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ARTICLE

Infantile colic

SUMMARY

Infantile colic is a common, self-resolving condition. It has important adverse associations including maternal depression, child abuse and early cessation of breastfeeding.

There are many proposed causes of colic, however none is definitive. Colic is likely to be an exacerbation of normal infant crying brought about by physiological and psychosocial factors.

There is no known single effective treatment for colic. The mainstay of management is exclusion of organic causes, explanation of the natural history of colic, parental support, offering strategies to deal with the infant's feeding and sleep, and exploration of settling techniques.

The probiotic *Lactobacillus reuteri* DSM17938 may be trialled for exclusively breastfed infants with colic. Its efficacy in formula-fed babies is unknown.

An allergy to cow's milk protein accounts for a minority of cases. Hypoallergenic formula, and dietary exclusion for breastfeeding mothers, should only be tried in infants with other clinical features of cow's milk allergy.

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Introduction

Infantile colic describes excessive crying of unknown cause in otherwise well infants. Colic affects up to 20% of infants,[1] and is one of the most common presentations to the primary health sector in early life. It resolves spontaneously after the first three to four months of life.

Colic is traditionally defined by the Wessel's criteria of crying or fussing more than three hours of the day for more than three days of the week.[2] The new Rome IV criteria define it as 'recurrent and prolonged periods of infant crying, fussing or irritability reported by caregivers that occur without obvious cause and cannot be prevented or resolved'.[3] The diagnosis can be assumed after exclusion of potential organic causes.

Although colic is considered to be benign, it is a major burden to families, health professionals and the health system. Colic is strongly associated with maternal depression[4] and is the strongest risk factor for shaken baby syndrome.[5] It is also a common cause of early breastfeeding cessation.[6] Crying beyond the usual colicky period can be linked to later sleep problems, allergic disorders, family dysfunction, and behavioural problems.[7,8]

Causes of colic

Despite years of research, the aetiology of colic remains elusive and there are many proposed theories. Does colic represent the most severe spectrum of normal infant distress, or is it a manifestation of underlying gastrointestinal, neurological or psychosocial disorders? Perhaps infant colic can be best regarded as an exacerbation of normal infant behaviour by a mixture of physiological and psychosocial factors.[9]

Colic should only be diagnosed after exclusion of organic causes. These occur in less than 10% of infants presenting with crying.[10,11] Most organic causes present with other associated features (Table 1).

Is it a gastrointestinal disorder?

The word 'colic' implies an abdominal origin. Postulated gastrointestinal mechanisms have included increased intraluminal gas, gut dysmotility, and visceral pain, but none is proven.[12,13] Recent research has focused on the role of gut microbiota, with more than a dozen case-control studies suggesting that infants with colic may have differences in gut microbiota compared to those without colic.[14,15] The majority of studies have found that Gram-negative organisms such as *Escherichia* species occur more frequently in colicky infants than in controls. Other studies have found fewer *Lactobacillus* species in those with colic.[14,15] In addition, some studies have suggested that infants with colic have increased gut and systemic inflammatory markers when compared to those without colic.[16] However, the pathophysiological evidence for the role of gut microbiota and inflammation is still far from conclusive.[17]

Gastro-oesophageal reflux

Gastro-oesophageal reflux has been regarded as having a role in irritable infants, however anti-reflux medicines are ineffective in reducing crying.[18,19] Studies have failed to show any correlation between

Table 1 **Organic causes to exclude in a crying infant**

Conditions to exclude	Additional clinical features
Cow's milk protein allergy	Significant vomiting Feeding difficulties Diarrhoea with mucus or blood Poor weight gain Extensive eczema First-degree family history of atopy
Gastro-oesophageal reflux disease	Frequent significant vomiting (>5 times per day) Haematemesis Feeding difficulties Poor weight gain
Lactose intolerance or overload	Watery, frothy, explosive diarrhoea AND perianal excoriation or ulcerations
Inguinal hernia	Vomiting Lump in inguinal region
Intussusception	Acute onset of vomiting, pallor, irritability Abdominal mass, rectal bleeding
Infection: urinary tract infection, meningitis, otitis media	Fever Lethargy Poor feeding, poor weight gain Perinatal risk factors for sepsis
Hydrocephalus	Increasing head circumference/macrocephaly Vomiting Lethargy
Hair tourniquet	Hair tourniquet around fingers or toes
Foreign body in eye	Acute distress, history of foreign body penetration in eye
Non-accidental injury	Bruising or petechiae Other features of physical injury

pathological gastro-oesophageal reflux and crying in infants less than three months old.[20] In the absence of frequent vomiting, haematemesis and poor weight gain, gastro-oesophageal reflux disease is an unlikely cause of infant crying.[21]

Cow's milk protein allergy

An allergy to cow's milk protein has been implicated as a cause of irritability,[22,23] but accounts for probably less than 5% of cases of colic.[24] It should be considered if the crying infant has feeding difficulties (during the day as well as at night), failure to thrive, significant vomiting, diarrhoea with mucus or blood, widespread eczema and a first-degree family history of atopy. The diagnosis can be confirmed if the symptoms resolve after excluding dairy food from the diet of breastfeeding mothers or using hypoallergenic formula (usually for a two-week trial period), together with reproduction of the symptoms on re-challenge with cow's milk protein.

Lactose intolerance and overload

Evidence for the role of lactose intolerance or overload in colic is mixed and inconclusive.[22,25-28] Lactose intolerance may be secondary to an underlying pathology such as cow's milk protein allergy or gastroenteritis. Lactose overload is usually a result of excessively frequent breastfeeding whereby the baby is snacking on the foremilk which has a high lactose content. Lactose intolerance or overload should be considered in the presence of watery, frothy, explosive diarrhoea with significant perianal excoriation or ulceration (due to acidic stools).

Possible neurological or psychosocial causes

Evidence for a neurological basis for colic is limited,[29] although recent studies have suggested colic may be associated with both childhood migraine later on in life and migraines in the mother.[30-32] Psychosocial factors such as infant temperament, mother–infant

interactions, maternal anxiety and depression may be important contributors to colic.[33,34] Maternal smoking may be a risk factor.[35,36]

Management options

Despite years of research, effective management options for colic are limited. Table 2 summarises the different proposed management options and the evidence for their effectiveness.

Drug therapies

Anticholinergic drugs, such as dicyclomine and cimetropium, reduce crying,[37-40] but have potentially dangerous adverse effects, including drowsiness, apnoeas and coma.[41] They are not recommended for infants younger than six months old. Despite its widespread use for colic, simethicone, an anti-foaming agent to reduce intraluminal gas, is not effective.[37-40,42] Proton pump inhibitors are conclusively ineffective.[18,19] Considering that there is increasing evidence of their association with adverse effects such as an increased risk of infections,[43] they should not be routinely used for managing colic. There have been no studies examining the effect of gripe water on colic.

Non-drug therapies

Many natural remedies have been tried, but not rigorously studied. Few have evidence of effectiveness.

Probiotics

Recent evidence has emerged of a possible role for probiotics in infant colic. These are 'live micro-organisms which, when administered in adequate amounts, confer a health benefit on the host'.[44] *Lactobacillus reuteri* DSM17938 reduced infant crying in four double-blind randomised trials, two open-label and one single-blinded trial of exclusively breastfed infants with colic, at a dose of 1 x 10^8 colony-forming units per day. These studies all had sample sizes under 80.[45-51] In contrast, an Australian double-blind randomised trial, the largest to date (n=167), including both breastfed and formula-fed infants with colic, concluded that *L. reuteri* was ineffective.[52] The negative findings were replicated in a more recent smaller double-blind trial of 20 breastfed infants with colic.[53]

In response to the conflicting results, a meta-analysis pooled raw data from four of the higher quality double-blind trials, involving 345 infants with colic (174 probiotic, 171 placebo).[54] The reduction in daily crying from baseline to 21 days in the probiotic group was 25 minutes more than in the placebo group (adjusted mean difference in change from baseline -25.4, 95% confidence interval (CI) -47.3, -3.5). The probiotic group was more likely to experience treatment success (adjusted incidence ratio 1.7, 95% CI 1.4, 2.2). Intervention effects were more pronounced in breastfed infants (number needed to treat 2.6, 95% CI 2.0, 3.6). The meta-analysis of individual participant data concluded that *L. reuteri* DSM17938 was effective in exclusively breastfed infants with colic. There was insufficient evidence to make conclusions for formula-fed infants with colic.[54]

Table 2 **Summary of evidence from randomised controlled trials for the management of colic**

Effectiveness	Intervention
Effective for exclusively breastfed infants with colic	Probiotic *Lactobacillus reuteri* DSM17938
Possibly effective	Hydrolysed formula
	Hypoallergenic diet in breastfeeding mothers
	Reduced stimulation
	Improved parental responsiveness
	Focused parent counselling
	Acupuncture
Ineffective	Simethicone
	Spinal manipulation
	Lactase
	Soy formula
	Fibre-enriched formula
	Carbohydrate alteration
	Increased carrying
	Car ride simulator
	Crib vibrator
Effective but possibly harmful	Dicyclomine, cimetropium
	Herbal mixtures
	Swaddling
Effective but short-lived effects	Sucrose

Other non-drug therapies

Next to *L. reuteri*, the best evidence for colic management is the use of hypoallergenic formulae or eliminating dairy foods from the diet of breastfeeding mothers. However, not all unsettled infants respond and most studies examining maternal elimination diets have methodological limitations.[37-40,55,56] These approaches are probably only effective for babies who have an underlying allergy to cow's milk protein.[56]

Behavioural therapies such as reducing stimulation, improving parental responsiveness and parental counselling can be effective. However, the evidence comes from unblinded studies which are prone to bias.[37-40]

Acupuncture has been suggested to be effective in two recent studies, however there were methodological limitations in both.[57,58] Herbal mixtures given to infants with colic may be effective,[59-62]

however the consumption of large quantities of herbal teas has the potential to reduce milk intake and put infants at risk of nutritional deficiencies.[39] Swaddling the baby may be effective, however there is concern that it can increase the risk of hip dysplasia.[63,64]

Sucrose is effective in reducing crying but its effects are short-lived.[37-40] The use of lactase, soy or fibre-enriched formulae, massage, music and spinal manipulation have all been shown to be ineffective for colic.[37-40,65]

Recommendations

The first step for managing colic is to exclude organic causes of crying by careful history and examination. Infants who have significant feeding difficulties and frequent vomiting, especially those who are struggling to gain weight, have a strong family history of allergy, and those with increasing irritability beyond three months should be considered for a limited trial of a hypoallergenic diet. Hypoallergenic formula or dietary elimination should only be continued if symptoms resolve and then reappear after a re-challenge with cow's milk protein.

It is important to explore the family's perceptions of their infant's crying, listen to their worries, acknowledge their feelings of anger, frustration and exhaustion, and avoid being dismissive of their concerns. Discussing the different hypotheses surrounding colic, and addressing each hypothesis in relation to the individual infant and family, can be helpful.

It is essential to screen for maternal postnatal depression and also pay attention to paternal well-being. Clinicians should explore parental coping mechanisms during times of extreme crying, explain the neurological consequences of shaken baby syndrome and suggest strategies to prevent it. All families should be offered support and help around the infant's feeding, settling, and sleep. Feeding difficulties must be addressed and managed. Strategies to soothe the infant should be explored, with recommendations to reduce environmental stimuli.

Families can often be reassured by understanding the self-resolving nature of colic, offering at least one review and more where necessary, putting in place strategies to increase emotional and social supports, and acknowledging that it may be difficult, if not impossible, to 'teach' their infant to 'self-soothe' during the first few months of life. Most of all, it is vital to recognise that the family is usually doing the best they can for their baby, to allay any feelings of failure or guilt, and to encourage them to take adequate breaks from their crying infant.

If the infant is exclusively breastfed, a three-week trial of the probiotic *L. reuteri* DSM17938 can be considered. It is important to discuss that even though the probiotic has been shown to be effective in breastfed babies in most trials across the world, it has not been shown to be effective in Australia and cannot be recommended for formula-fed infants. In addition, although the probiotic is considered safe without short-term adverse effects, its longer term effects are unknown.

Conclusion

The mainstay of management for colic is to help families cope with their infant's symptoms, reduce the risks of parental depression, child abuse and early breastfeeding cessation, and to prevent the possibility of long-term adverse effects. The myths surrounding colic should be explored, and the lack of evidence for any one effective intervention should be explained. All families must be offered strategies to manage their infant's feeding, settling and sleep, together with a recommendation to reduce environmental stimuli. Although evidence for these strategies is limited, they are not harmful or expensive. Other management strategies should be considered on a case-by-case basis suited to each individual family. <

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