

## FROM DRUG AND THERAPEUTICS BULLETIN

## Management of infantile colic



Drug and Therapeutics Bulletin  
THE INDEPENDENT REVIEW OF MEDICAL TREATMENT

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Cite this as: *BMJ* 2013;346:f4102  
doi: 10.1136/bmj.f4102

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This article was originally published with the title Management of infantile colic in *Drug and Therapeutics Bulletin* (DTB 2013;51:6-9, doi:10.1136/dtb.2013.1.0153). DTB is a highly regarded source of unbiased, evidence based information and practical advice for healthcare professionals. It is independent of the pharmaceutical industry, government, and regulatory authorities, and is free of advertising.

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Although infantile colic is considered to be a self limiting and benign condition, it is often a frustrating problem for parents and caregivers. It is a frequent source of consultation with healthcare professionals and is associated with high levels of parental stress and anxiety.<sup>1 2</sup>

Several published reviews of the literature have explored dietary, pharmacological, complementary, and behavioural therapies as options for the management of infantile colic.<sup>1 3</sup> Here, we assess whether these management options are supported by the literature and if there are any novel treatment options.

#### About infantile colic

Infantile colic has been defined as paroxysmal uncontrollable crying in an otherwise healthy infant less than 3 months of age, with more than three hours of crying per day in more than three days a week and for more than three weeks.<sup>4 5</sup> It is known to have a significant impact on infants and their families, with up to one in six families with children with symptoms of colic consulting healthcare professionals.<sup>6</sup>

#### Background

Despite the prevalence of the condition, the pathogenesis remains incompletely understood. One hypothesis has suggested that infantile colic is caused by the impact of abnormal gastrointestinal motility and pain signals from sensitised pathways in the gut viscera.<sup>2</sup> Another hypothesis is that inadequate amounts of lactobacilli and increased amounts of coliform bacteria in the intestinal microbiota influences gut motor function and gas production, which subsequently contributes to the condition.<sup>2</sup>

#### Box 1 | Differential diagnosis of colic symptoms in infants

##### Infection

Meningitis, urinary tract infection, otitis media

##### Gastrointestinal

Constipation, cow's milk protein allergy, gastro-oesophageal reflux disease, inguinal hernia, intussusception, anal fissure

##### Metabolic

Hypoglycaemia, inborn errors of metabolism

##### Neurological

Hydrocephalus

##### Trauma

Non-accidental injury, accidental trauma

More controversially, behavioural issues such as family tension, parental anxiety, or inadequate parent-infant interaction have also been explored as causative factors for infantile colic.<sup>1</sup> In addition, little is known about concomitant risk factors; however, maternal smoking, increased maternal age, and firstborn status are thought to be associated with the development of infantile colic. No association with feeding method has been noted.<sup>1</sup>

As a consequence of the lack of understanding of the cause of the condition, a wide spectrum of treatment modalities have been suggested, with each one targeted to address a postulated cause.

#### Diagnosis

Although infantile colic is by definition a benign condition, healthcare professionals should address parental concerns carefully, as the diagnosis is made by exclusion of more sinister causes. Examples of conditions to be excluded are listed in box 1.

A careful generic paediatric history should be taken. In particular this should include the relationship between an infant's behaviour and time of day and duration of crying episodes. Additional red flag features (see box 2) such as apnoeic episodes, cyanosis, respiratory distress, vomiting, or bloody stools should be elicited as these may be suggestive of more uncommon but serious causes, such as intussusception and pyloric stenosis. In addition, other more common conditions such as cow's milk protein allergy or gastro-oesophageal reflux disease, should be considered.

Routine observations such as pulse, respiratory rate and temperature should be performed. The infant's weight should be plotted and compared against previous measurements. In the absence of serial measurements, follow-up weight measurements recorded by a healthcare professional may be necessary to identify infants with faltering growth. A complete physical examination should be undertaken with full exposure to assess the presence of bruises or trauma and identify any visible evidence of non-accidental injuries. If non-accidental injury is suspected, the local clinician responsible for child safeguarding should be contacted immediately.<sup>7</sup> Red flags to be excluded are listed in box 2.<sup>8</sup>

If the history and examination reveal no abnormalities aside from inconsolable crying, there is usually no need for biochemical and radiological examinations.<sup>7</sup>

#### Management options

There are numerous issues with the methodological rigour of many intervention studies with several systematic reviews on infantile colic describing shortcomings in trial methodology. While some form of randomisation was performed with many of these studies, lack of a clear definition for infantile colic, absence of clinically

meaningful end points (aside from crying duration), and limited detail on sample size calculations, allocation concealment, and randomisation methods are likely to have affected the validity of the results. It is therefore appropriate to take a cautious approach in translating the outcomes of research to practical recommendations for managing infantile colic.

#### Diet modification

Based on the theory that infantile colic results from excessive gas production from poor gut digestion of cow's milk proteins, several nutritional interventions have been reviewed.<sup>2</sup>

In practice, any positive impact of diet modification may result from improving symptoms of colic secondary to a previously undiagnosed cow's milk protein allergy in the infant. Therefore, it is important that cow's milk protein allergy is considered during the assessment of an infant with inconsolable crying. There are currently no reported unwanted effects for any of the diet modification studies described below.<sup>9</sup>

#### *Hypoallergenic formula preparations for bottle fed infants*

In hydrolysed formulas, whole milk proteins are broken down to prepare them for digestion. These can range from partially hydrolysed to completely hydrolysed formula preparations, with the former often used for lactose intolerance and the latter used in the management of cow's milk protein allergy.<sup>9</sup>

Several systematic reviews have identified studies that demonstrated that completely hydrolysed formulas significantly improved clinical symptoms of infantile colic, such as crying time.<sup>1 9 10</sup> These studies used standard cow's milk formula as the comparator, and improvements were noted from seven days onwards. When carbohydrate and fat content compositions were varied in one study, both proved similarly effective in reducing colic symptoms, suggesting that changes to carbohydrate and fat content had no effect.<sup>9</sup>

In one systematic review, two randomised controlled trials noted that partially hydrolysed formulas reduced colic symptoms after 14 days of feeding. However, the trials did not involve a direct comparison with a regular cow's milk formula but compared partially hydrolysed formulas and soy based formulas.<sup>9</sup>

Where a suspicion of cow's milk protein allergy exists there is some evidence that the use of an empirical time limited trial of a completely hydrolysed formula is a reasonable option.<sup>1 9 10</sup> Correspondingly, while there is some literature advocating the use of partially hydrolysed formula,<sup>9</sup> its use for the dietary management of colic would not be recommended because partially hydrolysed formulas are not hypoallergenic and therefore will not address colic symptoms secondary to a protein allergy.<sup>10</sup>

#### *High fibre formula*

High fibre or fibre enriched formulas are those that are fortified, typically with a soy polysaccharide, to increase the dietary fibre concentration. A randomised controlled

#### Box 2 | Red flags signs and symptoms

##### Signs

Irritability, tachycardia, pallor, mottling, poor perfusion  
Petechiae, bruising, tachypnoea, cyanosis, nasal flaring  
Hypotonia, meningism, full fontanelle  
Weight <4th centile for age (or decreasing on the centile charts)  
Head circumference >95th centile (or increasing on the centile charts)

##### Symptoms

Bilious or projectile vomiting, bloody stool  
Fever, lethargy, poor feeding  
Perinatal risk factors for sepsis (premature rupture of membranes, maternal fever or infection, group B streptococcus)

trial identified by two systematic reviews found no significant difference in symptoms when comparing a high fibre formula with a standard formula.<sup>1 9</sup>

#### *Soy based formula*

Two systematic reviews noted several low quality studies that demonstrated a reduction in crying duration when comparing soy based formula with standard cow's milk formula after seven days of feeding.<sup>9 10</sup> However, because of concerns about the levels of phytoestrogens in soy based formula and that soy protein may be an allergen in infancy, its use in infantile colic is not recommended.<sup>10 11</sup>

#### *Hypoallergenic maternal diet for breastfed infants*

A hypoallergenic diet for breastfeeding mothers excludes cow's milk products and other possible trigger foods. In comparison to the use of a hypoallergenic infant formula, there is limited evidence supporting the use of hypoallergenic maternal diet, with several studies noting equivocal results.<sup>1 9 10</sup> This has been attributed to the use of an incompletely hydrolysed diet without a thorough exclusion of trigger foods that could have reduced the effect of the intervention.<sup>9</sup>

One systematic review identified a good quality randomised controlled trial in which mothers eliminated dairy foods, eggs, peanuts, tree nuts, wheat, soy, and fish from their diet.<sup>9</sup> The primary end point of the study was a reduction in "cry/fuss" duration of >25% from baseline, with more responders in the low allergen diet group compared with the control group (74% v 37%) and an absolute risk reduction of 37% (95% confidence interval 18% to 56%).<sup>10</sup> Two earlier studies reported similar findings, but neither separated the results for breastfed infants from hypoallergenic formula fed infants.<sup>9</sup>

On balance there is limited evidence to suggest that hypoallergenic diets in mothers may be helpful. If a time limited trial is undertaken, mothers should be advised to exclude trigger foods including cow's milk products from their diet and to ensure that they and their infant receive appropriate nutritional support, including cal-

cium and vitamin D intake. They should also be advised not to discontinue breast feeding while switching to the hypoallergenic maternal diet.<sup>1 9 10</sup>

### Lactase therapy

In lactase therapy, galactosidase (lactase) drops are mixed with breast or bottle milk feeds up to 24 hours prior to feeding the infant. A systematic review identified two randomised controlled trials where an improvement in symptoms was noted with the use of lactase therapy. In one randomised controlled trial, a relative decrease in crying time of 22.4% (95% confidence interval 13% to 44%) was noted.<sup>1</sup> This conflicted with several other randomised controlled trials noting no improvement with the use of lactase in either breast or formula milk. In one example, only a 40 minute reduction in crying time was observed compared with placebo.<sup>1</sup>

### Pharmacological management

It is hypothesised that the gut's peristaltic cholinergic activity is linked to gastrointestinal discomfort in infantile colic. Consequently, anticholinergics such as dicyclomine hydrochloride and cimetopium bromide, which reduce smooth muscle activity, have been studied. Neither of these drugs are licensed in the UK for use in infants.

In one systematic review, two studies investigating dicyclomine hydrochloride noted improvement in colic symptoms. However, severe adverse effects including respiratory distress and seizures led to its licence withdrawal in infants less than 6 months of age.<sup>7</sup> One study has reported significant improvements with the use of cimetopium bromide, with only drowsiness noted as a side effect.<sup>13-7</sup>

Simethicone (Infacol), which reduces intraluminal gas and is readily available over the counter, has been studied in two randomised controlled trials. No difference in reducing colic episodes was shown compared with placebo.<sup>1 3-7</sup>

### Complementary therapies and other interventions

In the absence of safe and effective pharmacological interventions, complementary therapies have taken a more prominent role in the management of infantile colic. These can range from conventional therapies, such as dietary supplements, sugar solutions, herbal extracts, or massage, to controversial options such as chiropractic treatment.

#### Herbal supplements

A systematic review identified several studies of herbal supplements such as fennel extract and mixed herbal tea that showed a reduction in symptoms of infantile colic.<sup>12</sup> However, the presence of several adverse effects such as vomiting, sleepiness, constipation, and loss of appetite was also noted.<sup>12</sup> Minimal information on extraction and preparation of herbs and lack of standardisation of dosage and formulations have also limited their use.<sup>2</sup>

#### Sucrose solutions

Two studies compared glucose solutions with placebo and found positive effects in relieving symptoms.<sup>2</sup> How-

ever, there are concerns about potential nutritional effects, in particular the content of sugar and alcohol, the lack of formulation standardisation, and the poor quality of the evidence.<sup>2 12 13</sup>

### Probiotics

Based upon the hypothesis that aberrant intestinal microflora affecting gut function and gas production may contribute to symptoms, the use of probiotics in infantile colic has become more common. Numerous studies have been identified in a systematic review.<sup>12 14 15</sup> One randomised double blind placebo controlled trial involving 46 infants used a suspension of freeze dried *Lactobacillus reuteri*. There were significantly more responders (50% reduction in crying time from baseline) in the *L reuteri* group on days 7 (20 v 8, P=0.006), 14 (24 v 13, P=0.007), and 21 (24 v 15, P=0.036). A further randomised controlled trial identified good weight gain and gastrointestinal tolerance.<sup>2</sup>

### Massage

One study noted a positive effect in massage using aromatherapy oils, however, the results were not separated between massage and aromatherapy.<sup>16</sup> While several other studies identified in a systematic review<sup>12 13</sup> showed some improvement on symptoms of colic, overall the quality of these studies is poor.

### Swaddling

Swaddling has traditionally been used by some parents to reduce crying in infancy. A systematic review noted that swaddling reduced crying symptoms compared with massage in excessively crying infants with cerebral damage.<sup>17</sup> However, there is a known associated risk of developing hip dysplasia, overheating or sudden infant death syndrome if placed in the prone position. The current evidence base therefore does not support the use of swaddling in the management of infantile colic.

### Chiropractic treatment

As a more controversial complementary therapy, chiropractic care is sometimes advocated as a treatment option for infantile colic. Chiropractic care can include, but is not limited to, cranial osteopathy and spinal manipulation therapy. The evaluation of treatment options in this field is challenging because of the absence of good quality randomised controlled trials. Additionally, adverse effects such as vertebral artery dissection have been reported anecdotally.<sup>18 19</sup>

It is hypothesised that chiropractic care can have a positive effect on symptoms; however, the literature has noted that this may be a consequence of improving parents' coping ability with the condition rather than true effectiveness of chiropractic care.<sup>20</sup>

In several systematic reviews, one good quality single blinded randomised controlled trial was identified noting no differences in outcomes between chiropractic care and placebo, which was infant holding by a nurse.<sup>21</sup> Several other studies were identified noting positive treatment effects, however, these were noted to be of low quality.<sup>12 18 19 21 22</sup>

Currently, therefore, there is limited evidence from the literature to recommend chiropractic care in infantile colic.

#### *Acupuncture*

Several randomised controlled trials evaluating acupuncture were identified, of which two trials noted a shorter duration and intensity of infantile colic symptoms.<sup>23 24</sup> Another good quality double blinded randomised controlled trial comparing acupuncture with a sham needle insertion noted no major effect on symptoms including feeding, bowel movement frequency, and sleep.<sup>25</sup>

#### **Behaviour modification**

Several behavioural interventions were identified that aimed to provide reassurance to parents and offer alternative methods to treat colic.<sup>3</sup>

One systematic review identified two controlled trials where the use of modified parent and infant interaction led to significant reduction in colic symptoms and additional benefits of early gains in development.<sup>1 26</sup> This has been attributed to increased maternal responsiveness and time spent with infants resulting in increased infant alertness. In another study, entire family involvement using an integrated care model led to the relief of infantile colic symptoms more readily than standard care.<sup>27</sup> The use of “contingent music” was noted to decrease symptoms in another study.<sup>1</sup>

It has been noted that the identification of effective coping strategies and consoling methods to assist parents in managing this stressful condition is imperative.<sup>28</sup> A systematic review identified two studies addressing this; one study used a home based nursing intervention, and another used counselling on specific management techniques and car ride simulation in infants over 6 weeks of age, leading to significant reductions in parental stress and anxiety.<sup>1 3</sup>

#### **Guidelines**

The National Institute for Health and Clinical Excellence guideline on postnatal care advises that holding the baby through the crying episode, and accessing peer support may be helpful; and that the use of hypoallergenic formula in bottle fed babies should be considered for treating colic, but only under medical guidance.<sup>29</sup>

A position statement by the Canadian Paediatric Society on dietary interventions commented that a minority of infants have symptoms of infantile colic secondary to cow’s milk protein allergy, and in such cases a maternal hypoallergenic diet for breastfed infants and an extensively hydrolysed formula for bottle fed infants may help.<sup>10</sup> In addition it concluded that there is no proven role for the use of soy based formulas or lactase therapy and insufficient data to make a recommendation on the effect of probiotics.

The Clinical Knowledge Summary noted that “although there are many studies of interventions for infantile colic, most are of poor methodological quality.”<sup>30</sup> The guidance suggests that clinicians should “only consider trying medical treatments if parents feel

unable to cope despite advice and reassurance.” Options listed include a one week trial of simeticone drops (breastfed infants or bottle fed infants); a one week trial of diet modification to exclude cow’s milk protein (dairy-free diet for the mother (breastfed infants) or hypoallergenic formula (bottle fed infants)); and a one week trial of lactase drops (breastfed infants or bottle fed infants). However, it should be noted that the Clinical Knowledge Summary guidance was last revised in 2007. A Map of Medicine health guide on infantile colic also cites the Clinical Knowledge Summary guidance.<sup>31</sup>

#### **Other issues**

There is evidence of inconsistent advice relating to early infant crying and colic in various media outlets such as parenting magazines.<sup>32</sup> Advice was noted to be “diffuse, varied, and generally unrelated to the current evidence based conceptualization of early infant crying.”

Advice for community pharmacists has summarised many of the options available over the counter (including those for which there is little evidence of efficacy, such as gripe water) and highlighted resources and support groups.<sup>33</sup>

#### **Conclusion**

Parents with infants with colic commonly consult a healthcare professional. Each case should be thoroughly assessed because of the wide range of other conditions that can present in a similar way. For the majority of cases simple reassurance is all that is required. If the clinician feels intervention is required there are a wide range of options available with a poor evidence base to support any of them.

Currently there are no effective and safe pharmacological management options available over the counter or by prescription. Simeticone, lactase drops, and probiotics are unlikely to be harmful, but there is little evidence to support their use. While complementary treatment options exist, there is currently insufficient evidence to recommend their use. The absence of strong evidence is similarly noted for behavioural modification interventions. Despite this, the absence of side effects makes the argument for a trial of such an intervention more compelling.

Where there is a suspicion of cow’s milk protein allergy, a short trial of hypoallergenic feeding, through a hypoallergenic formula in bottle fed infants may be considered. The improvement in infants with this approach may in part be as a result of treatment of undiagnosed cow’s milk allergy rather than symptomatic improvement of colic. In breastfeeding mothers there is limited evidence that a fully hypoallergenic exclusion diet may be helpful if undertaken carefully.

Infantile colic, while self limiting and benign, can cause considerable distress to parents, and it is therefore important that parental support is provided. Advice and guidance on where to obtain support outside conventional healthcare sources should be discussed with parents.

References are in the version on bmj.com.