gastrointestinal disorders

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Review

An Overview of the Management of Functional Gastrointestinal Disorders in Infancy

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Abstract: This review article will address the frequently encountered functional gastrointestinal disorders (FGIDs) occurring in infancy. The clinical features and management of infant regurgitation, infant colic, infant dyschezia, and functional constipation are discussed with reference to the most recent literature and evidence. Management should be focused on ruling out organic causes with careful history and examination, and then reassurance for the caregiver in this often very stressful period of parenting. There is often no or minimal pharmacological treatment necessary for FGIDs and treatment should be individualised for each patient and family.

Keywords: FGID; infant; constipation; dyschezia; regurgitation; colic

Citation: Rishanghan, L.; Hinds, R. An Overview of the Management of Functional Gastrointestinal Disorders in Infancy. *Gastrointest. Disord.* **2023**, *5*, 500–507. https://doi.org/10.3390/gidisord5040041

Academic Editor: Michio Hongo

Received: 12 September 2023
Revised: 10 October 2023
Accepted: 2 November 2023
Published: 15 November 2023

1. Introduction

Functional gastrointestinal disorders (FGIDs), now also called disorders of gut-brain interaction (DGBI), are seen frequently in the paediatric age group with recurrent and frequent gastrointestinal symptoms that cannot be attributed to structural or biochemical abnormalities [1]. These patients often seek help from not only their primary health care physicians, but also specialists and allied health care teams.

Current studies show FGIDs are frequent and reported all over the world. The most common FGIDs being regurgitation and colic in the infant age group [2,3]. Combined FGIDs are also commonly seen and can often cause significant negative impact on quality of life. Patients often require multiple doctor visits and even hospitalisation, a frequent change of milk formulas, shortened duration of breastfeeding, and other costly non-pharmacological interventions [4–6].

The pathophysiology behind FGIDs is multifactorial and results in disruption of the microbiota-gut-brain axis. This is related to a number of elements including visceral hypersensitivity, central hypervigilance, genetics, environmental factors, neuroimmune interactions, early life events, gastrointestinal motility, nutrition, changes in gut microbiota, and psychological factors [7].

For the purpose of this review article, we wanted to draw attention to the management of the most commonly clinically encountered FGIDs in children in their first year of life. We focus on infant regurgitation, infant colic, infant dyschezia, and functional constipation. This age group is particularly challenging because symptoms are based on parental reporting and physician assessment together.

2. Infant Regurgitation

2.1. Overview

Gastro-oesophageal reflux (GER) is a normal physiological process occurring in healthy infants. It should cause minimal or no symptoms and often occurs in the post-prandial period and lasts only a few minutes. Regurgitation is the passage of this refluxed gastric contents into the mouth where it can spill out. Other familiar terms can include "spilling",

"posseting", and "spitting up". Regurgitation is normally effortless and non-projectile [8]. Regurgitation can occur in healthy infants. It is important to distinguish vomiting from regurgitation, as both have different physiology. Vomiting is a central system reflex, whereas regurgitation is within the normal and healthy range of behaviour for an infant. GER occurs with transient relaxation of the lower oesophageal sphincter allowing retrograde passage of gastric contents. Gastro-oesophageal reflux disease (GERD) is again different and is seen when this regurgitation causes inflammation or damage [9].

The Rome IV criteria uses criteria for infant regurgitation of an infant (between 3 weeks and 12 months of age) to have both:

1. Regurgitation two or more times per day for three or more weeks.
2. No retching, haematemesis, aspiration, apnoea, failure to thrive, feeding or swallowing difficulties, or abnormal posturing [10].

Red flags noted with clinical evaluation of an infant should prompt further investigation and referral to the most appropriate speciality service. It is also important to consider risk factors such as prematurity, developmental delay, and congenital abnormalities of the oropharynx, chest, lungs, central nervous system, heart, and gastrointestinal tract. It is important to note that if regurgitation persists beyond one year of life, assessment to rule out anatomical abnormalities should be carried out [9]. See tables below for red flags of concern (Table 1) and differential diagnoses to consider (Table 2).

Table 1. Red flags for infant regurgitation [8].

Bilious vomiting	Fever
Gastrointestinal bleeding	Lethargy
Haematemesis	Hepatosplenomegaly
Haematochezia	Bulging Fontanelle
Abnormal posturing/irritability after feeds	Macro/microcephaly
Respiratory symptoms	Seizures
Cough	Abdominal tenderness or distension
Stridor	Documented or suspected genetic/metabolic
Wheeze	syndrome
Apnoea	Diarrhoea
Failure to thrive	Constipation

Table 2. Differential diagnoses for infant regurgitation/GER [11].

Gastrointestinal
Pyloric stenosis
Malrotation
Cow's milk allergy
Respiratory
Central nervous system
Hydrocephalus
Infection
Viral gastroenteritis
Urinary tract infection
Meningitis
Metabolic disorders
Renal tubular acidosis
Urea cycle defects
Hypocalcaemia
Drugs/Toxins

2.2. Management of Infant Regurgitation

Infants will most often grow out of their GER by 12 months of age and it is necessary to provide parents and caregivers with reassurance and non-pharmacological management strategies [12].

A paper by Beninga et al. reports initial approaches should include positioning after meals, thickening of feeds, and ensuring that they are not overfeeding. Positioning of infants in left lateral and prone position can help reduce symptoms, however, it is important to ensure supine position when asleep [9]. Horvath et al. reports evidence to support both thickened feeds and antiregurgitation formulas. These have been shown to have a positive effect on regurgitation including reducing the number of episodes, reduced duration of reflux episodes, and increased weight gain with no serious adverse effects noted [13].

A recent Nurko et al. paper published in 2022 also describes an association between GER and non-IgE mediated cow's milk protein allergy, with reports it can induce GER. For this reason, a two to four week-long trial of maternal dietary elimination of cow's milk or an extensively hydrolysed formula can be offered [14].

On the other hand, proton pump inhibitors are often recommended to parents by multiple sources including health care professionals despite literature showing they perform equivalent to placebo and can be associated with adverse effects such as increased respiratory tract infections, increased risk of all allergic diseases, and obesity in childhood [15,16].

Beninga et al. reports there is little evidence to support smaller and more frequent feedings, however, it is important to ensure parents are not overfeeding a child and this can be elicited with thorough history taking [9].

The use of alginates, found in over the counter medications such as Gaviscon, are recommended in the UK according to the NICE guidelines, however, this data is extrapolated from adult studies and a joint position paper from the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition (NASPGHAN) and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) does not recommend this as side effects have not been assessed [17].

To reiterate, care should be taken to alleviate and address fears about infant regurgitation and appropriate management plans should be put in place to encourage a confident and conservative approach for the caregiver.

3. Infant Colic

3.1. Overview

Crying in infants is normal and exists on a spectrum, and infant colic is thought to exist at the upper end of this spectrum [18]. It occurs most commonly between the ages of 1 to 4 months and is described as inconsolable crying. There is no obvious cause for the crying, which can lead to significant distress for caregivers. There is often more crying in the afternoon or evening, and the reason for this is unknown [19]. Multiple hypotheses for causes for infant colic exist including normal developmental phenomenon, central nervous system disbalance, environmental disturbance, and gastrointestinal discomfort. Newer research is looking at whether gut microbiome is implicated, however, the cause remains largely uncertain for all theories listed [10].

The Rome IV criteria uses the following diagnostic criteria:

1. An infant who is <5 months of age when the symptoms start and stop.
2. Recurrent and prolonged periods of infant crying, fussing, or irritability reported by caregivers that occur without obvious cause and cannot be prevented or resolved by caregivers.
3. No evidence of infant failure to thrive, fever, or illness [10].

It can be noted here that organic disease is found in less than 5% of children who present with colic symptoms [20].

3.2. Management of Infant Colic

In almost all cases of colic, the most important factor is to offer support for parents in this challenging time of a baby's development [21]. Parents often feel hopeless and anxious with their child's crying, often questioning their ability to be a parent. This leads to parental/caregiver exhaustion where they may have feelings of frustration towards a child they cannot soothe. The Period of PURPLE Crying is a well-known educational

program used around the world aimed at giving evidence-based guidance and information for parents and caregivers to prevent shaken baby syndrome. It helps to provide parents with an understanding of what is normal for their child (Table 3). It becomes important to assess the social supports available to families and ensure health worker support remains continually available [22].

Table 3. PURPLE crying [22].

Peak	Peak crying between 6–8 weeks, crying time resembles a bell curve where it gets worse and then should improve.
Unexpected	Often appears out of nowhere.
Resists soothing	May resist all attempts at soothing.
Pain like face	No evidence to suggest pain.
Long lasting	Can cry for hours.
Evening	Crying period often occur in the evening, but can happen any time of the night.

Heine et al. discusses how similar to regurgitation, there is evidence of colic associated with non-IgE mediated cow's milk protein allergy and for this a trial of maternal dairy exclusion for breastfed infants or extensively hydrolysed formula can be offered. Improvement should be noted within the first two weeks with relapse of symptoms on reintroduction of cow's milk. This should be offered in consultation with a specialist paediatrician with a dietitian, especially if further consideration needs to be made in switching to an amino acid-based formula [23].

There is no evidence to support treatments for GERD in infant colic as described by recommendations from British Medical Journal (BMJ) [24].

BMJ reports no evidence to suggest lactase therapy helped or was any better than placebo. There was low quality evidence to suggest soy formula improved crying duration but given levels of phytoestrogens and that soy may be an allergen in infancy, its use is not recommended [24].

Simethicone, which is often used, showed no benefit over placebo in randomised controlled trials [24].

Complementary therapies are becoming more popular recently with parents wanting to move towards more 'natural' treatments. Herbal supplements such as fennel extract or herbal tea have several adverse effects (vomiting, sleepiness, constipation) and are not recommended [24].

There have also been studies looking at the role of probiotic supplements in reducing or preventing colic given they are widely available and inexpensive compared to other treatments. There is growing evidence that intestinal microbiota of colicky infants is different to healthy controls, and the addition of probiotics is thought to help provide a healthier intestinal microbiota landscape. A Cochrane review found that there was some evidence of reduced crying time with the use of *Lactobacillus reuteri DSM 17938* in breastfed infants, however, recommended further studies to assess this. Reassuringly there were minimal adverse effects compared to placebo. The authors' conclusions were restricted as they felt conclusions had limited strength based on current studies available. They do note that these medications are available over the counter, so it is important to discuss probiotic supplementation with families to help make informed decisions [25].

There is limited literature evidence to suggest chiropractic care helps with infantile colic symptoms [26].

Given the risk of parental exhaustion, the clinician should ensure appropriate and timely follow up is in place not only to monitor the infant but also to alleviate any doubts the parents/caregiver may have about soothing their child.

4. Infant Dyschezia

4.1. Overview

Infant dyschezia is described as straining to pass stool, with screaming, crying, turning red or purple in the face. This usually lasts 10–20 minutes until a soft or normal stool is successfully passed. There are normally several stools passed daily, and symptoms should self-resolve over a few weeks [26,27]. The main feature differentiating dyschezia from constipation is the passage of normal stools daily.

The Rome IV diagnostic criteria include infants <9 months of age:

1. At least 10 min of straining and crying before successful or unsuccessful passage of soft stools
2. No other health problems [10]

4.2. Management of Infant Dyschezia

As this is a self-resolving problem, reassurance and helping parents to understand physiology is helpful. Symptoms occur when infants are unable to co-ordinate increase in intra-abdominal pressure with a relaxation of pelvic floor muscles. When these occur together, defecation is learned and symptoms improve. Laxatives are not required. It is also important to avoid rectal stimulation as it may condition the child to wait for stimulation to defecate [10,26].

5. Functional Constipation

5.1. Overview

Functional constipation occurs when children have negative or unpleasant associations with defecation, and as a result voluntarily withhold their faeces. This leads to hard stools, which become increasingly difficult to pass due to absorption of water while they remain in the colon [9]. During early infancy, feeding changes such as transition to formula from breastfeeding or introduction of solids can trigger functional constipation. The introduction of solids means slower transit time for food, which could reduce the frequency of bowel movements and contribute further to constipation. Moretti et al. reports that breastfed infants have less constipation and pass more frequent and softer stools [28]. Clinical history and assessment is mainly to look for red flags that may suggest an organic cause such as timing of meconium passage. Especially pertaining to this age group, it is important to rule out Hirschsprung's disease with careful history and examination as required. If this is suspected, early referral to a general surgical team is needed for consideration of rectal biopsies [29]. Other differentials include anatomic obstructions, spinal problems, metabolic, and other neuro-enteric abnormalities (see Table 4 below for further red flags and Table 5 for differentials) [9]. Joint guidelines from ESPGHAN and NASPGHAN have demonstrated that there is no role for routine laboratory testing for coeliac disease, hypothyroidism, and hypercalcaemia in a child with no red flags. They also report no evidence to support the use of abdominal radiography, digital rectal examination, and routine allergy testing or barium enema to aid with diagnosis [29].

Table 4. Red flags for constipation [29].

Constipation in a child <1 month old
Passage of meconium >48 h
Family history of Hirschprung disease
Trisomy 21
Failure to thrive
Bloody/mucoid stools
Bilious vomiting
Severe abdominal distension
Abnormal position or appearance of the anus
Abnormal lower limb neurology
Sacral dimples/sacral abnormalities

Table 5. Differential diagnoses for constipation [29].

Hirschprung disease
Cystic fibrosis
Hypothyroidism, hypercalcaemia, hypokalaemia
Cow's milk protein allergy
Anal achalasia
Imperforate anus
Anal stenosis
Spinal cord anomalies
Abnormal abdominal musculature
Pseudo-obstruction
Coeliac disease

The Rome IV criteria has two age groups for diagnosis, for infants up to one year of age they must have at least two of the following for one month:

1. Two or fewer defecations per week.
2. History of excessive stool retention.
3. History of painful or hard bowel movements.
4. History of large-diameter stools.
5. Presence of a large faecal mass in the rectum [10].

5.2. Management of Functional Constipation

Once functional constipation is recognised, it is important to intervene early as this contributes to successful resolution of symptoms [30].

ESPGHAN and NASPGHAN have put together a number of evidence-based recommendations [29].

These include encouraging normal fibre and fluid intake. There is no evidence to increase fibre or fluid intake above standard requirements. Current evidence does not support the use of fibre supplements [29].

Connor et al. supported by ESPGHAN/NASPGHAN guidelines demonstrate a two to four week-long trial of cow's milk protein avoidance or extensively hydrolysed formula may be indicated when laxative therapy has failed. Reintroduction should be offered if no improvement is noted with appropriate follow-up in place [31].

First line treatment should be with the use of nonstimulant or osmotic laxative such as polyethylene glycol (PEG) and lactulose. Michail et al. discusses how PEG is a non-toxic and highly soluble compound that is minimally absorbed in the GI tract, while lactulose is a non-absorbable sugar. They both promote water reabsorption into the GI tract making stools softer and easier to pass. Lactulose has been studied more than PEG in the infant age range, however, both are safe in this age group [29]. Lactulose is often used in infants <6 months age, and PEG for infants older than 6 months. Transient diarrhoea may occur but adjusting dosage should improve this. Stimulant laxatives are not recommended as they often lead to further cramping and if used for a prolonged period, the dose needs to be increased to have the same effect [32]. The main goal is ensuring passage of soft stools to allow painless defecation until symptoms improve. Maintenance treatment is often required for months to improve the negative association the infant can have with defecation. Parents should be reassured that children do not become reliant on osmotic laxatives given their mechanism of action. It was difficult to find studies looking at the long-term use of PEG, however, in clinical practice it is often prescribed for chronic use with no serious side effects.

Further recommendations from these joint guidelines show there is no evidence for the use of prebiotics or probiotics, but there is only limited published information on this in infants with constipation [29]. There was only low-quality evidence and no randomised controlled trials looking at alternative medicine, and therefore this is not recommended.

Although dietary interventions are often recommended, the importance of nutrition for growth and development cannot be overlooked and consultation with a dietitian is paramount [14].

6. Discussion

A step towards helping these families who have infants with FGIDs is with clearer education and guidelines, especially for those clinicians who will often be the initial point of contact such as child health nurses and pharmacists. Families often have conflicting advice from sources such as medical professionals, alternative health care practitioners, Google, social media websites, and other family members. Over the counter medications are pursued with significant out of pocket costs for therapies with questionable or no evidence. Given FGIDs could be managed primarily by primary health care physicians, which in turn would mean saving families from frequent emergency department visits or costly private specialist appointments, one solution would be well-defined national or international guidelines about diagnosis and management. These should incorporate strict diagnostic criteria, assessing current management strategies and appropriate controls for comparison. It is important to note that these guidelines would need to be regularly updated due to the exponential growth of knowledge we are having about FGIDs, specifically the role of gut microbiota and the gut-brain-axis.

This review highlights the approach to many FGIDs in infants is with parental reassurance, while ensuring organic causes are ruled out by thorough history and physical examinations. With initial presentations, it is important to keep differentials broad and consider risk factors and red flags before making the diagnosis of FGID. Referral to a specialist paediatrician or paediatric gastroenterologist should be the next step if there are concerns or symptoms do not resolve as expected. Often no further testing is required for these diagnoses, and management should be individually tailored while ensuring appropriate follow-up is in place. Most FGIDs in infancy will improve over time, which should provide optimism for parents and caregivers.

Author Contributions: Writing—original draft preparation, L.R.; writing—review and editing, R.H.; supervision, R.H. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: No new data were created or analyzed in this study. Data sharing is not applicable to this article.

Conflicts of Interest: The authors declare no conflict of interest.

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