



ANNOTATION

Diagnosing gastro-oesophageal reflux disease or lactose intolerance in babies who cry a lot in the first few months overlooks feeding problems

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Abstract: This paper explores two areas in which the translation of research into practice may be improved in the management of cry-fuss behaviours in the first few months of life. Firstly, babies who cry excessively are often prescribed proton pump inhibitors, despite evidence that gastro-oesophageal reflux disease is very rarely a cause. The inaccuracy of commonly used explanatory mechanisms, the side-effects of acid-suppressive medications, and the failure to identify treatable problems, including feeding difficulty when the diagnosis of 'reflux' is applied, are discussed. Secondly, crying breastfed babies are still prescribed lactase or lactose-free formula, despite evidence that the problem of functional lactose overload is one of breastfeeding management. The mechanisms and management of functional lactose overload are discussed. These two problems of research translation need to be addressed because failure to identify and manage other causes of cry-fuss problems, including feeding difficulty, may have adverse outcomes for a small but significant minority of families.

Key words: breastfeeding; crying baby; feeding problem; gastro-oesophageal reflux disease; proton pump inhibitor.

Introduction

Although excessive crying in otherwise healthy babies in the first few months of life is generally self-limiting and without adverse effects in the long term for most, it is also associated with premature breastfeeding cessation,¹ long-term behavioural problems, including feeding difficulty,^{2,3} child abuse,⁴ and for the mother, an increased risk of post-natal depression.⁵ Assessment should include a thorough history, including a feeding history, and a thorough physical examination, including weight gain. Investigations are not warranted, unless abnormalities are noted in the history and examination.⁶

Key Points

- 1 Proton pump inhibitors are no better than placebo in babies with cry-fuss problems in the first few months of life.
- 2 For 2 hours after a (breast or bottle) feed, gastric acid is buffered by milk, and gastric refluxate is not noxious. Back-arching at feed-time, feeding refusal, and crying when put down after a feed are not signs of oesophageal inflammation.
- 3 Feeding refusal in breast or bottle-fed babies and signs of functional lactose overload in breastfed babies require assessment and management by a feeding expert before cry-fuss problems entrench.

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Proton Pump Inhibitor Use Is Linked with Failure to Identify and Manage Feeding Difficulties in Crying Babies in the First Months of Life

Many babies with cry-fuss problems under 3–4 months of age are prescribed proton pump inhibitors (PPIs). There is no data available in Australia, but in the USA, PPI prescriptions increased sevenfold in infants under 1 year between 1999 and 2004; 50% of these babies were under 4 months of age, and use of a child-friendly liquid formulation increased 16 fold.⁷

Randomised controlled trials, systematic reviews and two international consensus statements by paediatric gastroenterologists conclude that PPI use is no better than placebo in crying babies in the first few months of life and that acid-peptic or allergic gastro-oesophageal reflux disease (GORD) is very rarely a cause of crying in this population.^{8–14} It may help to consider the problem of inappropriate PPI prescription in crying babies from three perspectives.

Firstly, the mechanisms previously used to explain why GORD causes babies to cry in the first weeks and months of life are not credible. Intra-oesophageal pH monitoring and multichannel intraluminal impedance and manometry, separately or in combination, correlate poorly with symptoms and are not reliable diagnostic tools in this population. Multiple unpredictable variables including cough, positioning, volume and frequency of feeds, and crying itself affect the frequency and/or pH of reflux.¹⁵ Crying babies under 3–4 months of age with vomiting, back-arching and aversive feeding behaviours very rarely have macroscopic oesophageal lesions on endoscopy; there is no evidence that microscopic changes, including of eosinophilic oesophagitis, cause oesophageal pain and crying in this

population.^{8,10,16} Gastric acid is buffered for 2 hours after feeds of either breastmilk or formula, so gastric refluxate during this period will not irritate oesophageal mucosa.^{15,17–19} High levels of autonomic nervous system arousal and crying in infants cause oesophageal dysmotility; the reverse causality hypothesis that oesophageal dysmotility or distension causes infant crying is not supported by evidence.^{20–22} Back-arching and crying when put down are normal infant neurobehavioural cues. In breastfed infants, back-arching and pulling away from the breast occur when positional instability or other feeding problems disrupt the infant's reflex feeding sequence.²³ Screaming with a red face, flexed hips and knees, and flailing fists does not necessarily or even usually signal abdominal pain.²⁴ Frequent vomiting is normal once serious conditions have been excluded – including food protein-induced enteropathy syndrome, which is very rare in exclusively breastfed babies.²⁵ Vomiting occurs in 40% of babies, peaks at 4 months of age and occurs more frequently with the high levels of autonomic nervous system arousal associated with excessive crying.^{21,26,27} Night waking is normal in babies in the first months of life, as long as satiety has been addressed.

In summary, feeding refusal, back-arching at the breast and crying when put down after a feed do not signal oesophageal pain. Rather, feeding refusal requires prompt intervention by a feeding expert, such as a lactation consultant or speech pathologist, before crying behaviours and disrupted maternal–infant relations entrench.^{3,28–30}

Secondly, PPIs place infants at increased risk of lower respiratory tract infection¹¹ and food allergy.^{31,32} Because PPIs are no better than placebo for cry-fuss problems, exposing the unsettled infant to even a modest risk of medication side effect is indefensible. Anecdotally, prescribing doctors argue that mothers report improvement with PPIs and worsened crying when the PPI is stopped. These reports should be considered in light of the powerful placebo effect, the difficulty stressed and exhausted parents have in objectively quantifying their babies' crying, the therapeutic effects of active listening and validation, the self-limiting nature of the problem and the side effects of PPI withdrawal, including rebound acid hypersecretion and upper gastrointestinal tract symptoms, which have been demonstrated in adults.³³

Thirdly, and most importantly, interpreting cry-fuss behaviours, feeding refusal, back-arching, crying when put down, vomiting and frequent night waking in babies in the first months of life through the lens of a presumed GORD, whether acid-peptic or allergic, means that various other treatable factors that have been shown to relate to excessive crying in the first few months of life, including feeding problems, may be overlooked.^{6,30,34–36}

Prescribing Lactase or Lactose-Free Formula for Breastfed Crying Babies in the First Few Months of Life Is Linked with Failure to Identify and Manage Functional Lactose Overload

Prospective studies, randomised controlled trials and observational studies demonstrate that breastfed crying babies are at increased risk of premature weaning, and that regardless of

feeding method, there are strong links between infant crying and feeding problems.^{1,3,6,36} Crying babies also have lower levels of plasma cholecystokinin, which is released when a lipid-rich meal reaches the stomach to cause feelings of satiety.³⁷ A large multicentre study shows that infants with persistent crying are at increased risk of feeding problems later in childhood.³ Although the investment in research concerning human lactation and infant feeding problems has comprised only a fraction of the investment in research concerning GORD in crying babies over the past two decades internationally, feeding problems linked with cry-fuss behaviours include feeding refusal, as discussed above, oral motor dysfunctions and poor milk transfer, and functional lactose overload.^{30,37–39}

Functional lactose overload presents with excess flatus, explosive frothy stools, tympanic abdomen and crying in breastfed infants. The lipid proportion in a breastfeed is dynamic and dependent on the way feeding is managed by each unique mother–baby pair. The initial part of a breastfeed is high in volume with proportionally low lipid content; further into the feed, the suckling infant takes smaller volumes of more lipid-rich milk. This richer lipid fraction of the meal not only triggers release of plasma cholecystokinin in the infant, signalling satiety, but also modulates intestinal contractility, slowing down gut transit. Unduly rapid intestinal transit of the normal lactose load in a breastfeed, occurring in the context of an inadequate lipid fraction, results in functional lactose overload, because lactase in the small intestine does not have time to properly digest the lactose load. Undigested lactose then reaches the colon and ferments.^{39,40} Although functional lactose overload is one example of a common breastfeeding management problem, studies investigating infant crying generally, and studies that claim to show the efficacy of lactase in reducing crying in particular, fail to control for breastfeeding management.⁴¹

The best way to ensure breastfeeding homeostasis is to encourage cue-based feeding, which may be frequent in the first days and weeks.^{42,43} Simplistic attempts to limit functional lactose overload by instructing mothers to feed only from one breast over a stipulated period of time may cause other problems, for example inadequate supply or mastitis. The transfer of low-volume, lipid-rich milk is compromised when mothers are told not to allow 'comfort sucking', or to limit feeds to a defined time period, or to always offer the fuller side first or to always feed from both sides. These widespread practices, which are not evidence based, may result not only in functional lactose overload but in failure to identify important problems that underlie poor milk transfer and excessively long feeds. Optimal management of functional lactose overload is more likely to be achieved through individual assessment and management, if necessary by a feeding expert, rather than through a 'one-size-fits-all' solution.

Because a breast pump does not extract as much of the low volume, lipid-rich milk, babies receiving significant amounts of expressed breastmilk may also develop functional lactose overload.⁴⁰ Babies who do not achieve good satiety due to inadequate lipid intake may quickly want more milk. In older breastfed babies, a cycle of overproduction may result: the infant feeds very frequently, stimulating the breast to produce more milk but still receives inadequate 'cream'.

Mothers should be encouraged to offer cue-based care and be informed of the importance of the lipid-rich 'creamy dessert'. They should be encouraged to pay attention to breast comfort when deciding which breast to offer first, without adhering to any particular rule. Mothers can be reassured that the cluster feeds commonly required by babies in the evenings are usually low-volume, high lipid feeds that result in good satiety and assist with sleep. In older babies with functional lactose overload and high maternal supply, management should be individually tailored.⁴⁰

While a decline in lactase-specific activity commonly occurs as early as 3–5 years of age in humans, congenital lactase deficiency is rare. Infants can acquire a transient, secondary lactose intolerance from damage to the intestinal villi, most commonly due to gastroenteritis or cow's milk allergy. If the baby is formula fed, this secondary lactose intolerance responds to lactose-free formula, although infants with cow's milk allergy who are mistakenly diagnosed with lactose intolerance could experience perpetuation of their gut lesion if the lactose-free formula contains cow's milk protein. If the baby is breastfed, weaning is not indicated, although a maternal dairy elimination diet may have a role.³⁵ The trend to diagnose lactase insufficiency or lactose intolerance in crying babies in the first weeks and months of life, accompanied by treatment with either lactase or a lactose-free formula, confuses functional lactose overload, a common breastfeeding management problem, with either congenital lactase insufficiency or secondary lactose intolerance.

Conclusion

Even if doctors explain that the condition is innocuous and treatment ineffective, the GORD label increases parents' desire to medicate their crying baby.⁴⁴ An Australian study of the perspectives of 24 health professionals from 11 disciplines, who are experts in infant crying, reports their consensus view that unsettled infant behaviour is still commonly inappropriately medicalised and that many health professionals have significant knowledge gaps concerning management of this common yet complex problem.⁴⁵ This view is corroborated, for example, by Australian and international research demonstrating that even doctors and nurses with positive attitudes to breastfeeding have significant knowledge gaps concerning the identification and management of breastfeeding problems.^{46–49} Key informants emphasised the importance of early intervention for treatable problems such as feeding difficulty, in both breastfed and formula-fed unsettled babies, and of improved cross-professional communication.⁴⁵

The diagnoses of GORD and lactose intolerance in healthy crying infants are examples of delayed translation of research into practice. These diagnoses are linked with failure to identify and manage other contributing problems including feeding issues.⁵⁰ Due to the neuroplasticity of the neonatal brain, unmanaged feeding difficulties may quickly entrench cry-fuss problems in the short term. Aversive feeding behaviour in this neurodevelopmentally sensitive post-birth period may result in impaired mutual regulation of feeding and disrupted maternal–infant relations in the long term.^{28,29,51,52} Clinicians should adopt a 'both . . . and' approach: infant crying in the first few months

of life is self-limiting in most cases (and does not require treatment with PPIs, lactase or lactose-free formula), and families with crying babies require assessment and management of the various factors that interact and contribute to unsettled behaviours, including feeding problems, as early as possible.⁶

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Question 1

The following is a sign of gastro-oesophageal reflux disease (GORD) in infants in the first 3–4 months of life:

- Crying and fussing
Cry-fuss problems are not caused by acid-peptic GORD in well, afebrile babies in the first few months of life.
- Vomiting
Once serious underlying medical conditions are excluded, such as pyloric stenosis or food protein-induced enteropathy syndrome, frequent vomiting is normal infant behaviour and peaks at 4 months.
- Back-arching at feed-times or feeding refusal
Back-arching is an infant cue, not a signal of oesophageal discomfort or pain. Feeding refusal, whether breast or bottle fed, is a sign of feeding difficulty and requires assessment by a feeding expert.

- d. Crying when put down after a feed
Crying when put down after a feed is not a sign of oesophageal discomfort or pain.
- e. **Haematemesis**
Haematemesis may be a sign of gastro-oesophageal reflux disease in babies.

Question 2

Proton pump inhibitor use has NOT been linked with

- a. Lower respiratory tract infection in babies
Proton pump inhibitors (PPIs) increase the risk of lower respiratory tract infection in babies in the first year of life.
- b. **Hip fractures in babies**
Long-term PPI use has been associated with increased risk of hip fracture in adults, but no link has been demonstrated in infants.
- c. Withdrawal symptoms
Withdrawal symptoms such as rebound acidity and upper gastrointestinal tract symptoms are associated with abrupt cessation of PPIs in adults, and for this reason, gradual weaning off PPIs is advised for young infants.
- d. Increasing prevalence of food allergy
It is hypothesised that the dramatic increase in prevalence of food allergy over the past 20 years may be caused by PPI use because PPIs increase gastric pH, which inhibits the breakdown of larger proteins and increases gastric permeability, which increases the absorption of these undigested proteins, sensitising the immune system.

- e. Unidentified and unmanaged feeding difficulty
Randomised controlled trials and observational studies link cry-fuss problems with unidentified and unmanaged feeding problems.

Question 3

The following breastfeeding advice may predispose to functional lactose overload:

- a. Allow breastfed babies to have cluster feeds in the evening
Cluster feeds allow the baby to receive low-volume, high lipid, which increases satiety and decreases the risk of functional lactose overload.
- b. Pay attention to breast comfort when deciding which breast to offer
Feeding from one breast only over a prescribed number of hours may create other problems such as mastitis or low supply, so mothers should make decisions about which breast to offer by paying attention to breast comfort.
- c. **Always offer both breasts at each feed**
This may be necessary to establish good supply initially, but may also result in functional lactose overload in some babies. Functional lactose overload is resolved by individually tailored breastfeeding management.
- d. Allow 'comfort' sucking at the breast
'Comfort' sucking allows transfer of low-volume, lipid-rich milk. If the baby is requiring excessively long feeds, the mother and baby should be assessed for the quality of milk transfer and underlying feeding problems.
- e. Allow baby to finish at the breast
This is more likely to allow the baby adequate low-volume, lipid-rich breast milk.