

Functional gastrointestinal disorders. How to manage them without medication

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ABSTRACT

Functional gastrointestinal disorders (FGIDs) are characterized by symptoms attributable to the gastrointestinal tract that cannot be explained by the presence of structural or biochemical abnormalities. During the first year of life, FGIDs can cause great discomfort in infants and concern in their parents. The diagnosis of FGIDs is based on clinical criteria determined by experts and on a comprehensive case-taking process and physical exam to rule out organic causes. The objective of this update is to describe strategies for the management of the most frequent FGIDs during the first year of life: colics, regurgitations, dyschezia, and constipation, in light of new pathophysiological insights, to avoid unnecessary tests and medications.

Key words: gastric regurgitation, colic, constipation, dyschezia, infant.

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INTRODUCTION

Functional gastrointestinal disorders (FGIDs) or disorders of gut-brain interaction are characterized by chronic or recurrent gastrointestinal (GI) symptoms that cannot be explained by structural or biochemical abnormalities.¹ They are called functional because symptoms are not caused by organic alterations.²

During the first year of life, infants may develop functional disorders such as regurgitation, rumination, vomiting, colic, diarrhea, and constipation,¹ without altering their height and weight growth or maturational development. Clinical manifestations are transient and resolve spontaneously; this is achieved thanks to the postnatal maturation and adaptation process of the gut-brain interaction.

The prevalence of FGIDs is highly variable across different published studies due to their various designs, populations, and symptom definitions used. Experts agree that the probable prevalence of regurgitation is 30%; of colic, 20%; and of constipation, 15%,³⁻⁵ and state that, from birth to 6 months old, approximately 1 in 2 infants develops FGIDs.

Given the absence of biomarkers or specific tests, diagnosis is based on clinical criteria that experts have defined at various meetings held in Rome, the last one in 2016: the Rome IV criteria¹ (Table 1).

The objective of this update is to provide tools to better manage FGIDs in the first year of life. Pediatric gastroenterologists conducted a review of the bibliography from the last 5 years on colic, regurgitation, and constipation, the most frequent FGIDs in infants under 1 year of age, in order to describe the advances in pathophysiological knowledge, the latest diagnostic criteria, and management recommendations.

PATHOPHYSIOLOGY

The pathophysiological mechanisms are not completely known; however, the biopsychosocial model (genetic, cultural, environmental, and psychosocial factors) provides probable causes such as alterations in GI motility, in gut microbiota (GM), and in the gut-brain axis, associated with low-grade inflammation processes and visceral hypersensitivity. At this stage of life, the psychosocial aspects of the environment, the family, and the parenting nucleus are fundamental factors. Caregivers play a vital role in

conveying their perception of their child's level of discomfort. However, there is currently no way to measure pain in their caregivers' accounts or distinguish child behaviors that underlie caregivers' perceptions of them.¹

Moreover, there is a direct relationship between early and psychosocial factors in an individual's life and their influence on GI physiological functioning and gut-brain interaction, which together determine the clinical presentation of FGIDs from infancy to adulthood.⁶⁻⁹

The gut microbiota plays a crucial role in integrating the gut-brain axis, the central nervous system (CNS), and the enteric nervous system (ENS). Modifications in the gut microbiota, called dysbiosis, are described in children with FGIDs. Several lines of evidence indicate that the gut microbiota may be involved in the pathogenesis and pathophysiology of FGIDs, through its metabolic capacity in the intestinal lumen and potential interaction with the host, via immune mechanisms.^{1,7-9}

Increased intestinal permeability, dysbiosis, and alterations in the immune function of the gut mucosa result in an increased access of antigens to the submucosa, associated with mast cell activation, and increased release of inflammatory cytokines. This alters the sensitivity receptors of the gut mucosa and myenteric plexus, with subsequent visceral hypersensitivity.^{1,6-9}

Nociceptive development is also relevant since studies in humans and animals have shown that painful stimuli are identified by the brain at 24 weeks of gestation. Preterm and term newborns have a low pain threshold, which increases with age and, as a result, they may respond equally well to a diaper change as to an invasive procedure. In addition, they lack inhibitory control, an elementary key to modulate the experience of pain, and therefore lack the ability to put the experience of pain in perspective. It has been shown that newborns are not only able to process pain at the cortical level, but can experience painful stimuli differently and more severely, with an immediate response, generating physiological responses with production of cortisol and stress hormones, and different behavioral responses such as specific facial expressions and movement patterns.^{1,7,8}

Another important consideration is the long-term effect of pain suffered early in life, and its subsequent relationship with the development

of altered pain perception, since these children would be predisposed to visceral hyperalgesia, as is particularly the case in relation to functional abdominal pain.^{1,7,8}

INFANTILE COLIC

FGIDs in infants share some signs and symptoms, including irritability, often accompanied by crying, sometimes inconsolable. How do they start? Is it hunger? Is it pain? Is it gas? Is it a disease we do not know about? The answers to these questions are what parents seek as the main reason for pediatric consultation.^{2,6,10,11} The first probable cause is colic, which usually occurs with greater intensity between the 5th and 6th week of life and then gradually decreases towards the 12th week, until it disappears spontaneously.¹² It usually occurs in the evening hours, and begins and ends abruptly, for no apparent reason. The reasons for the onset of this problem are still unknown. Environmental, family, CNS, GI tract, and gut microbiota causes are associated.^{1,2,6,9}

Psychosocial aspects are very important in the cascade of events that appear in crying infants. Some authors propose a certain disorder in the relationship between the newborn and the environment. Parental anxiety, postpartum depression, and parental insecurity could account for its onset.^{1,2,9,11}

The great family anguish explains the involvement of other actors (family, friends, social networks) who, in an attempt to help, question the mother's milk production, which leads to the use of unnecessary formulas that threaten the maintenance of breastfeeding. Other times, this situation results in overfeeding, which leads to vomiting and adds more drama to the situation. A worse scenario occurs when, with vomiting already present, the use of medications is suggested, which, far from being beneficial, are detrimental to the gut microbiota.^{2,10,11}

Other factors involved include the immaturity of the CNS, the ENS, and the GI tract at this early stage of gut microbiota colonization and intestinal immune system development.¹⁰ Recent studies show that infants with colic who are breastfed or formula-fed have a different gut microbiota (dysbiosis), with decreased stability and diversity.^{9,13,14}

The pediatrician's assessment is fundamental, since the diagnosis is clinical. Organic causes are described in only 5% of infants with colic^{9,14} (Tables 1 and 2).

Gastroesophageal reflux (GER) at this stage of life is not a cause of pain and crying. Cow's milk protein allergy (CMPA) in infants may present with irritability, crying, and colic, but in general there are other associated symptoms, and its diagnosis requires confirmatory challenge testing.²

Treatment guidelines

Since 95% are healthy infants, what should we do? How can we support the family?

Education: The most important thing is to be empathetic and supportive and allow the parents to let off steam, giving them confidence and security.^{1,2,4,9}

Consultation will allow us to:

1. Assess the bond between parents and with their baby, and detect risk behaviors.^{15,16}

2. To encourage breastfeeding, assess and improve the sucking technique.
3. Encourage a healthy nutrition, rest, and good hydration in the mother.
4. Reinforce the importance of avoiding overfeeding and overstimulation.^{1,2,4,6}

Nutritional management: The importance of maintaining breastfeeding should be conveyed. Breast milk (BM) contains oligosaccharides (prebiotics) and healthy bacteria (probiotics) that promote the development of the gut microbiota and an adequate GI maturation. If an infant's weight progresses adequately, the use of milk formulas should be discouraged.^{4,15-17} If supplementation is necessary, the use of lactose-free formulas is not appropriate. The role of lactose in the presence of colic has been questioned and has not been demonstrated.⁶

TABLE 1. Rome IV criteria: clinical criteria for the diagnosis of gastrointestinal disorders

Infantile colic

An infant who is < 5 months of age when the symptoms start and stop. Recurrent and prolonged periods of infant crying, fussing, and irritability reported by caregivers. Crying for 3 hours or more a day, for 3 days or more in the past 7 days. Episodes that occur without obvious cause and cannot be prevented or resolved by caregivers. No evidence of failure to thrive, fever, or illness.

Regurgitation, physiological gastroesophageal reflux

An otherwise healthy infant who is 3 weeks to 12 months of age with regurgitation 2 times or more per day for more than 3 weeks. No retching, hematemesis, aspiration, apnea, failure to thrive, feeding or swallowing difficulties, or abnormal posturing.

Functional constipation

A child who is younger than 4 years with a minimum of 1 month with at least 2 of the following signs or symptoms: 2 or less bowel movements per week, history of excessive fecal retention, history of painful and hard bowel movements, history of large-diameter stools, presence of a large fecal mass in the rectum.

Dyschezia

An infant who is younger than 9 months of age with, at least, 10 minutes of straining and crying before successful or unsuccessful passage of soft stools. Otherwise healthy.

Source: Developed by the authors.

TABLE 2. Warning signs observed in infants with colic, irritability, and crying

	GENERAL	<ul style="list-style-type: none"> • Weight loss. Fever. Excessive irritability and pain.
	NEUROLOGICAL	<ul style="list-style-type: none"> • Developmental delay. Muscle hypotonia or hypertonia.
	GASTROINTESTINAL	<ul style="list-style-type: none"> • Vomiting and poor weight gain. • Sandifer posturing. Gastrointestinal bleeding. • Diarrhea and abdominal bloating.

Source: Developed by the authors.

Some studies have shown benefits with formulas consisting of low-lactose, partially hydrolyzed protein, beta-palmitate, and prebiotics and/or probiotics.^{18,19}

Drug treatment: There is no scientific evidence that pharmacological intervention (simethicone, proton pump inhibitors, and herbal medicines, among others) is helpful.^{1,20}

In children with inconsolable crying that does not improve with previous guidelines, there is another option: the use of probiotics. *Lactobacillus reuteri* is the probiotic that has been shown to be most effective.^{21,22} Although there is scientific evidence showing its usefulness, especially in exclusively breastfed infants, further longitudinal and comprehensive studies are required to determine its precise indication.¹

REGURGITATION AND PHYSIOLOGICAL GASTROESOPHAGEAL REFLUX

GER is the involuntary retrograde movement of gastric contents into the esophagus. When high enough, it is called regurgitation, which can reach the esophagus, mouth and/or nose. It is common in healthy infants. Its peak incidence is between 2 and 4 months of life. It disappears spontaneously between 6 and 12 months of age.^{9,23}

A healthy infant who regurgitates is known as a “happy spitter or regurgitator.” In the first months, there are anatomical predisposing factors (frequent aerophagia, low lower esophageal sphincter [LES] pressure, limited gastric capacity, lack of motor coordination of the digestive

tract in the first months of life), but a poor feeding technique and overfeeding are the most frequent triggers.^{1,24,25}

History taking provides data that help to rule out organic causes (Table 3).²

When gastric regurgitation generates complications with damage or inflammation (esophagitis, apnea, reactive airway disease, pulmonary aspiration, feeding and swallowing difficulties, or failure to thrive) and is accompanied by warning signs, it is called gastroesophageal reflux disease (GERD).^{23,25}

The recognition of functional regurgitation, based on clinical criteria, avoids unnecessary medical visits, tests, and therapies.^{1,24,25} (Table 1).

Treatment guidelines





Education: It is very important to provide parents with information about the natural history of regurgitation and warning signs. It should be made clear that GER is physiologic and resolves spontaneously around 1 year of age.²

An upright or left lateral position in the immediate postprandial period may reduce this symptom. The prone position is contraindicated because of the increased risk for sudden infant death.^{26,27}

It is recommended NOT to expose the infant to tobacco smoke: nicotine decreases LES pressure and increases regurgitation and GER.^{1,2,26}

Nutritional management: Breastfeeding is the best option in the management of infants with GER because it improves gastric emptying and

TABLE 3. Warning signs observed in infants with vomiting

	GENERAL	<ul style="list-style-type: none"> • Weight loss; fever; lethargy; excessive irritability and pain.
	NEUROLOGICAL	<ul style="list-style-type: none"> • Bulging fontanelle; rapid head circumference increase; seizures; macro- or microcephalus; developmental delay.
	GASTROINTESTINAL	<ul style="list-style-type: none"> • Billious and heavy, persistent vomiting, with poor weight gain. • Onset before 15 days of life or after 6 months of age or persisting after 18 months of age. • Vomiting or nausea or choking with feeding. • Sandifer posturing; hematemesis; diarrhea; rectal bleeding; abdominal bloating.
	RESPIRATORY	<ul style="list-style-type: none"> • Intermittent sleep, with ineffective cough. Respiratory conditions, bronchospasm. Dysphonia.

Source: Developed by the authors.

contains factors that favor an adequate maturation of the GI system; therefore, breastfeeding should never be interrupted. It is important to correct the frequency and volume of feedings, and to recommend an appropriate breastfeeding technique.^{2,11,20}

In the case of formula-fed infants, correct preparation should be advised and the impact of overfeeding should be explained. Administration of a thickened or “anti-regurgitation” formula may be considered in cases with persistent and distressing symptoms. Studies have shown that it reduces the number of NON-acid reflux episodes (pH > 4) and decreases the height the reflux reaches in the esophagus.^{2,11,27}

Anti-reflux formulas contain thickeners, such as carob seed flour, corn starch, potato or rice. Carob seed flour is not hydrolyzed by salivary amylases and maintains its effect in the stomach, has no nutritional value, does not increase calories, and has a fiber effect, thus avoiding the constipation caused by other thickeners. The use of homemade thickeners is not recommended, because they can generate an increase in osmolarity and thus worsen gastric emptying and symptoms.^{6,11,27}

Extensively hydrolyzed formulas should only be used in infants who do not respond to treatment and in whom CMPA is suspected due to the presence of other symptoms.^{11,23}

Drug treatment: Drugs used for reflux disease are not indicated for the treatment of functional physiological reflux. In addition, they may have adverse effects.

Proton pump inhibitors (omeprazole, esomeprazole, lansoprazole, pantoprazole) may have adverse effects in 35% of cases, with diarrhea or constipation, headache, abdominal pain, fever, and mild to severe infections, especially pneumonia and osteoporosis.

H2-receptor antagonists (famotidine, cimetidine) may cause mild effects, but with a frequency of 1-19%.

In the case of prokinetics (metoclopramide, domperidone, erythromycin, and cisapride), the effects are related to the passage of the blood-brain barrier or electrocardiographic disturbances, such as QT prolongation.^{15,21,28}

There is often intense pressure from families to start anti-reflux therapies or perform diagnostic testing because of the perceived severity of symptoms; however, in the absence of warning signs, diagnostic testing and/or acid suppression therapies are NOT necessary.^{20,24,28}

CHRONIC FUNCTIONAL CONSTIPATION AND DYSCHEZIA

Functional constipation is often defined as the result of repetitive attempts at voluntary fecal retention by the child, who tries to avoid a discomforting sensation of bowel movement, usually due to fear of having bowel movements. The diagnosis of functional constipation is based on clinical criteria^{1,16} (Table 1).

It is important to differentiate functional constipation from infant dyschezia.¹⁰ The latter is defined as the lack of coordination of defecation dynamics between intra-abdominal pressure and pelvic floor relaxation. It is a benign, transient, functional disorder that occurs in infants younger than 9 months, usually beginning in the first months of life. It is characterized by the lack of bowel movements for several days, episodes of intense crying and reddening of the face during repeated attempts to have a bowel movement, with pushing that lasts a few minutes and stops when the stools are passed, which will be pasty or liquid, without an enlarged consistency. This disorder is self-limited and does not require medical treatment or diagnostic tests.¹

In the pathophysiology of functional constipation, 2 major aspects are involved, which are in turn interrelated.^{1,6,29-31}

- **Pain mechanism:** It is associated with most FGIDs, in which neurodevelopmental nociception and other determining factors have an impact on the magnitude of this experience. Pain is related to some previous experience passing large stools with a bigger consistency, and/or having a rectal injury.^{30,31}
- **Fecal retention cycle:** Pain during bowel movements plays a determining role for the infant's conditioned behavior, and the need to avoid it appears with the defecation mechanism versus the desire to prevent it. The retentive behavior leads to an increase in the absorption of water by the colon, which generates an enlarged stool consistency, accommodation of the rectal wall to its contents, and disappearance of the urge to defecate once the mechanism is altered (Figure 1).

The most common triggering factors of functional constipation are:

- Weaning and the introduction of formula containing palmitic acid at the alpha position (poorly absorbed and hydrolyzed by pancreatic lipase) may cause calcium soaps and harden stools.

- A diet with poor fiber contents and water intake.
- Pain from previous anal and perianal injuries.
- Chronic medications, such as anti-cough medicine, opioid derivatives, atropine.^{6,11,20,21}

As in all FGIDs, complete case taking and physical examination are the cornerstones for an adequate diagnosis.^{2,6,11,20,29,31} The Bristol stool scale is helpful in identifying stool characteristics³² (Tables 4 and 5).

Treatment guidelines

The goal of treatment is basically to soothe pain so that the fear of bowel movements disappears and thus a regular pattern of defecation is reestablished.^{1,2}

Education: Infants with dyschezia do not require treatment with laxatives or stimulation

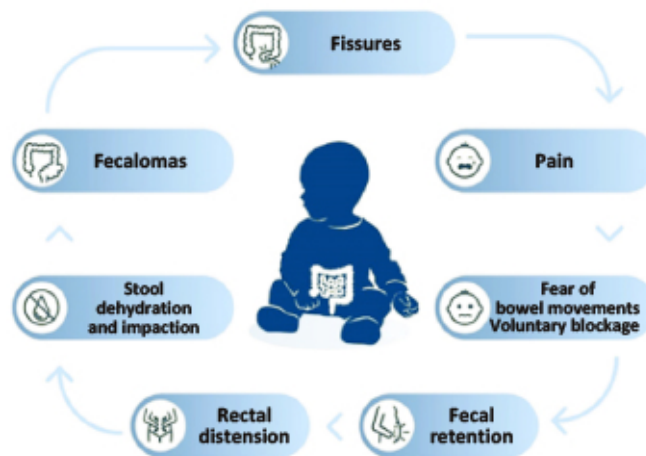
(neither suppositories nor enemas), since they may increase pain or discomfort, which will worsen the condition. Management should focus on reassuring the parents about delayed bowel movements, and explain to them that it is only a lack of coordination in defecation.^{1,11}

In infants with functional constipation, parents should be advised on how to decrease stool consistency and size to reduce pain with nutritional or medication management.^{1,11}

Nutritional management: Breastfeeding should be continued because it favors a decrease in stool consistency. Breastfed infants account for only 1% of constipated infants.¹¹

If the infant is not breastfed, the physician should check formula preparation and consider the use of formulas with prebiotics and/or synbiotics, and with beta palmitate and/or

FIGURE 1. *Fecal retention cycle*



Modified from: Bautista Casanovas A, Espin Jaime B. Introducción. In: Espin Jaime B (coord.). Guía de Estreñimiento en el Niño. Madrid: Argón; 2015:1-5.

TABLE 4. *Warning signs observed during case taking according to the constipation diagnostic algorithm*

- Passage of meconium after 24/48 hours.
- Early age at initiation of breastfeeding.
- Poor weight/height gain.
- Diarrhea and explosive bowel movements after delayed emptying.
- Pain and abdominal bloating.
- Rectal bleeding.
- Prior treatments. Failure after 3 months.
- Family history of: Hirschprung disease, food allergies, celiac disease, CF, thyroid and renal abnormalities.
- Chronic medication use.
- Emotional problems/abuse.

Source: Developed by the authors.

CF: cystic fibrosis.

magnesium in normal ranges.^{2,11,18,19}

If complementary feeding has already begun, the physician should check the amount of dietary fiber, increase fluid intake, and control the volume of dairy products to facilitate the acceptance of other foods.^{1,11,30,31}

Drug treatment: Maintenance of a healthy perianal skin.

In children with fecal impaction or functional fecal retention with pain due to stools with enlarged consistency and size, the use of osmotic laxatives is indicated to hydrate stools.^{1,2,11,31}

CONCLUSIONS

In children with FGIDs, parental concern, which depends on their perception of the symptoms and the discomfort demonstrated by the infant, motivates medical consultation and leads to a challenging diagnostic process. Taking into account the established clinical diagnostic criteria (Rome IV), based more on experience than on evidence, unnecessary tests and drugs will be avoided.

According to the guidelines, the recommendation is to offer support to parents or caregivers, through explanation and pathophysiological understanding, to reduce their anxiety and reinforce their empathy and confidence. Adequate infant nutrition, prioritizing breastfeeding above all, and advice on how to reduce predisposing factors are the keys to optimize the management of FGIDs in infants. ■

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TABLE 5. Warning signs observed during physical examination according to the constipation diagnostic algorithm

- Abdominal tenderness and/or bloating.
- Rectal bleeding.
- Palpable fecal mass in the abdomen. Empty rectal ampulla.
- Rectal and sacral region exam, malformations, anal position, perianal folds, erythema, fissures.
- Lumbosacral region exam, sacral dimple, strand of hair, gluteal line deviation, sacral agenesis.
- Clinical signs of malabsorption/ impaired weight and height, recurrent sores.
- Clinical signs of allergy, including atopic eczema, rhinitis, bronchospasm, erythema.
- Suspected genetic disorder or neuromuscular disease. Muscle tone alterations.
- Developmental delay, signs of hypothyroidism.

Source: Developed by the authors.

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