Functional gastrointestinal disorders (fgids) And cow's milk allergy (cma) in infants

This factsheet will focus on functional gastrointestinal disorders (FGIDs), non-IgE mediated cow's milk allergy (CMA) and the overlap in these conditions. There are a number of FGIDs which can occur in infants and toddlers and we will focus on three of the most common: colic, constipation and reflux (otherwise known as infant regurgitation)[1]. Although we'll consider each disorder separately, in clinical practice, many infants will present with a combination of FGIDs[2].

FGIDs:

FGIDs are defined by the ROME IV criteria as: 'disorders of the digestive system in which symptoms cannot be explained by the pres- ence of structural or tissue (or biochemical) abnormality, based on clinical symptoms[3].

A study looking at the prevalence and health outcomes of FGIDs in infants from birth to 12 months of age found the global prevalence to be as follows: colic 20%, functional constipa- tion 15% and reflux 30%[4]

Normal Crying and Fussing Versus FGIDs

Crying and fussing are normal during infancy. The duration of crying reaches an average peak of 2¾ hours/day when the infant is around six weeks old[5]. Less that 5% of crying and distress infants have an organic cause behind their symptoms[6]. However, if there is parental concern, it is important to look out for red flags such as[7]:

- Extreme or high-pitched cry
- Symptoms persisting beyond 4 months
- Presence of frequent regurgitation, vomiting, diarrhoea and/or weight loss
- Failure to thrive
- Family history of atopy or migraine
- Abnormal physical examination
- Fever or illness
- Severe parental anxiety or depression
- Others (according to clinical judgement)

Diagnostic Criteria for FGIDs:

Colic

Diagnostic criteria for infant colic are as follows[1]:

1. 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
2. Infant < 5 months of age when the symptoms start and stop
3. No evidence of infant failure to thrive, fever, or illness

For clinical purposes, a diagnosis must include all of the criteria listed above.

Constipation

For a diagnosis of functional constipation, infants up to 4 years old must have experienced at least two of the following for at least one month[1]:

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

For diagnosis of children < 9 months of age, it is important to differentiate between constipation and infant dyschezia (at least 10 minutes of straining and crying before successful or unsuccessful passage of stools in the absence of other health problems).

Infant Regurgitation (Reflux)

Infant regurgitation refers to retrograde involuntary movement of gastric contents in and out of the stomach and is often referred to as gastroesophageal reflux. When the reflux is high enough to be visualized it is called regurgitation. Reflux is diagnosed when both of the following criteria are fulfilled in an otherwise healthy infant aged 3 weeks to 12 months[1]:

1. Regurgitation 2 or more times per day for 3 or more
2. No retching, hematemesis, aspiration, apnea, failure to thrive, feeding or swallowing difficulties, or abnormal posturing weeks

Gastroesophageal reflux (GER) becomes gastroesophageal reflux disease (GERD) when troublesome symptoms or complications occur as a result of GER, and will need further support.

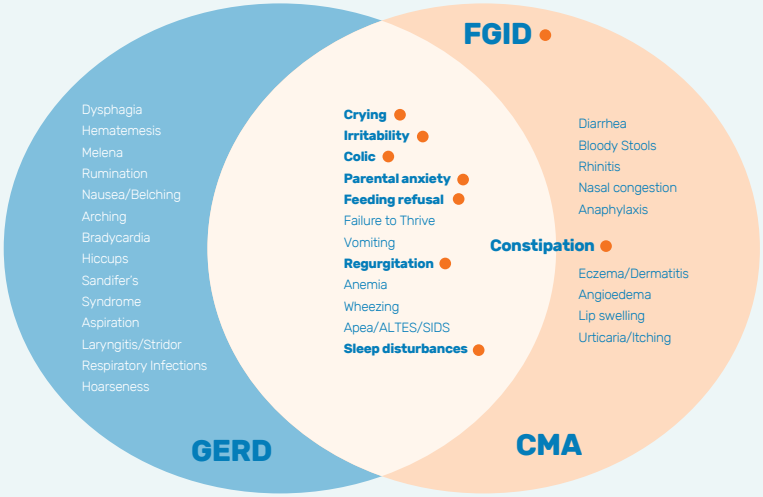
Non-IgE Mediated CMA

Unlike FGIDs, in order for a CMA diagnosis to be made, infants need to display several of the symptoms listed below[8]:

- Crying
- Irritability
- Colic
- Parental anxiety
- Feeding refusal
- Regurgitation
- Constipation
- Sleep disturbances

The symptoms above are common in otherwise well infants as well as in children with GERD and FGIDs. This can make diagnosis difficult and thus clinical judgement is required (Figure 1).

CMA is a risk factor for developing FGIDs later in life such as irritable bowel disease (IBD)[9] and it is therefore important that is is recognised and appropriately managed. One study found that 44% of patients (n=52) who had CMA experienced gastrointestinal (GI) symptoms compared to 20% of controls (n=53)[9]. Of the CMA patients, 19% of fulfilled the Rome III criteria for FGIDs compared to none in the control group[9].



"Figure 1. Overlap between CMA and FGIDs"

Dietary and Clinical Management

The management of CMA or any FGID begins by listening to the parents and acknowledging their distress[10].

Colic

Most of the time, treatment of colic involves supporting parents to cope with this period of development. It is important to explain normal crying patterns to parents. If there are parental warning signs, such as parental anxiety or depression, provide support and reassurance as needed[10].

In breastfed (BF) infants, avoid overfeeding and over-stimulation and consider using the probiotic Lactobacillus reuteri DSM17938[10]. In formula fed (FF) infants, consider using a partially hydrolysed or a lower lactose formula along with a prebiotic[10].

Constipation

Functional constipation is rare in BF infants[10] however, if it does occur, provide parental reassurance and encourage mothers to continue with BF if they are able to10. In FF infants, as well as providing parental reassurance, check that the formula is being correctly prepared and that infants are receiving the correct volume[10].

Consider using a partially hydrolysed whey formula (pHF), with prebiotics, probiotics, magnesium, beta palmitate or that is palm oil free to reduce symptoms of constipation[10]. If symptoms persist in FF infants, laxatives such as lactulose may be recommended[10].

If the infant is on complimentary feeding, it is important to check their fluid and fibre intakes[10].

Infant Regurgitation (Reflux)

Reflux is very common in the first few months of life and usually reduces without intervention by 12 months[11]. If there are no red flags, reflux should be managed conservatively.

It is important to ensure that the infant is not being overfed. If necessary, feeds can be thickened using an age-appropriate thickener[10,12]. Reflux is not a reason to stop BF and it should be continued where possible[10]. A BF advisor will be able to check the mother's feeding technique. This is important as an insufficient latch may produce reflux symptoms.

If these techniques with colic, constipation are ineffective and you suspect CMA, guidelines recommend 2-4 weeks of extensively hydrolyzed formula (EHF) in FF infants or trialing the mother on a CM elimination diet in BF infants[10,12]. In those who have non IgE-CMA, removing CM from the diet improves symptoms of reflux[13]. If the diet is observed to be beneficial, a cow's milk-based formula challenge should be planned to confirm the diagnosis of CMA.

Non-IgE Mediated CMA

If symptoms persist despite first-line measures, they are likely to be allergy related. Trial exclusion diets must only be considered if the history and examination strongly suggest CMA[10].

It is also important to ensure that oral-motor-skill development is maintained as those with non- IgE mediated allergies can be at greater risk of developing feeding difficulties[14].

Managing non-IgE mediated CMA begins with a 2–4-week CM elimination diet, followed by reintroduction to confirm the diagnosis[10]. Clinicians and parents should aim to follow the World Health Organization's guidance on BF[15] as breastmilk is the gold-standard form of nutrition for infants. BF supports a baby's microbiome via the entero-mammary pathway whereby gut bacteria is transferred from the mothers' GI tract through the breastmilk[16]. Bacteria are also transferred when the infant sucks on the mother's nipple[16].

In a BF CMA infant, guidelines recommend that the mother follows a CM-free diet[17,18]. It is important to support the mother to ensure they have an adequate intake of calcium, vitamin D and iodine[18,19]. Support the mother to continue breastfeeding where possible and provide education around food labelling law, hidden sources of CM and recipes.

In FF CMA infants, there are three categories of suitable formula[20]:

- Extensively Hydrolysed Formula (EHF) e.g. EHF-whey, EHF-casein
- Amino Acid Formulas (AAF)
- Non-Milk Proteins e.g., soya (suitable after 6 months of age), rice hydrolysate

EHF is recommended as a first-line intervention for the majority of CMA infants[21]. AAF is indicated in eosinophilic esophagitis, anaphylaxis, faltering growth and failure to thrive on an EHF[21]. Supplementation of vitamins A and D, calcium, iron and zinc should be considered[22].

Globally there is a high prevalence of FGIDs amongst infants, although its aetiology is unclear[4]. Interestingly, research shows that CMA may lead to FGIDs later in life . Differentiating between FGIDs and CMA is challenging but important, and a diagnosis must be confirmed by an elimination diet followed by a food challenge[10]. In the absence of red flags, testing and pharmacological treatment should be avoided.

Considerations for Clinical Practice

- Consider the impact that a change of feed has on the infants real or perceived symptoms and on the psychological health of the parent.
- Make sure you have enough time in the consultation to listen to the parents to help you to make decisions
- Any change of feed should bring you closer to a diagnostic answer
- Follow-up to ensure that the diagnostic diet is correct, and that re-challenge occurs.

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