal manipulation versus holding:
The review (search date not reported) [27] identified one RCT. [29] The RCT (86 infants) compared spinal palpation by a chiropractor versus holding of the infant by a nurse (in each case 3 times over 8 days). [29] The parents, who were blind to the intervention, rated symptom severity on a 5-point scale and recorded crying in a diary. The RCT found no significant difference between spinal palpation and holding for crying reduction (mean reduction in crying by day 8: 3.1 hours for both groups; P = 0.98). [29]

Harms: The RCTs gave no information on adverse effects. [28] [29]

Comment: It is unclear whether reduced crying reflected the effects of interventions or spontaneous improvement.

OPTION WHEY HYDROLYSATE FORMULA

Duration of crying
Compared with cows' milk formula Whey hydrolysate milk may be more effective at reducing the duration of crying (low-quality evidence).

For GRADE evaluation of interventions for colic in infants, see table, p 11 .

Benefits: **Whey hydrolysate milk versus cows' milk formula:**
We found two systematic reviews (search dates 1996 [1] and 1999 [7]) and one subsequent RCT. [30] The systematic reviews found no RCTs of adequate quality. The subsequent, double-blind RCT (43 infants) found that whey hydrolysate milk formula significantly reduced the time that babies cried each day compared with standard cows' milk formula, measured by a validated parental diary (crying reduced by 63 minutes/day, 95% CI 1 minute/day to 127 minutes/day; P = 0.05). [30] Parents' blinding to the intervention was checked. When asked, six indicated that they were aware of allocation, but two of these falsely identified the formula. When these infants' results were removed from the analysis, the crying time with whey hydrolysate formula was still significantly reduced compared with standard cows' milk formula (crying reduced by 58 minutes/day; P = 0.03). Further statistical data were not provided for this result. [30]

Harms: **Whey hydrolysate milk versus cows' milk formula:**
No harms were identified in the subsequent RCT. [30]

Comment: This RCT has wide confidence intervals and blinding may have been unmasked in four parents. [30]

Clinical guide:
There is insufficient evidence for the effect of different formulas of bottle milk on colic in infants to warrant changing milks in a baby who is thriving on a standard formula milk. An exception to this general rule is that infants with colic in atopic families might benefit from a change to a hypoallergenic formula. Breastfeeding mothers should generally be encouraged to continue breastfeeding.

GLOSSARY

Cranial osteopathy Involves gentle manipulation of the tissues of the head by an osteopath.

Jadad scale This measures factors that have an impact on trial quality. Poor description of the factors, rated by low figures, is associated with greater estimates of effect. The scale includes three items: was the study described as randomised? (0–2); was the study described as double blind? (0–2); was there a description of withdrawals? (0–1). [5]

Casein hydrolysate milk is a hypoallergenic milk made of cows' milk and containing predominantly casein proteins.

Crib vibrator device/car ride simulators These attempt to sooth crying infants, and involve attaching a small motor underneath the crib to vibrate it, and a box to the side of the crib to produce white noise. are a type of crib vibrator device designed to simulate the sound and motion of a car travelling at 55 miles an hour.

Low-quality evidence Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Moderate-quality evidence Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Reassurance Informing the parent that infantile colic is a self-limiting condition resolving by 3–4 months of age, and is not caused by disease or any fault in parental care.

Simethicone (activated dimeticone [dimethicone]) This has defoaming properties, which can aid dispersion of wind in the gastrointestinal tract.

Soya-based infant feeds Contain proteins from soya beans; the feeds are used as lactose-free vegetable milks for those with lactose or cows' milk protein intolerance.

Very low-quality evidence Any estimate of effect is very uncertain.

Whey hydrolysate milk is a hypoallergenic milk made from cows' milk and containing predominantly whey proteins.

SUBSTANTIVE CHANGES

Simethicone versus placebo: One systematic review added comparing the effects of simethicone versus placebo on duration of crying or presence of colic in infants. [19] This review superseded two earlier reviews, but added no further evidence. Categorisation unchanged (Unknown effectiveness) as there remains insufficient good-quality evidence to assess simethicone.

Spinal manipulation versus simethicone: One systematic review added, which included the same RCT as the previously included review, therefore no new data was added. [19] Categorisation unchanged (Unknown effectiveness).

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Competing interests: PL is the first author of one RCT and two systematic reviews referenced in this review.

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TABLE **GRADE evaluation of interventions for colic in infants**

Important outcomes			Duration of crying caused by colic, adverse effects						
Number of studies (participants)	Outcome	Comparison	Type of evidence	Quality	Consistency	Directness	Effect size	GRADE	Comment
What are the effects of treatments for colic in infants?									
1 (66) [8]	Duration of crying	Advice to carry infant *v* general advice	4	–2	0	0	0	Low	Quality points deducted for sparse data and incomplete reporting of results
1 (42) [9]	Duration of crying	Advice to reduce stimulation *v* no advice	4	–2	0	0	0	Low	Quality points deducted for sparse data and uncertain validity of outcome measure
1 (122) [11]	Duration of crying	Casein hydrolysate milk or hypoallergenic diet for breastfeeding mother *v* cows' milk or control diet for mother	4	–2	0	–1	0	Very low	Quality points deducted for sparse data and incomplete reporting of data. Directness point deducted for inclusion of different interventions
1 (38) [12]	Duration of crying	Counselling plus reassurance *v* crib vibrator device plus reassurance *v* reassurance alone	4	–2	0	–1	0	Very low	Quality point deducted for sparse data and incomplete reporting of results. Directness point deducted for range of interventions advised as part of counselling
1 (20) [13]	Duration of crying	Counselling *v* elimination of cows' milk or soya milk with casein hydrolysate	4	–1	0	–1	0	Low	Quality point deducted for sparse data. Directness point deducted for range of interventions advised as part of counselling
1 (58) [14]	Duration of crying	Infant massage *v* crib vibrator device	4	–1	0	–1	0	Low	Quality point deducted for sparse data. Directness point deducted for inclusion of babies without colic
1 (53) [16]	Duration of crying	Low-lactose milk *v* standard milk	4	–2	0	–1	0	Very low	Quality points deducted for sparse data and methodological flaws. Directness point deducted for uncertain lactose intolerance in babies
3 (136) [20] [21] [22]	Duration of crying	Simethicone *v* placebo	4	–2	–1	0	0	Very low	Quality points deducted for sparse data and methodological flaws. Consistency point deducted for conflicting results
1 (41) [28]	Duration of crying	Simethicone *v* spinal manipulation	4	–2	0	0	0	Low	Quality points deducted for sparse data and lack of blinding
1 (86) [29]	Duration of crying	Spinal palpation *v* holding	4	–1	0	0	0	Moderate	Quality point deducted for sparse data
1 (43) [30]	Duration of crying	Whey hydrolysate milk *v* cows' milk formula	4	–2	0	0	0	Low	Quality points deducted for sparse data and flawed blinding

Type of evidence: 4 = RCT; 2 = Observational; 1 = Non-analytical/expert opinion. Consistency: similarity of results across studies
Directness: generalisability of population or outcomes
Effect size: based on relative risk or odds ratio