Clinical review

Infantile colic

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Interventions

Likely to be beneficial:

Whey hydrolysate milk

Trade off between benefits and harms:

Anticholinergic drugs

Unknown effectiveness:

Soya substitute milk

Casein hydrolysate milk

Low lactose milk

Sucrose solution

Herbal tea

Reduction of stimulation of the infant

Unlikely to be beneficial:

Simethicone

Increased carrying

Background

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

Incidence/prevalence Infantile colic causes one in six families to consult a health professional. One population based study (409 breastfed or formula fed infants) found the incidence of infantile colic to be 3.3-17%, depending on the definition used and whether the symptoms were reported prospectively or retrospectively. The incidence was 9% using the definition given above.[2] One randomised controlled trial (RCT) (89 breast and formula fed infants) found that, at 2 weeks of age, the incidence of crying more than three hours a day was 43% in formula fed infants and 16% in breastfed infants. The incidence at 6 weeks was 12% and 31% respectively.[3]

Aetiology The cause of infantile colic is unclear. It may be part of the normal distribution of crying. Other possible explanations are painful gut contractions, lactose intolerance, gas, or parental misinterpretation of normal crying.[1] One large survey found that the social factors that influenced reporting of infantile colic included the age at which the woman had her first child, the time she had spent in full time education, and her occupation. Older women who had spent the longest in full time education and in non-manual occupations were the most likely to report infantile colic.[4]

Prognosis Infantile colic improves with time. One study found that 29% of infants aged 1-3 months cried for more than three hours a day, but by 4-6 months of age the prevalence had fallen to 7-11%.[5]

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

Outcomes Duration of crying or colic, as measured on dichotomous, ordinal, or continuous scales. Parents' perceptions of severity (recorded in a diary).

Methods

Clinical Evidence update search and appraisal January 2001. We searched Cinahl, the Cochrane Library, Embase, and Medline for publications using reduction in crying or colic as the main outcome. Trials were excluded for the following reasons: infants studied had normal crying patterns, infants were older than 6 months, interventions lasted less than three days, trials had no control groups or had low Jadad quality scores.[6] Sometimes we pooled results from RCTs with different but comparable outcomes; effect sizes were calculated using a random effects model.

Question What are the effects of treatments for infantile colic?

Option Anticholinergic drugs

Summary Two systematic reviews have found that anticholinergic drugs (dicyclomine or dicycloverine) significantly reduce infantile colic but may be associated with more frequent minor adverse effects.

Benefits

We found two systematic reviews.[1 7] The first systematic review (search date 1996, 5 RCTs, 177 infants) found that anticholinergic drugs (most frequently dicyclomine 5 mg

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four times daily) were more effective than placebo (standardised mean difference of effect size 0.46, 95% confidence interval 0.33 to 0.60; see comment below).[1] The clinical importance of this result is unclear. A second systematic review (search date 1999, four of the same RCTs) found similar results (3 of 4 RCTs found that dicyclomine was more effective than placebo).[7]

Harms

Two of five RCTs[8][9] in the systematic reviews[1][7] compared harms of dicyclomine versus placebo. The first RCT (crossover design, 30 infants) found more drowsiness with dicyclomine than with placebo (4/30 v 1/30; P = 0.16).[8] The second RCT (crossover design, 25 infants) found more loose stools or constipation in infants on dicyclomine versus placebo (3/25 v 1/25; P = 0.3).[9] Case reports of harms have included breathing difficulties, seizures, syncope, asphyxia, muscular hypotonia, and coma.[10]

Comments

Most RCTs used dicyclomine; dicycloverine was used in only one of the RCTs. Only one RCT stated measures to make the control syrup taste the same as the drug syrup.[8] The first review is limited because it pooled different outcome measures from RCTs and included crossover studies.[1] The crossover design is unlikely to provide valid evidence because infantile colic is an unstable condition, and the effects of dicyclomine may continue even after a washout period.[11]

Option Simethicone

Summary Two systematic reviews of the same three RCTs found no evidence that simethicone reduced infantile colic.

Benefits

We found two systematic reviews (search dates 1996 and 1999, same 3 RCTs, 136 infants with infantile colic), which found no evidence that simethicone was more effective than placebo.[1][7] One RCT was of unsatisfactory quality. The second RCT (double blind, crossover, 83 infants) compared 0.3 ml of simethicone against placebo before feeds.[12] It found no significant difference for colic when rated by carers (28% improved with simethicone, 37% with placebo, 20% with both; effect size for simethicone versus placebo −0.10, −0.27 to 0.08). The third RCT (double blind, crossover trial, 27 infants) compared simethicone with placebo and found no improvement as rated by parental interview, 24 hour diary, or behavioural observation (effect size 0.06, −0.17 to 0.28).[13]

Harms

None reported.

Comment

The crossover design limits the validity and clinical utility of the RCTs.

Option Replacement of cows' milk with soya

Summary One small RCT has found that soya replacement of standard formula milk reduced crying time.

Benefits

We found two systematic reviews (search dates 1996 and 1999, 1 RCT).[1][7] The RCT (19 infants) found that soya milk compared with standard milk formula reduced the duration of crying (4.3-12.7 hours with soya milk v 17.3-20.1 hours with formula milk; mean difference 10.3 hours, −16 to −4 hours).[14]

Harms

None reported.

Comment

Mothers were not told which milk the babies received, but differences between the milks could be detected by smell and texture.

Option Replacement of cows' milk with casein hydrolysate

Summary Two RCTs comparing cows' milk formula against casein hydrolysate found insufficient evidence.

Benefits

We found two systematic reviews (search dates 1996 and 1999, identified the same 2 RCTs).[1][7] The first RCT (double blind, crossover, 17 infants) studied the effect of each of three changes of infant diet for four days.[15] Colicky, bottle fed infants received casein hydrolysate and cows' milk alternatively. By the third change there was no notable difference in the incidence of colic between groups, but 47% of infants left the study before completion. The second RCT (122 infants) compared bottle fed infants given casein hydrolysate versus cows' milk formula. It also compared breastfed infants with mothers on a hypoallergenic diet against controls on an unmodified diet.[16] Thirty eight infants were bottle fed, but the RCT did not report how many of these babies received the active diet. This RCT pooled the results of breastfed and bottle fed babies and found that the active diet reduced infant distress as measured by parents on a validated chart. The number of bottle fed infants was too small to establish any important effect in the bottle fed subgroup.

Harms

None reported.

Comment

None.

Option Replacement of cows' milk formula by whey hydrolysate

Summary One RCT found limited evidence that replacing cows' milk formula by whey hydrolysate reduces infant colic.

Benefits

We found two systematic reviews (search dates 1996 and 1999)[1][7] and one subsequent RCT.[17] The systematic reviews found no RCTs of adequate quality. The subsequent, double blind RCT (43 infants) found that whey hydrolysate formula (23 infants) compared with standard cows' milk formula reduced the time that babies cried each day, measured by a validated parental diary (crying reduced by 63 (1 to 127) minutes a day).[17]

Harms

None identified in the RCT.

Comment

Parents may not have been blind to the intervention. When asked, six indicated that they were aware, but two of these falsely identified the formula. When these infants' results were removed from the analysis, the calculated reduction in crying time with whey hydrolysate formula versus standard cows' milk formula was 58 minutes a day (P = 0.03).[17]

Option: Low lactose milk

Summary We found insufficient evidence from RCTs on the effects of low lactose milk.

Benefits

We found two systematic reviews (search dates 1996 and 1999, 2 RCTs),[1 7] and one additional small RCT.[18] The first RCT in the systematic reviews (double blind, crossover, 10 weaned infants) compared four options: bottle feeding using pooled breast milk, lactase treated breast milk, formula milk, and lactase treated formula milk.[19] It found no evidence that low lactose milk reduced the time, severity, or duration of colic, as recorded by parents. The second RCT (12 breastfed infants) compared lactase against placebo drops given within five minutes of feeding; it found no differences in the duration of time spent feeding, sleeping, or crying. The additional small crossover RCT (13 infants) compared lactase treated milk against milk with placebo drops added.[18] It found that the lactase treated milk reduced crying time (1.1 (0.2 to 2.1) hours a day).

Harms

None reported.

Comment

The RCTs are too small to allow confident conclusions to be drawn. The babies were not selected on the basis of a history of confirmed lactose intolerance.

Option Sucrose solution

Summary We found limited evidence from one small RCT that sucrose solution may benefit infantile colic.

Benefits

We found one systematic review (search date 1999, 1 RCT).[7] The small crossover RCT (19 infants), compared 2 ml of 12% sucrose solution against placebo given to babies when they continued to cry despite comforting.[20] Parents, blind to the intervention, scored the effect of the treatment on a scale of 1-5. Treatments were crossed over after 3-4 days and again after 6-8 days. The RCT found that parents were more likely to rate improvement with sucrose than with placebo (12/19 (63%) with sucrose *v* 1/19 (5%) with placebo; absolute risk increase (ARI) 58%, 10% to 89%; number needed to treat (NNT) 2, 95% CI 1 to 10; RR 12, 3.0 to 19).

Harms

None reported.

Comment

Publication bias has not been excluded.

Option Herbal tea

Summary One small RCT found limited evidence that herbal tea is effective for infantile colic.

Benefits

We found two systematic reviews (search dates 1996 and 1999, 1 RCT[21]).[1 7] The RCT compared herbal tea containing extracts of chamomile, vervain, licorice, fennel, and balm-mint in a sucrose solution (33 infants) against sucrose control (35 infants) given by parents up to three times daily in response to episodes of colic. Coding was known only to the pharmacist, and the taste and smell of the tea and placebo were similar. Parents rated response using a symptom diary. The RCT found that, at seven days, herbal tea eliminated colic in more infants than sucrose controls (number of infants free of colic: 19/33 (58%) with herbal tea *v* 9/5 (26%) with sucrose; ARI 32%, 7% to 53%; RR 2.2, 1.3 to 3.1; NNT 3, 2 to 14).

Harms

None reported.

Comment

One additional RCT, evaluating herbal drops, was not considered suitable for inclusion. The possibility of publication bias has not been excluded.

Option Behavioural modification

Summary Two systematic reviews found conflicting evidence from four small RCTs of the effects of behavioural modification of parents in response to their baby's crying.

Benefits

We found two systematic reviews (search dates 1996 and 1999, 4 RCTs).[1 7] **Focused counselling versus non-specific reassurance:** One RCT (22 infants) assessed maternal anxiety and the hours of crying each day by questionnaire. It found no evidence that counselling mothers about specific management techniques (responding to crying with gentle soothing motion, avoidance of over stimulation, using a pacifier, and prophylactic carrying) was any better than reassurance and support.[22] **Focused counselling versus car ride simulation:** The same RCT also allocated 16 infants (mean age 6.8 weeks) to car ride simulation for up to one hour. There were no important differences between this group and the control group (11 infants) for crying times or maternal anxiety.[22] **Focused counselling versus elimination of cows' milk protein:** One RCT (20 infants) found that counselling parents to respond to their baby's cries by feeding, holding, offering a pacifier, stimulating, or putting the baby down to sleep decreased duration and extent of crying more quickly than substitution of soya or cows' milk with hydrolysed casein formula. Mean decrease in crying as recorded by parent diary was 2.1 hours/day with counselling versus 1.2 hours/day with dietary change.[23] **Increased carrying versus general advice:** The third RCT (66 infants) randomised mothers of babies with colic to carry their infant, even when the infant was not crying, for at least an additional three hours a day or to a general advice group (to carry, check baby's nappy, feed, offer pacifier, place baby near mother, or use background stimulation such as music). The first group carried their babies for 4.5 hours a day compared with 2.6 hours a day in the general advice group. There was no effect on daily crying time (mean difference −3 minutes, −37 minutes to 32 minutes).[24] **Reducing stimulation versus non-specific interview:** The fourth RCT (42 infants, median age 10 weeks) allocated mothers of infants to a low stimulation group (mothers were advised to reduce stimulation by not patting, lifting, winding, or jiggling the baby, or by reducing auditory stimulation) or a group that was given an empathetic interview. For infants under 12 weeks, advice to reduce stimulation versus no advice improved a change rating scale for more infants (after 7 days 14/15 (95%) improved with advice *v* 6/12 (50%) with control; ARI 43%, 8% to 49%; RR 1.9, 1.2 to 2.0; NNT 2, 2 to 13).[25] Improvement in the change rating scale was defined as a score of +2 or better on a scale from −5 to +5 that was meant to indicate perceived change in crying since the start of the trial. It is unclear if this scale has been validated (see comment).

Harms

None reported.

Comment

Mothers given advice to reduce stimulation were also given permission to leave their infants if they felt 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.

Glossary

Behavioural modification—Changing the way in which parents respond to their babies crying from colic

Hypoallergenic diet—In bottle fed infants, a hypoallergenic diet uses a casein hydrolysate formula. In breastfed infants, a hypoallergenic diet involves a maternal diet, free of artificial colourings, preservatives, and additives, and low in common allergens (milk, egg, wheat, nuts, etc)

Jadad scale—This measures factors that impact on quality of the trial. Poor description of the factors, rated by low figures, are 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 and drop-outs? (0-1)[6]

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.

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A memorable patient
"Let's wait and see"

It happened on a Saturday morning. I was on call for the intensive care unit when I received the referral of a potential admission. The patient was an elderly man with an acute exacerbation of his chronic obstructive airways disease.

On my arrival on the medical ward, I immediately saw that he was in extremis. Very little information was available to provide the basis for an informed decision as to his suitability for intensive care admission and ventilatory support. The only option was to admit him to the intensive care unit.

After he was anaesthetised, intubated, and ventilated, a helpful colleague commented on some lung function tests in the medical record of which I was unaware. The results were dismal, and my hopes of successfully weaning the patient from mechanical ventilation were dashed. I was filled with the horror of this man being ventilated week after week and the implications of this for him, his family, and my standing on the intensive care unit.

Later that day, his relatives visited. During my discussions with them, I learnt that he was an active man involved in heavy gardening. This was not, in my opinion, in keeping with those infamous lung function tests. I thus adopted an attitude of "let's wait and see."

As the week progressed, he improved, requiring less ventilatory support until he was successfully weaned from the ventilator. He even avoided the need for tracheostomy, which had been predicted. When he was ready to be discharged to the medical ward I went to see him and his wife. He thanked me for taking him to the intensive care unit when he needed it most. His wife was delighted with his recovery.

This case shows the unpredictability of medicine. We cannot always correctly predict how our patients will respond to our interventions, and we must always consider the individual rather than the collective. Test results are important, but so is taking a full history. With increasing demand on critical care services, this case illustrates some of the difficulties in setting rigid admission policies based on patient groups. I felt guilty about my reluctance to take him to intensive care at the outset, but I'm glad that I did.

Christopher Sharpe *specialist registrar in anaesthetics, West Suffolk Hospital, Bury St Edmunds*

We welcome articles of up to 600 words on topics such as *A memorable patient, A paper that changed my practice, My most unfortunate mistake*, or any other piece conveying instruction, pathos, or humour. If possible the article should be supplied on a disk. Permission is needed from the patient or a relative if an identifiable patient is referred to. We also welcome contributions for "Endpieces," consisting of quotations of up to 80 words (but most are considerably shorter) from any source, ancient or modern, which have appealed to the reader.