Infantile Colic: Recognition and Treatment

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Clinical Presentation and Prevalence of Infantile Colic

Infantile colic (IC) is a syndrome characterized by paroxysms of irritability and inconsolable crying and screaming, accompanied with associated motor behaviors such as clenched fists, drawn-up legs, and a red face.[1] During the crying episodes, infant is generally inconsolable, which can be severely distressing for the parents.[2] Hence, 10–20% of pediatrician visits of infants aged 2 weeks to 3 months is due to IC. Presentation of IC is usually seen in the second or third week after birth, and it peaks at 5 to 8 weeks of age.[1] A plethora of studies have shown the prevalence of IC to be between 2% and 73% depending on study design, definition of colic, and method of data collection.[3,4] For infants younger than 12 months of age, the prevalence is estimated between 2%- 73%. Additionally, occurrence of infantile colic in the first 3 months of life may range from 3% to 28% as shown by prospective studies and from 8% to 40% based on retrospective studies. Although IC usually resolves spontaneously by 4 months of age, it may have certain negative consequences as shown in Box 1.[5,6]

Diagnostic Criteria

The currently used diagnostic criteria for IC are the Rome IV criteria, which include:[7]

- Paroxysms of irritability with fussing or crying that start and stop without obvious causes
- No evidence of failure to thrive, fever, or illness in infants from birth to 5 months of age
- Symptoms lasting ≥3 hours a day and occur ≥3 days a week for ≥1 week
- A prospective behavior diary should be maintained by parents that confirms that the total crying/fussing time was ≥3 hours in any 24-hour period.

Box 1: Adverse outcomes associated with infantile colic

- A disturbed parent–infant interaction
- Child abuse leading to neurologic morbidity and mortality
- Recurrent abdominal pain
- Migraine
- Allergy
- A trigger for shaken baby syndrome
- Hyperactivity
- Learning problems
- Development of postpartum depression in mothers
- Feeding changes
- Medication use
- Pediatrician or emergency department visits
- Hospitalization
- Loss of parental working days

Adapted from: 1. Steutel NF, Benninga MA, Langendam MW, *et al*. Developing a core outcome set for infant colic for primary, secondary and tertiary care settings: a prospective study. *BMJ Open*. 2017; 7:e015418. **2.** Gelfand AA. Infant Colic. *Seminars in pediatric neurology.* 2016;23(1):79-82.

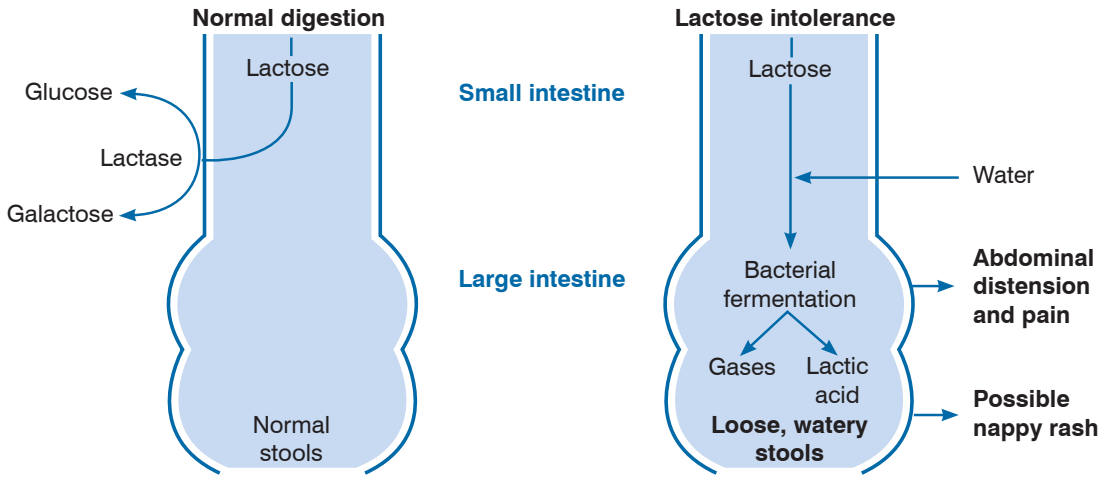
Etiology and Pathogenesis

The pathophysiology of infant colic is incompletely understood, and has been credited to various factors such as:

1. Lactose Intolerance

Lactose is a disaccharide sugar that is abundant in mammalian milk. It is naturally metabolized by the enzyme lactase in the mucosal brush border of the intestine into absorbable sugars, namely glucose and galactose.[8] Hence, a diminution in intestinal lactase activity results in malabsorption of lactose. Lactose malabsorption results in significant accumulation of lactose in the colon, thereby acting as a substrate for gut bacteria such as lactobacilli and bifidobacteria.[9] Bacterial fermentation of lactose results in rapid production of hydrogen and lactic acid which incurs various deleterious effects. Non-digested lactose creates an osmotic load that draws fluid and electrolytes into the intestinal lumen, resulting in loose stools or osmotic diarrhea.[9,10] In addition, the hydrogen gas also distends colon resulting in pain.[9] However, not all lactose malabsorption results in lactose intolerance. In actual fact, only about one-third to half of lactose maldigesters are also intolerants.[11] Development of lactose intolerance depends largely on the rate and quantity of lactose reaching the colon and the type of colonic flora.[8,12] Pathophysiology of lactose intolerance is shown in Figure 1.

Figure 1: Pathophysiology and symptoms of lactose intolerance



Adapted from: 1. Bhatnagar S, Aggarwal R. Lactose intolerance. *BMJ : British Medical Journal*. 2007;334(7608):1331-1332. **2.** Mattar R, de Campos Mazo DF, Carrilho FJ. Lactose intolerance: diagnosis, genetic, and clinical factors. *Clinical and Experimental Gastroenterology.* 2012;5:113-121. **3.** Misselwitz B, Pohl D, Frühauf H, Fried M, Vavricka SR, Fox M. Lactose malabsorption and intolerance: pathogenesis, diagnosis and treatment. *United European Gastroenterology Journal*. 2013;1(3):151-159.

Types of Lactose Intolerance

Lactase deficiency may be classified as primary, secondary, congenital, and developmental.[8]

a) Primary Lactase Deficiency

Primary lactase deficiency is relative or absolute absence of lactase that develops in childhood at various ages and is the most common cause of lactose malabsorption prevalent in approximately 70 % of world population. In primary lactase deficiency, a physiological decline in lactase concentrations occurs at the age of weaning.[10] In babies there may not be enough of naturally occurring lactase enzyme to digest milk (including both breast milk and baby formula derived from cow's milk). Expression or production of lactase becomes normal by age of 4 to 6 month. In situations of overfeeds, lactose overload may also contribute to lactose intolerance.[13,14]

Box 2: Etiological factors contributing to development of secondary lactase deficiency

- Celiac disease
- Gastroenteritis
- Persistent diarrhea
- Crohn's disease
- Acute infections (such as rotavirus) or parasitic infection (giardiasis or cryptosporidiosis)
- Small bowel overgrowth
- Cancer chemotherapy
- Post bowel surgery

Adapted from: 1. Heyman MB; Committee on Nutrition. Lactose intolerance in infants, children, and adolescents. *Pediatrics.* 2006 Sep;118(3):1279-86. **2.** Usai-Satta P, Scarpa M, Oppia F, Cabras F. Lactose malabsorption and intolerance: What should be the best clinical management? *World Journal of Gastrointestinal Pharmacology and Therapeutics.* 2012;3(3):29-33.

b) Secondary Lactase Deficiency

This type of deficiency can present at any age but is more common in infancy. It generally occurs secondary to infections or diseases that may cause small intestinal injury. Various etiological factors contributing to secondary lactase deficiency are listed in Box 2.[10,11] These conditions deplete the lactase-containing epithelial cells from the tips of the villi.[10] The epithelial cells that replace these areas are immature and lack lactase, leading to secondary lactase deficiency and lactose malabsorption. Moreover, young malnourished infants are highly susceptible to small intestinal atrophy that also results in deficiency of lactase.[10]

c) Congenital Lactase Deficiency

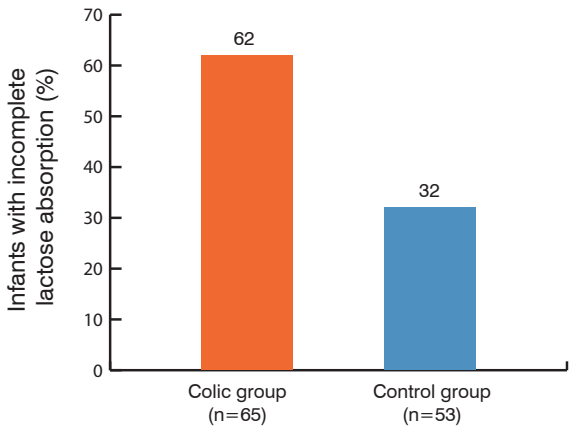
Congenital lactase deficiency is a single autosomal recessive disorder which is extremely rare and affects newborn infants. It presents with intractable diarrhea as soon as human milk or lactose-containing formula is introduced. Affected infants have minimal or absent lactase in an otherwise normal intestinal mucosa. Unless recognized and treated quickly, the condition is life-threatening because of dehydration and electrolyte losses.[8,10]

d) Developmental or Transient Lactase Deficiency

This type of lactase deficiency is commonly seen in infants born prematurely.[15] The immature gastrointestinal tract, until at least 34 weeks' gestation, is deficient of lactase and other disaccharidases.

The infants suffer from this problem only for a short time after they are born (about 3-4 months) as there is natural increase in the production of lactase enzyme with maturity, which eventually make them grow out of lactose intolerance symptoms and its colic.

Figure 2: Number of infants with incomplete lactose absorption (breath hydrogen concentration > 20ppm)



Adapted from: Miller JJ, McVeagh P, Fleet GH, Petocz P, Brand JC. Breath hydrogen excretion in infants with colic. *Archives of Disease in Childhood*. 1989;64(5):725-729.

Infant Colic Due to Lactose Intolerance: Breath Hydrogen Response

Infantile colic with lactase deficiency causes carbohydrate malabsorption which leads to an increase in the gut fermentation of the undigested carbohydrate, resulting in elevated levels of hydrogen excreted in the breath. Studies have shown remarkably greater breath hydrogen values in colicky infants as compared to non colicky infants.[16,17] As per a study done by Moore *et al*, approximately 78% of colicky infants show signs of lactose Intolerance (positive breath H_2 tests) at 6 weeks and 89% at 12 weeks. Additionally, transient lactose Intolerance was shown to occur due to deficiency of lactase enzyme in small intestine at birth.[16] Miller *et al* investigated breath hydrogen as an index of incomplete lactose absorption in 118 infants, 65 of which had colic and 53 were controls. Infants were either breast fed or given a formula feed containing lactose. Breath samples were collected using a face mask sampling device preprandially, and 90 and 150 minutes after the start of a feed. Study results showed significantly higher breath hydrogen concentration in colic group (29 ppm) as compared to control group (11 ppm). The percentage of infants with incomplete lactose absorption (breath hydrogen concentration > 20 ppm) in the colic group was significantly higher as compared to the control group (Figure 2).[17] The breath hydrogen test thus provides a sensitive, reliable and semi quantitative index of incomplete carbohydrate absorption.

2. Colonic Microflora

Abnormal colonic microbial flora result in increased nutrient fermentation and reduced levels of dehydroxylated bile acids in the colon.[1] Additionally, early increased levels of pathogenic bacteria and reductions of lactobacilli, bifidobacteria or butyrate-producing bacteria produce intestinal pain and inflammation in the infant, in turn causing excessive crying. Studies have shown more frequent colonization with *E.coli* and other coliform bacteria and lower counts of lactobacilli in infants with colic symptoms compared with children not suffering from colic.[18,19]

3. Gastrointestinal Immaturity

Immaturity of the enteric nervous system during development, particularly during the first few weeks of life may cause abnormal motor and sensory functions of the intestine leading to intestinal hypermotility in infants with colic.[1,9]

4. Psychosocial Factors

The occurrence of colic has been associated with an irritable and hypersensitive infant. Studies have attributed an inadequate infant-family relationship or parental anxiety as causes of development of IC.[1]

5. Food Hypersensitivity

Allergens like wheat, cow's milk, peanuts and eggs stimulates mucosal immune responses and mucosal IgE containing plasma cells in infants with colic.[9] Cow's milk given as a formula or used by the lactating mother has been found to result in excessive and unexplained crying by healthy infants, commonly in the evenings.[20]

6. Poor Feeding Technique

7. Maternal Smoking[21]

8. Gut Hormones (increased ghrelin and motilin)

Current Approaches to Management

A stepwise approach to the management of infantile colic is shown in Figure 3.[14]

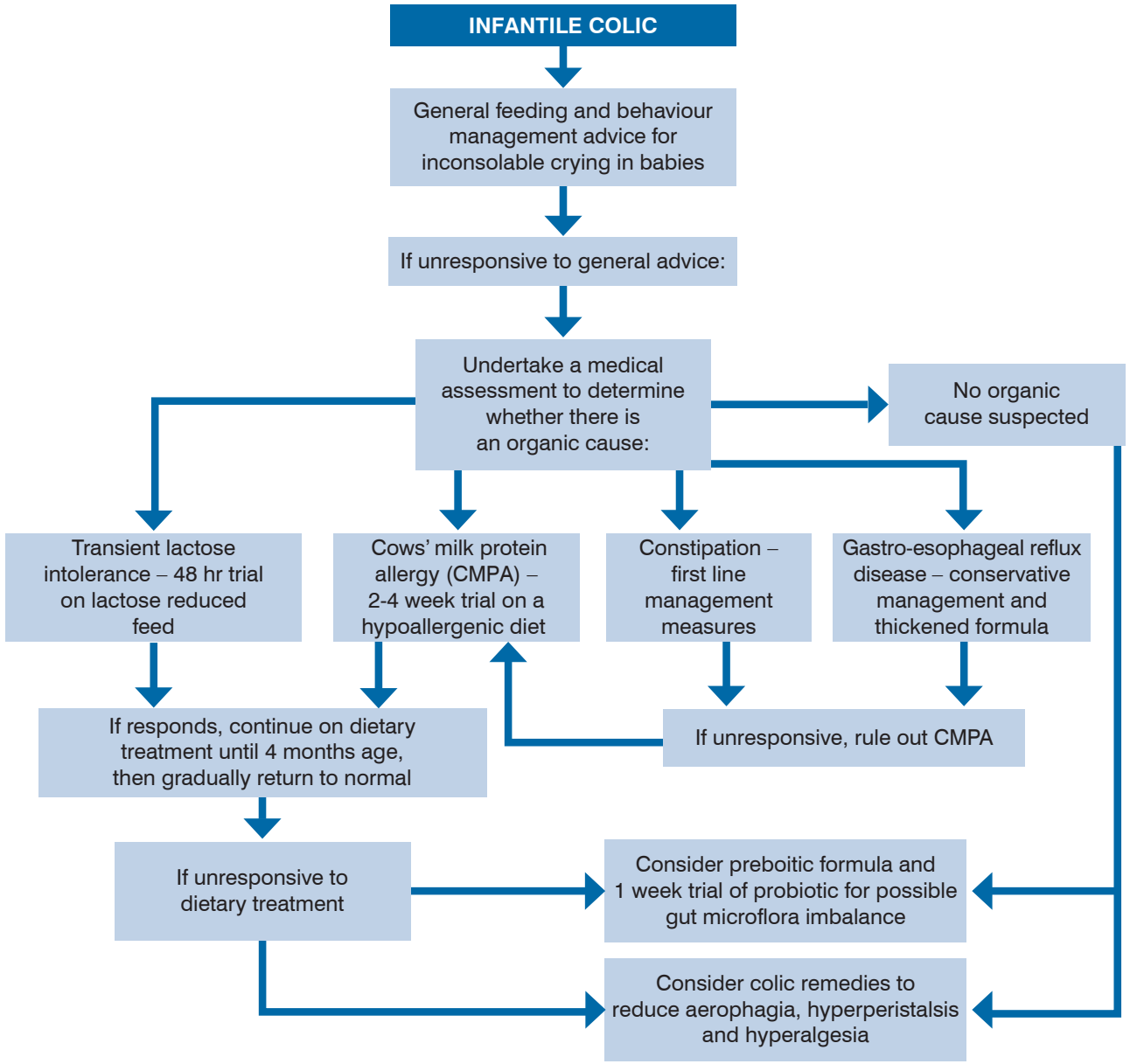
1. **Parental reassurance** and support is vital for effective management of infantile colic. Parents should be educated about the benign and self-limited nature of colic, and offer resources for support.[21] Additionally, early response to crying, sucking on a pacifier, using eye contact and interactive playing may be useful behavior modification therapy.[9]

2. **Dietary modifications** by avoiding potential allergens like cow's milk, egg, peanuts and wheat, may decrease the occurrence of infantile colic and is recommended in breast fed infants with colic.[9]

3. **Pharmacological alternatives** for the management of infantile colic are shown in Table 1.

4. **Management of lactose intolerance: Role of lactase enzyme:** Management of lactose intolerance is individualized based on the type of intolerance. A flow chart for the therapeutic management of lactose

Figure 3: A stepwise approach to management of infantile colic



Adapted from: Waddell L A. Management of infantile colic: an update. *The journal of family health care.* 2013; 23(3):17-22.

malabsorption is shown in Figure 4.[22] In general practice, for infant colic, it may not be feasible to go for test like H-2 breath test, stool acidity test etc. to exclude lactase deficiency as a reason or cause. Hence NICE (The National Institute for Health and Care Excellence) recommends that after excluding any organic cause of colic e.g. esophageal reflux, constipation, infectious intestinal lesions etc, lactase drops should be used before each feeding till a week. If the symptoms improve (lesser crying), then lactase can be given till 4-6 months of infancy. After 4-6 months, production of sufficient amount of lactase resumes.[23] After this period use of lactase drops should be gradually tapered off. Additionally, lactase drops can also be used to aid lactose digestion in infants and children with lactase deficiency due to secondary causes. Lactase activity returns to normal following healing of damaged epithelium i.e. between 6 to 8 weeks.

Clinical Studies on Lactase Enzyme Supplementation

A number of studies have validated the efficiency of lactase enzyme supplementation for colicky infants.[24,25] One such study was conducted by Kanabar *et al*, wherein 53 infants with colic were either treated with placebo or pre-incubated lactase feed. Study results showed that the total crying time and breath hydrogen levels were at least 45%

Table 1: Therapeutic alternatives for the management of infantile colic	
Therapeutic options	**Clinical remarks**
Lactase enzyme	This therapy has shown significant reduction in crying time and the levels of breath hydrogen[1]
Simethicone	No proper definition of colic or details on how cases were selected in the study available[1]
Dicycloverine, dicyclomine	Treats colic; however, associated with serious adverse effects. Therefore, dicyclomine is contraindicated in infants below 6 months of age[1]
Cimetropium bromide	Infants treated with cimetropium bromide have shown reduction in crying duration, in comparison to placebo[2]
Probiotics	Multiple studies have shown a reduction of average crying time to less than 3 hours a day with probiotics' use[3]
Hydroxyzine hydrochloride	This therapy suppresses exaggerated response to stimuli and demonstrates skeletal and smooth muscle hypotonic effect. Trials validating its use in infantile colic are lacking[4]
Decreased stimulation	For example- quiet room, associated with substantial improvement. However, study was biased as infants without true colic were also enrolled[1]
Hypoallergenic diet	Alleviates symptoms; however, a large drop-out rate has been reported in the hypoallergenic milk group[1]
Herbal tea	Eliminates colic. There is lack of data on its tolerability profile and infants may consume large amount of tea in place of milk[1]
Hydrolyzed whey formula	Findings suggest about 25% reduction in duration of symptoms.[1]

Adapted from: 1. Kanabar D. Current treatment options in the management of infantile colic. *Prescriber*. 2008;19(7):24–8. **2.** Biagioli E, Tarasco V, Lingua C, Moja L, Savino F. Pain-relieving agents for infantile colic. *Cochrane Database of Systematic Reviews* 2016, Issue 9. Art. No.: CD009999. **3.** Anabrees J, Indrio F, Paes B, AlFaleh K. Probiotics for infantile colic: a systematic review. *BMC Pediatrics*. 2013;13:186. **4.** Kopel HM. Hydroxyzine as a pre-operative sedative: a double blind study with apprehensive children. *Anesthesia Progress*. 1971;18(6):127-133.

Summarizing Benefits of Lactase (Yamoo) Drops

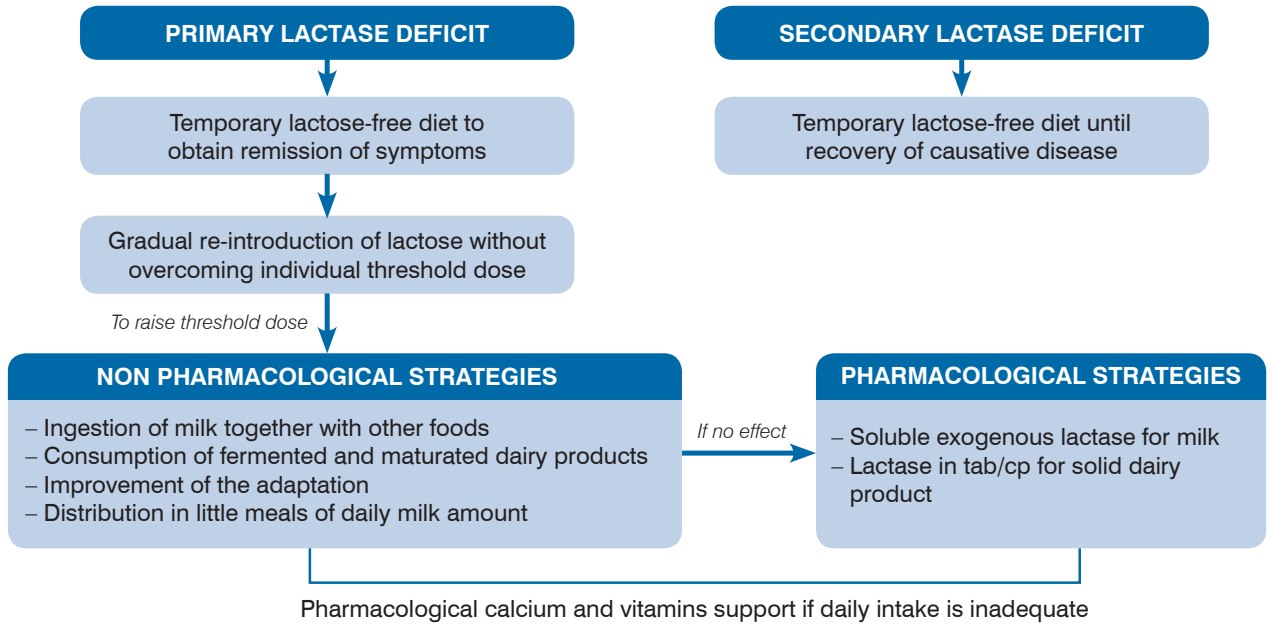
- Recommended as per International Guidelines (NICE guidelines)
- Generally Recommended As Safe (GRAS) – Natural Enzyme Food Supplement (In India approved by FSSAI-Food safety and Standard Authority of India, In Europe by EFSA-European Food Safety Authority)
- Relieves symptoms of infantile colic like excessive crying (by 45%)
- Improves parent and child bonding, parental care and reduces risk of child abuse
- In Rotaviral and other GI infections, reduces diarrhea and colicky symptoms (due to transient lactose intolerance), enabling improved nutritional intake
- Easy to use, great tasting natural supplement that promotes mother's milk (and can also be used with formula feeds)
- Yamoo (Lactase) is derived from *Aspergillus Oryzae*. This source is best and is recommended by all food regulatory body, both in India and in International countries (FSSAI in India and EFSA in Europe. In US too regulatory bodies like USFDA recommends this source as GRAS
- Yamoo drop is ph independent. It is safe and natural way to prevent infant colic and symptoms of lactose intolerance.

lower in the treatment group as compared to the placebo group.[24] Another randomized, double blind crossover trial of lactase and placebo drops was done in 13 babies who were randomly allocated to add either lactase or placebo drops to their formula feeds for 1 week, followed by 2 days 'wash out'. In the second week, the addition was changed so that subjects served as their own control. The formulas were refrigerated for 24 hours prior to ingestion and the parents were asked to maintain a diary of their crying time. A significant reduction in crying time (1.14 h/day) was seen with lactase as compared to placebo.[25]

Conclusion

In conclusion, infantile colic, typically manifested as excessive crying in infants, is a severely distressing condition for parents and a leading cause for pediatrician visits. Its etiology has not been completely understood, however, majority of infants develop colic due to lactose intolerance. Lactose malabsorption results in significant accumulation of lactose in the colon, which are fermented by bacteria resulting in rapid production of hydrogen and lactic acid that incurs various deleterious effects. Additional causes include abnormal colonic microbial flora, gastrointestinal immaturity and psycosocial factors among others. Lactase supplementation in addition to parental reassurance is an effective strategy for management of infantile colic. Studies have demonstrated that lactase when given with feeds reduces crying time by 45%. Lactase supplementation can be continued till 4 months during infancy, subsequent to which the babies may start producing sufficient amount of lactase.

Figure 4: Therapeutic management of lactose malabsorption



Adapted from: Montalto M, Curigliano V, Santoro L, *et al.* Management and treatment of lactose malabsorption. *World Journal of Gastroenterology : WJG.* 2006;12(2):187-191.

Method of Administration of Yamoo Drops

- Yamoo Bottle is of 15 ml. Each 1 ml contains lactase enzyme 600 FCC units

Dosage of Drops in Infants

- *Direction I (for Breast feed):* Add 4 to 5 drops of Yamoo Drops to few ml of expressed breast milk. The foremilk contains most of the lactose. Hence we recommend waiting only for few minutes and then giving this mixture to baby and then breastfeed as normal. (This method forms a "coating" for the baby's digestive system which allows the remaining breastmilk to be digested normally)
- *Direction II (for formula/ animal's milk feed):* Add 4 to 5 drops of Yamoo Drops to infant formula, when it is warm (30°C to 40°C). Add 4-5 drops of Yamoo Drops to infant's feed containing lactose/milk when it is warm (30°C to 40°C), mix well and then feed the baby.

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