

Review Article



Functional Gastrointestinal Disorders in Infancy: Impact on the Health of the Infant and Family

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Conflict of Interest

The authors have no financial conflicts of
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ABSTRACT

Functional gastrointestinal disorders (FGIDs) such as infantile colic, constipation and colic occur in almost half of the infants. The aim of this paper is to provide a critical and updated review on the management of FGIDs and their impact on the health of the infant and family to health care physicians. Guidelines and expert recommendations were reviewed. FGIDs are a frequent cause of parental concern, impairment in quality of life of infants and relatives, and impose a financial burden to families, health care, and insurance. Therefore, primary management of the FGIDs should be focused on improving the infants' symptoms and quality of life of the family. If more than parental reassurance is needed, available evidence recommends nutritional advice as it is an effective strategy and most of the time devoid of adverse effects. The role of healthcare providers in reassuring parents and proposing the correct behavior and nutritional intervention by avoiding inappropriate use of medication, is essential in the management of FGIDs.

Keywords: Constipation; Functional gastrointestinal disorders; Infant; Infantile colic; Nutrition therapy; Gastro-esophageal Reflux

INTRODUCTION

Functional gastrointestinal disorders (FGIDs) cause distress to infants and parents and lead to a cascade of infant and parental discomfort, repetitive consultations with health care providers, frequent changes in milk formula and other costly non-pharmacological treatments [1]. Doctors often recommend medications without proven efficacy, which possibly induce adverse reactions. Furthermore, parents seek help from family members, friends, and social media exchanges, which are often inappropriate.

This review is intended to provide a comprehensive literature overview of the impact of FGIDs on individuals and society.

At birth, the microbiota, nervous and immune systems in the gastrointestinal (GI) tract exist in the immature state. Generally, FGIDs are categorized into 7 different groups: infant regurgitation, infant colic, functional constipation, functional diarrhea, cyclic vomiting syndrome, infant dyschezia, and infant rumination syndrome. The diagnosis of a functional

disorder virtually eliminates the organic disease as a cause of the symptoms, and is, in principle, a diagnosis made by elimination of organic disease.

From birth to six months of age, approximately one infant out of 2 develops at least one FGID or related signs and symptoms [2-4]. Regurgitation, infantile colic, and functional constipation are the most common FGIDs in infancy. Functional diarrhea, dyschezia, rumination syndrome, and cyclic vomiting syndrome occur less frequently. Over 50% of the infants present with more than one FGID [6].

METHOD

Guidelines and position papers, along with Embase, MEDLINE and the Cochrane database of the last 10 years were reviewed and adapted with the intention to develop a practical approach and management of regurgitation, colic, and constipation in infants for health care providers.

Family life and economic impact

The impact of the symptoms of FGID varies from mild to extremely distressing for both the infant and parents. The symptoms may cause parental anxiety, poor quality of life, short and long-term health consequences, shortened duration of full breastfeeding, numerous changes in the formula, medical consultations, and associated significant healthcare costs [1-6].

The interaction between parent and infant, particularly father-infant, has been reported to be less optimal in the presence of an FGID. Also, the interaction between the parents is more often dysfunctional compared to control families [7]. Infantile colic has been associated with postpartum maternal depressive symptoms and insecure mother-child-bonding [8]. For these reasons, any medical consultation should include assessment of the management of the family and level of anxiety in conjunction with a complete physical examination [9]. All FGIDs and excessive crying, in particular, are extremely distressing and have been associated with behavioural disturbances and even infantile abuse.

FGIDs have a significant impact on personal and public healthcare expenses, because of huge consultation fees of health care professionals, drug prescriptions, over-the-counter or home remedies, use of special milk formulas and prolonged diet, and loss of income due to absenteeism from work [10].

In the USA, in the past 5 years (2006–2011), the national cost for constipation-related emergency department visits experienced an increase to \$1.6 billion (121%), and the highest number of visits was for the infant's group [11]. In the UK, the total annual cost to the National Health Service for the purposes of infant crying and sleeping problems in the first 12 weeks after birth is estimated at £65 million [12]. However, the cost of the management of FGIDs in infants was calculated at £72.3 million per year [1].

Diagnostic criteria

Diagnostic criteria for FGIDs based on international consensus were first published in 1989. The Rome criteria have been updated regularly (most recently in 2016) and include infantile FGIDs [9].

Etiology at a glance

When parents consult a health care specialist, they expect information on the cause of the referral symptoms. However, it is more obvious to provide a comprehensive explanation in case of an organic disease than in the case of an FGID. It is not easy to explain to a parent (and also for a parent to accept) that everything is normal and functional, transient and often auto-resolving in the presence of infant distressing symptoms.

In cases of reflux and regurgitation, provoking factors include over-amounts of feeding over a short period of time, reduced length of the intra-abdominal esophagus, the obtuse angle of His, prolonged horizontal feeding, and incorrect postprandial position [13]. Both GI and behavioral hypotheses contribute to colic [14,15]. GI hypotheses involve immaturity of gut function such as dysmotility, dysbiosis, gut hormones, and food hypersensitivity or allergy. Behavioral hypotheses include inadequate parent-infant interaction, maternal anxiety, and difficult infant temperament. To convince the parents that crying does not always reflect pain releases the caregiver of the feeling of inadequacy parental care and fear for the disease. Hypotheses regarding functional constipation include family predisposition and dietary factors such as the formation of calcium soaps, insufficient fiber intake, and liquid intake [16,17].

Management of FGIDs

Parents of infants with FGIDs are understandably keen to find a quick and easy solution and will often opt for medication hoping for rapid relief from symptoms [18]. The new era of social media-induced parental expectations for instant solutions have placed healthcare professionals under high pressure (often unneeded), given importance to investigations or recommended pharmacological treatments which are likely to bring little benefit in the absence of disease with possible adverse effects [19]. There is a widespread overuse of medication in the management of FGIDs such as regurgitation and infantile colic [18,20,21]. The cornerstone of the management of FGIDs in infants is parental reassurance, anticipatory guidance, education on natural evolution and different contributing factors, and adequacy of nutrition. Nutritional advice (feeding technique, volume and frequency, and change in the formula) can also be considered and should always stress the benefits of breastfeeding and offer appropriate support to continue breastfeeding. Overfeeding, especially in formula-fed infants, is a frequent cause of infant distress.

Management of regurgitation

Regurgitation is very common in infancy and usually improves spontaneously within the first year after birth. A full medical history and physical examination with anthropometry will rule out alarming or warning signs indicative of organic disease (**Fig. 1**).

The most important warning signs are severe vomiting, irritability, crying, fussiness, feeding problems, atopic dermatitis, constipation, diarrhea, failure to thrive, hematemesis, back arching, Sandifer syndrome, neurological abnormalities and/or neurodevelopmental delay. Physiological regurgitation should not be diagnosed in infants with vomiting and poor weight gain or abnormal physical examination [19,22]. More than half of the infants regurgitate daily and 20% of them are reported to do that more than 4 times per day. Physiologic regurgitation does not start before the age of one week or after the age of six months. Apparently, the main goal of management is to provide effective parental reassurance endorsed by symptom relief with thickened feeds in formula-fed infants while avoiding adverse effects of the drug management and complications of the regurgitations [9].

Infant with regurgitation/suspicion of GERD

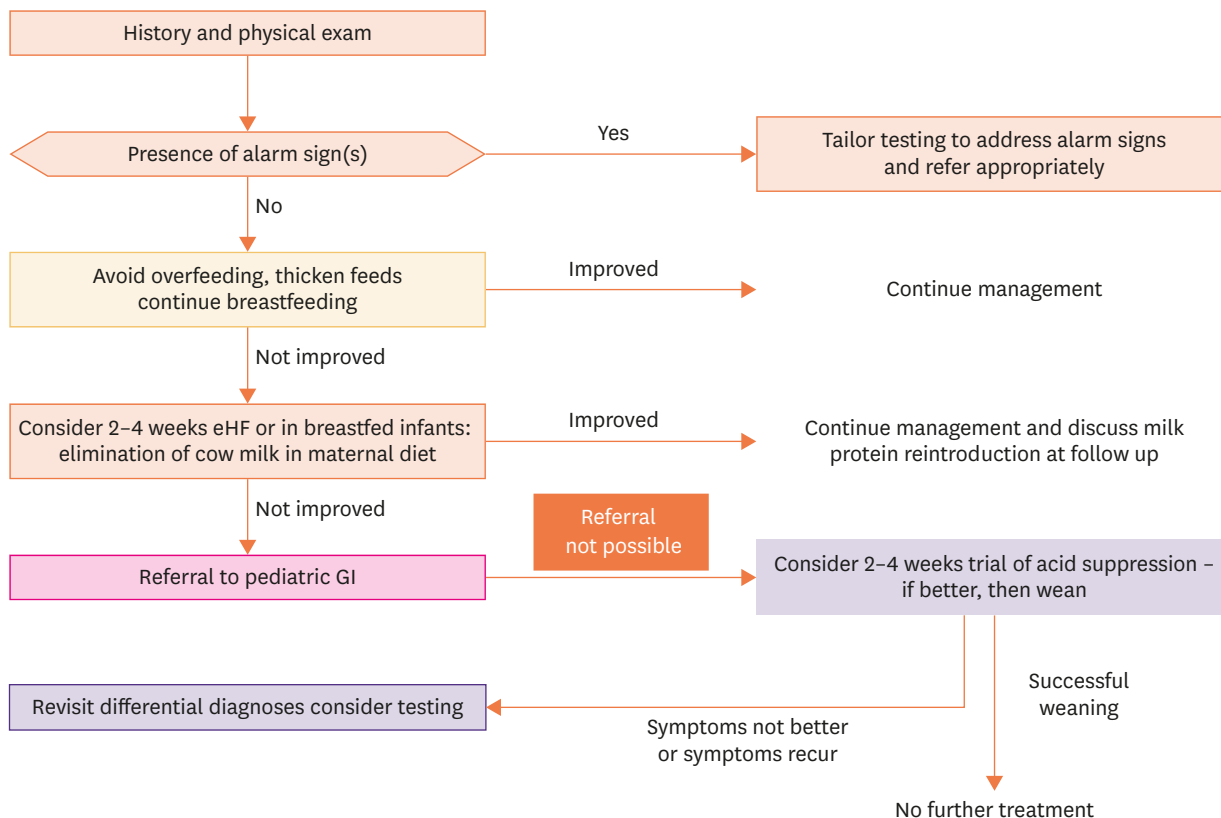


Fig. 1. Management of regurgitation.
GERD: gastroesophageal reflux disease, GI: gastroenterologist.

Special attention should be given to volume, as many infants drink too large volumes; also, the duration of feeding should be given importance as too fast or too slow may distress the infant. Medication and investigations are not required in the management of uncomplicated regurgitation. If the infant is in a very distressed state, mainly after a feeding or between the feeds, treatment with alginate may be given a chance [23]. A survey in Italy revealed that 56% of general pediatricians prescribe proton pump inhibitors for infants with gastroesophageal reflux (GER) symptoms associated with unexplained crying and/or irritability, and 38% of the pediatricians prescribe PPI in infants with uncomplicated recurrent regurgitation and vomiting [24]. According to a report from New Zealand, off-label prescription of proton pump inhibitors in infants is a common practice: 5.2% of children born in 2012 received a proton pump inhibitor before the age of one year despite the absence of a diagnosis of (severe) gastroesophageal reflux disease (GERD) [21]. About 25% of children develop at least one adverse effect as a consequence of the administration of H² receptor antagonists, and about one child in three develops adverse effects related to proton pump administration [25]. GI dysbiosis and consequent small bowel bacterial overgrowth are likely to be the most frequent adverse effect [26,27].

Management of infantile colic

Frequent and extensive auto-medication by parents of infants with colic has been reported [28,29]. Consequently, management should focus on sustaining parents to cope with their child's excessive crying and distressed behavior by informing them that in general, crying

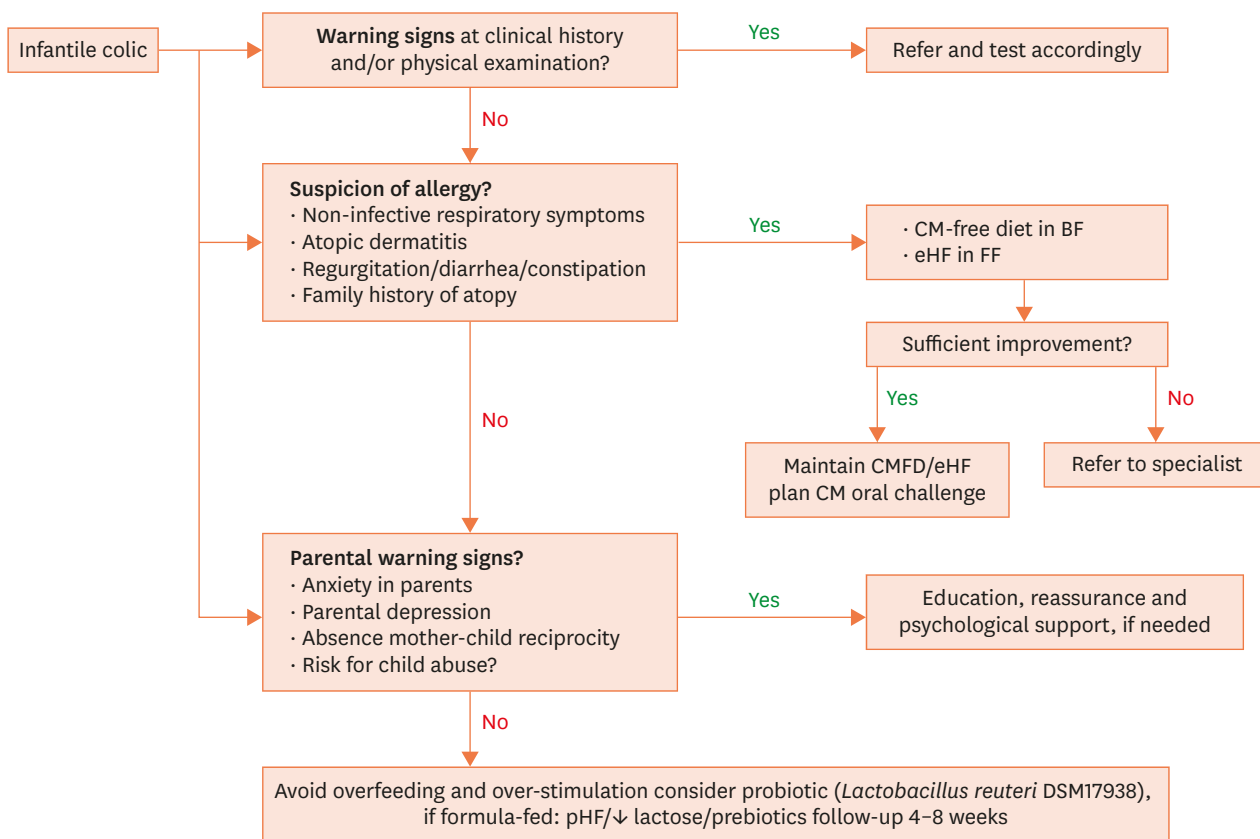


Fig. 2. Management of infantile colic.

CM: cow's milk; BF: breastfeeding; eHF: extensively hydrolyzed formula; FF: formula feeding; CMFD: cow milk free diet; pHF: partially hydrolyzed formula.

peaks at about 4 to 6 weeks after birth, may last up to three hours per day in otherwise normal infants and steadily diminishes from 12 weeks onwards [2,9,30]. Physical examination and history should focus on the most important warning signs, such as severe vomiting, back arching, Sandifer syndrome, gastrointestinal bleeding, failure to thrive, abdominal distention, bloating, and any other signs of further organic causes (Fig. 2).

The CoMiSS™ score, which is a questionnaire assessing regurgitation, crying time, stool pattern, skin, and respiratory signs, can be of help to suspect the possibility of underlying cow's milk protein allergy (CMPA) in infants with negative allergy tests [31]. The link between CMPA and FGIDs in the absence of other symptoms or signs of atopy remains a matter of debate [32,33]. If CMPA is suspected in a formula-fed infant, a 2 to 4 weeks trials of an extensively hydrolyzed formula is recommended. If the diet is observed to be beneficial, a cow's milk-based formula challenge should be planned to confirm the diagnosis and to test acquired tolerance to cow's milk protein; unnecessarily prolonged diet should be avoided. In the absence of suspicion of CMPA or warning signs of organic disease, caregivers should be reassured and supported, and observation of feeding and parent-infant interaction might be helpful [19]. According to the NICE guidelines, a 2 weeks trial with lactase can be considered, although the evidence for this recommendation is virtually missing. The evidence for benefits from pain relieving agents, prokinetic drugs or over-the-counter remedies such as simethicone is very sparse to non-existing [34,35]. Several trials on proton pump inhibitors indicated the same conclusion that anti-acid medication is ineffective in reducing the crying

and distress in an infant that does not present with frequent overt regurgitation and vomiting or GERD. A systematic review and meta-analysis demonstrated the absence of the benefit of proton pump inhibitor administration in crying and irritable infants [36]. Infants with GERD are often distressed and cry a lot, but crying and distress as a single manifestation, particularly in the absence of overt regurgitation or vomiting, is exceptionally a symptom of GERD. In formula-fed infants, when CMPA is an unlikely diagnosis, a partial hydrolysate with prebiotics and beta-palmitate; or a synbiotic formula with reduced lactose and partially hydrolyzed protein may be beneficial [14,37]. A fermented formula with prebiotics may be beneficial for the prevention of infantile colic, as was reported for *Lactobacillus reuteri* DSM17938 [38,39]. However, there is a lack of sufficient evidence to recommend routine use of these kinds of formulae.

An individual participant data meta-analysis concluded that *Lactobacillus reuteri* DSM17938 can be recommended in colicky breastfed infants [40]. Insufficient data exist for formula-fed infants [40]. Chronic inflammation might be one of the pathophysiologic mechanisms causing colic. However, informing parents about the natural evolution of infantile colic seems the only explanation available to generate reassurance. One should not forget that infant crying and distress is the risk factor for parental violence towards the infant and towards each other. Therefore, hospitalization of the infant, preferably in the absence of the usual caregivers leads to an interruption in the vicious circles inducing parental sleep deprivation and anxiety and may be successful. Adequate sleep for mother enables her to relax and recover from the enormous fatigue. Interruption of the vicious circle might also calm the infant. It is equally important to have the mother staying with her baby in the hospital before returning home, in order to allow her to become confident and convinced that crying is not a manifestation of pain or organic disease and it decreases substantially.

Management of functional constipation

Constipation is seldom in exclusively breastfed infants although some of them defecate less than once a week. Constipation is different from dyschezia. Dyschezia refers to condition in infants presenting with severe distress and discomfort when defecating, but produce stools with normal consistency. The goal of treatment of functional constipation is to restore a regular defecation pattern and prevent relapses. In the absence of suspicion of an organic condition such as anorectal malformations, Hirschsprung's disease or cystic fibrosis, and in the absence of warning signs such as failure to thrive, intermittent diarrhea or abdominal distension, parental reassurance is required, which should eventually be endorsed by a nutritional intervention (**Fig. 3**) [19].

The Brussels Infant and Toddlers Stool Scale (BITSS) was developed to better describe stool composition in non-toilet trained infants [41]. A formula with a (partial whey) hydrolysate, (a mixture of) prebiotics, probiotics, synbiotics, and beta-palmitate and/or formula with high magnesium content (but within normal ranges) may offer some benefit under the condition of constipation. Palm-oil, which is often added to infant formula can cause the formation of calcium soaps and induce constipation. Palm-oil free infant formula may reduce symptoms of constipation. Nutritional advice may be insufficient for formula-fed infants presenting with constipation and laxatives may be required as first-line treatment. In the case of fecal impaction, immediate pharmacological intervention to obtain disimpaction is recommended [10]. Laxative administration such as lactulose, polyethylene glycol, paraffin oil, and others might be indicated for infants with chronic constipation.

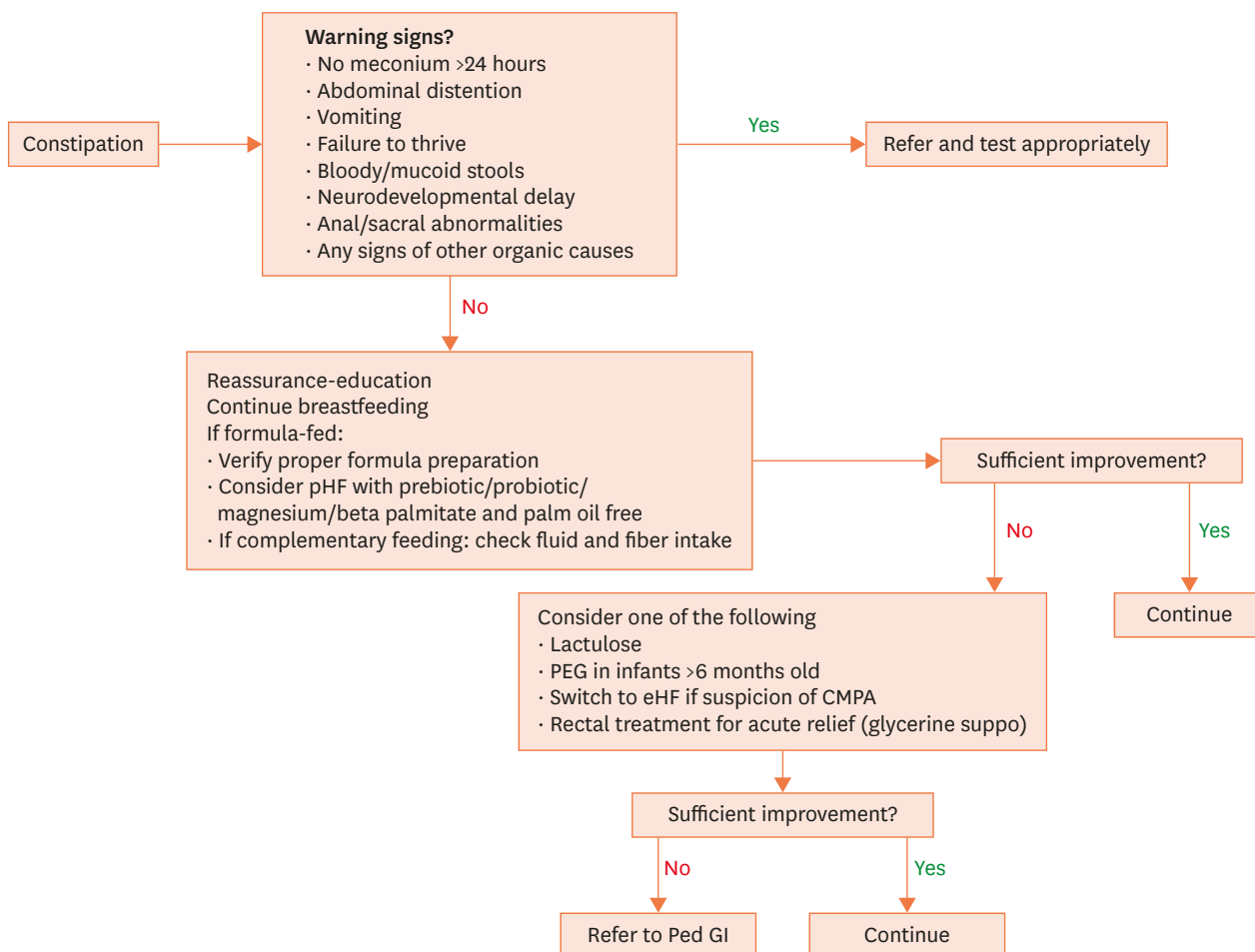


Fig. 3. Management of infant constipation.
PEG: polyethylene glycol; CMPA: cow's milk protein allergy; suppo: suppository; Ped GI: pediatric gastroenterologist.

CONCLUSION

Symptoms and signs of FGIDs represent a frequent and important burden to infants and parents and have a negative impact on their quality of life. The cornerstone of optimal management of FGIDs in infancy is based on parental education and reassurance, which can be accompanied by appropriate nutritional recommendations. FGIDs are not an indication to stop breastfeeding, but it should be supported actively. In formula-fed infants, special formulas may be considered if reassurance and advice on nutrition based on appropriate volume and frequency of milk intake does not lead to sufficient improvement. In the absence of organic disease, it is unlikely that any pharmacological intervention will be helpful. Moreover, medication may cause adverse effects. FGIDs often lead to a vicious cascade of distressed infants, concerned parents, increased medical consultation, over-prescription and use of over-the-counter medications resulting in an escalation in healthcare costs.

It is hypothesized that appropriate management will contribute towards disruption of the cascade of parental anxiousness accompanied with a negative impact on the family's life and will alleviate the distress in infants. Nutritional guidance is essential with some evidence regarding efficacy as it is devoid of the risks of inducing adverse effects.

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