

Lactase (Colief®), simeticone (Dentinox Colic Drops® and Infacol®) and gripe water in the management of infantile colic

This is one of a number of bulletins providing further information on medicines contained in the PrescQIPP DROP-List (Drugs to Review for Optimised Prescribing). This bulletin focuses on lactase (Colief®), simeticone (Dentinox Colic Drops® and Infacol®) and gripe water. It provides the rationale for restricting or stopping the supply of these products on NHS prescriptions, and advising parents of their limited roles in managing infantile colic.

Further bulletins, including the DROP-List¹ are available on the PrescQIPP website: www.prescqipp.info

Recommendations

- The most useful intervention for infantile colic is support for parents and reassurance that infantile colic will resolve. Only consider other remedies if parents feel unable to cope despite advice and reassurance.²
- Other remedies for infantile colic could include a trial of lactase (Colief®) or simeticone (Dentinox Colic Drops® and Infacol®). Treatment should be stopped if there is no response after one week.²
- Colief® is classified as a Borderline Substance.³
- Parents of infants that do not meet the ACBS approved indication (see main text for full criteria) should be advised to buy Colief® over the counter if they want to try it.
- They should be made aware that the evidence supporting Colief® is limited⁴⁻⁷ and should be given specific advice about how to use the product appropriately.
- Simeticone, in the form of Infacol® or Dentinox Colic Drops®, is readily available from pharmacies and other retail outlets.
- Parents wishing to try it should be advised to purchase it over the counter.
- They should be made aware that there is currently no convincing evidence that simeticone treatment helps^{8,9} but that some parents like to try it and assess their baby individually for signs of benefit.
- Gripe water should not be prescribed for infantile colic as it is not licensed for this condition^{10,11} and there are no clinical data to support using it.

Background

The PrescQIPP DROP-List is an accumulation of medicines that are regarded as low priority, poor value for money or medicines for which there are safer alternatives. There are also medicines which could be considered for self care with the support of the community pharmacist included on the DROP-List. Lactase (Colief®), simeticone (Dentinox Colic Drops® and Infacol®) and gripe water feature on the DROP-List as items which have limited clinical value and in many cases should be purchased over the counter.

Nationally over £1 million was spent on lactase (Colief®), simeticone (Dentinox Colic Drops® and Infacol®) and gripe water over the course of a year (ePACT February - April 2015). As with all prescribing, individual patient circumstances need to be borne in mind, however, with assistance from practice nurses, support from CCG medicines management teams and the experiences of CCGs that have already undertaken this work, it is hoped that practices will participate in realising the cost savings.

Rationale for restricting/stopping lactase (Colief®), simeticone (Dentinox® Colic Drops and Infacol®) and gripe water prescribing

Infantile colic

Infantile colic is defined for clinical purposes as repeated episodes of excessive and inconsolable crying in an infant that otherwise appears to be healthy and thriving.² NICE Guidance recommends that a baby who is crying excessively and inconsolably, most often during the evening, either drawing its knees up to its abdomen or arching its back, should be assessed for an underlying cause, including infant colic as an urgent action.¹² The condition can have significant impact on infants and their families, and some parents will consult a healthcare professional for advice.¹³

The underlying cause of infantile colic is unknown, but suggested mechanisms include:^{2,13}

- A transient intolerance to lactose or to the protein in cow's milk, leading to poor digestion of these compounds and excessive gas production.
- Gastrointestinal causes (e.g. gastro-oesophageal reflux).
- Abnormal gastrointestinal motility and pain signals from sensitized pathways in the gut viscera.
- An imbalance in the types of intestinal microflora present, influencing gut motor function and gas production.
- Parenting factors and behavioral issues have also been explored.

A range of different treatments has been suggested, targeting different potential causes of the condition. However, the lack of understanding about the cause of infantile colic presents problems for researching and developing treatments.¹³ A recent Drug and Therapeutics Bulletin states there are numerous issues with the methodological rigour of many intervention studies in this area. They advise taking a cautious approach in translating the outcomes of research to practical recommendations for managing infantile colic.¹³

Healthcare professionals, including GPs and health visitors, are a source of advice and support for parents of excessively crying babies.² NICE advise that healthcare professionals should reassure parents of babies with colic that the baby is not rejecting them and that colic is usually a phase that will pass. They state that parents should be advised that holding the baby through the crying episode, and accessing peer support may be helpful.¹² This is reflected in the Clinical Knowledge Summary (CKS) for infantile colic which says the most useful intervention for infantile colic is support for parents and reassurance that infantile colic will resolve.² CKS only advise considering other remedies if parents feel unable to cope despite advice and reassurance. They take a pragmatic approach in suggesting the following options:

- A 1-week trial of simeticone drops (breastfed or bottle-fed).
- A 1-week trial of diet modification to exclude cow's milk protein:
 - » For breastfed babies: dairy-free diet for the mother.*
 - » For bottle-fed babies: hypoallergenic formula.
- A 1-week trial of lactase drops (breastfed or bottle-fed).

They further advise that treatment should only continue if there is a response (such as the duration of crying shortens) and to consider trying another option if there is no response to one medical treatment.

*Breastfeeding mothers should take a calcium supplement if they are going to remain on a dairy-free diet long term.

CKS recommend seeking advice from a paediatrician if:

- The parents are not coping despite advice, reassurance, and primary care interventions.
- There is diagnostic doubt.
- The parents are unable to wean the child off treatment by the age of 6 months.

The use of both lactase and simeticone are considered in more detail below. Gripe water, which is not licensed for colic^{10,11} but has traditionally been used for it, is also considered.¹⁴

Please note, the following are beyond the scope of this bulletin and are covered in PrescQIPP B67. Appropriate prescribing of specialist infant formulae, available at:

<http://www.prescqipp.info/infant-feeds/viewcategory/217-infant-feeds>

- The use of low lactose/lactose free formulae for transient lactose intolerance.
- The management of potential cow's milk protein intolerance or allergy.

Lactase (Colief®)

Colief® is a dietary supplement containing the enzyme lactase, which is added to breast milk or infant formula to reduce its lactose content.¹⁵ GPs may be asked to prescribe it, by parents or other health care professionals, for the symptoms of infantile colic. Lactase use is based on the theory that some infants develop an intolerance to lactose, usually temporarily, due to a transient deficiency in lactase.⁴ Cow's milk protein allergy is a distinct condition to lactose intolerance and is managed differently.

There is some limited evidence from a few small studies that adding lactase to breast milk or infant formula to lower the lactose content may be of benefit if the lactase is given time to incubate in the milk before the feed is given.

A double-blind, crossover study in 10 bottle-fed infants gave cow's milk formula or breast milk that had been pre-treated (and then frozen) with lactase or placebo. No significant difference was detected between lactase and placebo for the percentage of days with colic or for the daily duration of colic.⁵

In another double-blind crossover study, 12 breastfed infants were given either lactase or placebo (directly into the infant's mouth) within 5 minutes of starting feeding. No significant difference was detected between treatments for mean duration of crying and fussing.⁶

A double-blind crossover study, funded by industry, gave 13 formula-fed infants milk pre-treated with lactase or placebo (added to the feed 24 hours before being fed to the infant). A statistically significant reduction of 1.14 hours in mean daily crying was found with lactase compared to placebo.⁷

A double-blind crossover study in 53 infants, funded and co-authored by industry, included both formula-fed and breastfed babies. Two drops of lactase (or placebo) were added to formula-feeds 4 hours before being given. If breastfeeding, mothers were instructed to express a small amount of milk before starting a feed and add four drops of lactase (or placebo) to the expressed milk. They breast fed as usual and gave the expressed and treated milk at the end of the feed. No statistically significant difference in crying time was found between lactase and placebo in the intention-to-treat analysis of those with available data (n=46). When 14 babies whose mothers were non-compliant were excluded from the analysis a statistically significant difference in the mean cry time between active and placebo was reported.⁴

The Department of Health (DH) recommend that formula feeds should be freshly made up as needed to reduce the risk of infection for the baby. They advise that feeds should only be made in advance and stored if there is no choice.¹⁶ The manufacturer of Colief® gives information on how to use the product in a way that is consistent with the DH advice¹⁷ and parents should be instructed to follow these directions. However it should be noted that studies that have shown any positive effect of lactase on colic symptoms have pre-treated the milk of formula-fed infants with lactase in a way that can not be recommended currently.

Colief® is not a licensed medicine, but rather a dietary supplement. It has been classified as a Borderline Substance, and can be prescribed on an NHS prescription (prescription must be endorsed 'ACBS') only in the following circumstances:

*'For the relief of symptoms associated with lactose intolerance in infants, provided that lactose intolerance is confirmed by the presence of reducing substances and/or excessive acid in stools, a low concentration of the corresponding disaccharide enzyme on intestinal biopsy or by breath hydrogen test or lactose intolerance test.'*³

Where the ACBS criteria are not met, parents should be advised to purchase Colief® if they wish to try it. They should be made aware that the evidence supporting its use is limited, and be given specific advice about how to use the product appropriately.

Simeticone (Dentinox Colic Drops® and Infacol®)

Simeticone (activated dimeticone) is an antifoaming agent. It is licensed for infantile colic but the BNF for Children states that evidence of benefit is uncertain and annotates the available products (Infacol® and Dentinox Colic Drops®) as preparations less suitable for prescribing.³

Its use in colic is based on the theory that symptoms are caused by gas in the intestine;^{18,19} the antifoaming action is intended to cause gas bubbles to coalesce to make them easier to eliminate.¹⁹

Studies of simeticone have not demonstrated benefit in infantile colic.²

- Out of 3 randomised controlled trials of simeticone for the treatment of colic, only 1 small study of 26 infants (with methodological limitations) showed any possible benefit. The simeticone group had significantly fewer crying attacks on days 4 to 7 of therapy compared with placebo. The 2 other trials (n=27 and n=83) found no significant difference between simeticone and placebo.^{2,8}
- A systematic review rated the methodological quality of the same three studies, and also pooled their data in a meta-analysis. The one study showing a positive benefit of simeticone versus placebo was rated of insufficient quality. The pooled data did not show a significant difference between simeticone and placebo, which did not change when only trials of sufficient quality were analysed.⁹ A more recent systematic review similarly concluded that the evidence did not support simeticone treatment for infantile colic.²⁰

CKS suggest considering a 1-week trial of simeticone, despite the lack of evidence to support efficacy. This is on the basis that as a placebo it may still be worth a try as it is licensed for the indication and unlikely to cause adverse effects. They state that the simple act of being able to give their baby something may help parents cope better with the crying.²

Both Infacol® and Dentinox Colic Drops® are readily available from pharmacies and other retail outlets. If a trial of simeticone is felt to be appropriate, parents should be advised to purchase it over the counter. They should be made aware there is currently no convincing evidence that the treatment helps but that some parents like to try it and assess their baby individually for signs of benefit.

Gripe water (or gripe mixture)

Gripe water is a traditional remedy which varies in exact constituents, but generally includes sodium bicarbonate with or without essential oils such as dill or fennel.¹⁴ Gripe water has traditionally been used for colic,¹⁴ although it is not licensed for this indication.^{10,11} For example, Woodward's Gripe Water – Alcohol Free & Sugar Free® (which contains sodium bicarbonate and terpenless dill seed oil) is licensed for the symptomatic relief of distress associated with wind in infants up to one year old.¹⁰

The use of gripe water is not supported by clinical trial evidence,²¹ and its use in infants has been questioned by some.²²

It should be noted that gripe water has a significant sodium content. Infants aged seven to twelve months should receive no more than 1g salt daily and infants of six months and under should receive less than 1g daily, which corresponds to approximately 16.7mmol of sodium.²³ Potential sodium intake is illustrated in the two examples on the following page.²³

Product	Approximate sodium content	
	Per 5ml dose*	Per maximum daily dose*
Boots Gripe Mixture 1 Month Plus liquid®	0.6mmol	7.2mmol
Woodward's Gripe Water – Alcohol Free & Sugar Free®	0.7mmol	8mmol

*Consult the relevant product information for dosing information.

Gripe water is not licensed to treat infantile colic and there are no clinical data to support using it in this condition, therefore prescribing is not recommended and should stop. Parents who want to try gripe water for their child's colic should be given support and advice on more appropriate ways to manage infantile colic. If they still wish to try it they should be offered appropriate advice for safe usage.

Key points

- Where a diagnosis of infantile colic has been made, the most useful intervention is support for parents and reassurance that the condition will resolve.²
- Several remedies are available which target different suggested causes of infantile colic. Some of the treatments may be worth a trial in some circumstances, but they should be discontinued if no benefit is seen.²
- Colief® is a dietary supplement (not a licensed medicine) containing lactase. There is limited evidence that adding lactase to breast milk or infant formula to lower the lactose content may be of benefit if the lactase is given time to incubate in the milk before the feed is given.
- Colief® is classified as a Borderline Substance.³ Parents of infants that do not meet the ACBS approved indication should be advised to buy Colief® over the counter if they want to try it.
- Parents should be made aware that the evidence supporting Colief® is limited, and should be given specific advice about how to use the product appropriately.
- Simeticone is an antifoaming agent that is the active ingredient in Infacol® and Dentinox Colic Drops®. Both are licensed medicines for use in infantile colic.³
- Studies of simeticone have not demonstrated benefit in infantile colic.
- If a trial of simeticone (Infacol® or Dentinox Colic Drops®) is felt to be appropriate, parents should be advised to purchase it over the counter. They should be made aware that there is currently no convincing evidence that the treatment helps but that some parents like to try it and assess their baby individually for signs of benefit.
- Gripe water should not be prescribed for infantile colic as it is not licensed for this condition^{10,11} and there are no clinical data to support using it.

Costs

The costs of Colief®, Dentinox Colic Drops® and Infacol® are listed for comparison in table 1.

Table 1: Lactase and simeticone products price comparison³

Product	Cost per pack	Amount used per dose	Estimated cost per dose (pence)
Colief®	7ml = £8.40	2 to 4 drops	10.5p to 21p*
Dentinox Colic Drops®	100ml = £1.73	2.5ml	4.3p
Infacol®	50ml = £2.71	0.5 – 1ml	2.7p to 5.4p

*Based on manufacturer's estimate of 160 drops per pack²⁴

Savings

Nationally over £1 million was spent on lactase (Colief®), simeticone (Dentinox Colic Drops® and Infacol®) and gripe water over the course of a year (ePACT February - April 2015).

Prescribing 80% less of these products would save almost £811,000 in England over 12 months. This equates to savings of £1,421 per 100,000 patients.

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Additional PrescQIPP resources



Briefing



Data pack



Implementation resources

Available here: <http://www.prescqipp.info/resources/viewcategory/337-infantile-colic-drop-list>

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Non-subscriber publication October 2015.

At the time of publication the PrescQIPP NHS Programme was hosted by Papworth NHS Trust and the Eastern Academic Health Science Network.

Contact help@prescqipp.info with any queries or comments related to the content of this document.

This document represents the view of PrescQIPP CIC at the time of publication, which was arrived at after careful consideration of the referenced evidence, and in accordance with PrescQIPP's quality assurance framework.

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