MANAGEMENT OF FUNCTIONAL GASTROINTESTINAL DISORDERS (FGIDs) IN INFANTS - Prof. S. Salvatore

Parallel to the ESPGHAN 2019 congress held on June 5-8th in Glasgow (UK), more than 170 pediatricians from 25 countries gathered on June 6th for our Novalac symposium. During this event, Prof. Silvia Salvatore from the department of Pediatrics (University of Insubria, Varese, Italy), delivered a presentation related to the management of functional gastrointestinal disorders (FGIDs) in infants.

«Why do we have so many FGIDs in infants?

As demonstrated in the biopsychosocial model, many factors can interfere with baby wellness. Functional gastrointestinal disorders (FGIDs) result from the complex interaction between biological and psychosocial factors. They come from genetics in addition to environmental factors such as early life events (antibiotic use, infection, inflammation, allergies, etc.), family coping style, family stress... Knowing these factors will help managing these FGIDs."

Prof. Silvia Salvatore from the department of Pediatrics (University of Insubria, Varese, Italy)

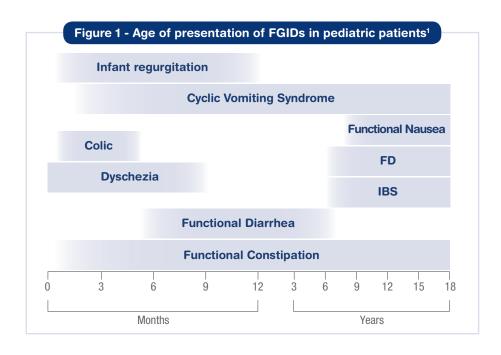


In the past decade, new insights have been gained about the different functional gastro-intestinal disorders (FGIDs) in infants and toddlers.

New Rome IV diagnostic criteria of FGIDs have been defined by a scientific expert committee in 2016¹.

The main FGIDs are infant regurgitation, infant colic, functional diarrhea, functional constipation, infant dyschezia.

Figure 1 shows the age of presentation of FGIDs in the pediatric age group¹.



About **30-50**% of infants present with symptoms of FGIDs during the first 12 months of life.

These FGID symptoms can have **important consequences on the families and the society**. They vary from mild to extremely distressing for the infant and parents and may lead to a cascade of infant discomfort and crying, parental anxiety, poor quality of life, short- and long-term health consequences, shortened duration of full breastfeeding, frequent formula changes and medical consultations, overuse of drugs and high associated healthcare costs²⁻⁹. FGIDs result from **complex interactions between biological, psychological, and social factors**.

Scientific and medical experts have developed and discussed practical recommendations and algorithms to manage FGIDs^{4,7}. The most relevant recommendations for the pragmatic management of FGIDs can be summarized as follows:

- Observe: the infant, the parents and the meal.
- **Educate and reassurance**: provide information on natural history of FGIDs, infant growth and feeding.
- Avoid: overload, smoking, tests, drugs.

1 OBSERVATION FOR ANY ALARM SIGNS

The first step in the management of FGIDs is to make sure the symptoms are functional. Thus, **any abnormal signs should be excluded** when reviewing the history of symptoms and onset of FGIDs, when evaluating the meal, parents' interaction, performed tests, when assessing growth and development, and during physical examination.

2 EDUCATION ON FGIDs

Parental education and reassurance is recommended as the first line of management of FGIDs⁷:

- Nutritional advice should emphasize the benefits of breastfeeding and appropriate support should be offered whenever necessary. Parents should be aware that breastfeeding provides the most ideal nutrition for infants.
- Overfeeding infants may exacerbate their symptoms and should be avoided.
- Colic and regurgitation are temporary problems during the first months of life and then spontaneously decrease and resolve in most infants within the first year.
- Pharmacological approaches are not necessary for infantile colic and regurgitation and could harm infants. Gastric acid inhibitors such as proton pump inhibitors (PPI) or prokinetic drugs have been shown to have side effects, such as an increased rate of infection, and are mostly ineffective for these conditions. Drug treatment is exceptionally used in case of functional constipation.

2.1 Breast milk for FGIDs: the best functional and personalized food

Breastfeeding should be recommended and supported, even when infants display persistent and severe FGIDs. Breast milk is a perfect orchestra for micro/macro nutrients and for immune properties (Figure 2).

Figure 2 - Protective effects of breastfeeding¹⁰



Passive immunity by the IgA antibodies

- Protection against infections
- Reduce risk of CD



Regulation of gut permeability

- Reduce of gastrointestinal infections
- Prevent of tissue transglutaminase expression



Bioactive antimicrobial factors

- Maturation of gut
- Development of the infant's innate and acquired immunities



Exerted of immuneregulatory

 Via suppression of autoimmunogenic T-cell



Antimicrobial and anti-inflammatory agents

- Blocking of the inflammatory cytokines production by lactoferrin
- Protection against infections via oligosaccharides

2.2 Special milk formulas in FGIDs, for whom?

Iln non-breastfed infants, special milk formulas may be considered in case of FGIDs.

Each infant is unique, but each infant formula is unique, too. Thus, infant formula that shows clinical benefits should be chosen. Special milk formulas are specific for infants with a particular gastrointestinal symptom. Key nutrients in special milk formula include protein, fat, carbohydrates, prebiotics and probiotics, and have different properties of interest for specific situations.

The role of proteins in the management of FGIDs

The nature of proteins (casein or whey) and their degree of hydrolysis (native, partial or extensive) will differently impact gastric emptying. Whey proteins are emptied faster than caseins, thus those last ones are better to improve satiety.

Partial hydrolyzed formula (pHF) for FGIDs?

Some studies show no benefit of pHF on FGIDs whereas others show benefits on colic, regurgitation and sometimes stool consistency. However, tested formulas differed not only by the nature of the proteins but also by other components (GOS/FOS, lactose content, etc.). Based on these conflicting results, no recommendation can be made on the use of pHF for FGID management.

• Extensively hydrolyzed formula (eHF) for FGIDs?

For a faster gastric emptying, eHF should be selected. eHF will also treat 90 to 95% of infants having CMA and reduce lactose related symptoms. However, there are some disadvantages regarding the use of eHF in case of FGIDs: different eHFs exist on the market, there are limited data on the long-term outcomes, eHFs can also influence taste development, and the cost of these formulas is not negligible.

How to differentiate FGIDs from cow's milk allergy (CMA)?

The diagnosis of CMA and its distinction from FGIDs is quite challenging since their age is overlapping, they do not have specific symptoms, CMA is frequently non-IgE mediated, and a possible association and confounding response may exist^{11–14}.

The Cow's Milk-related Symptom Score (CoMiSS), which considers general manifestations, dermatological, gastrointestinal and respiratory symptoms, was developed as an awareness tool for cow's milk-related symptoms¹⁵. Symptomatic children who score 12 or higher on the CoMiSS score with the presence of at least three symptoms and the involvement of two organ systems, are considered at a high risk of CMA. But the CoMiSS awareness tool is not a diagnostic test for CMA. It does not replace a food challenge with a cow's milk-free diet.

Thickened formulas for infants with regurgitation

Studies in infants with persistent regurgitation and poor weight gain have shown that **thickened formulas significantly reduce by half the number of regurgitation episodes**, increase the number of infants without regurgitation and increase weight gain compared to standard formulas¹⁶. Commonly used thickening agents include carob/locust bean gum, corn starch and rice starch.

A commercial thickened formula has the advantage to be homogeneous, to have a nutritionally balanced composition, and a higher viscosity in the stomach, but it is more expensive and there might be a risk of over use. In contrast, a "home-brew" thickened formula is cheaper and easy to prepare, but there is a higher sucking effort for the infant, a delayed gastric emptying, an inconsistency in composition and it has a too high viscosity and many calories.

For some babies with persistent symptoms or regurgitating while breastfed, the thickening agent alginate has been recently shown to significantly decrease the number and extension of both acid and non-acid reflux episodes and associated symptoms in infants with suspected GER-disease¹⁷.

How to manage infant colic?

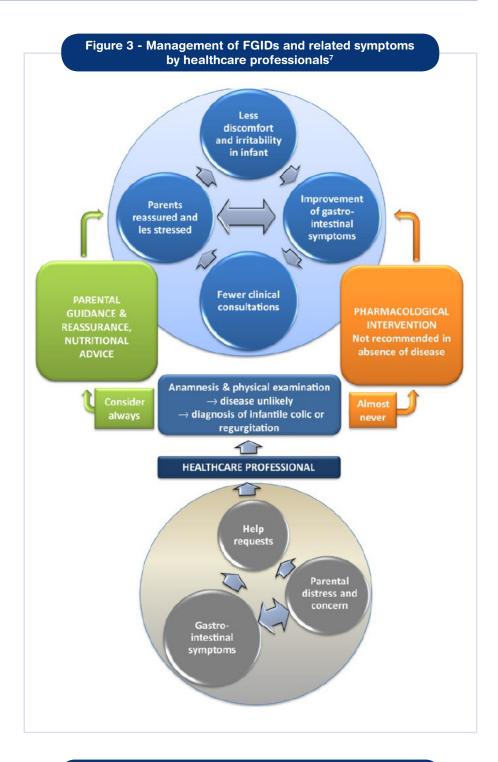
Infant colic results from normal developmental process. It is described as a behavioral syndrome in infants younger than 5 months old involving long periods of crying and hard-to-soothe behavior¹.

Parental reassurance is used as the first line of management of infant colic1. There is no evidence that pharmacologic intervention are useful. Some studies suggest that particular probiotic supplements are effective for breastfed infants with colic but there are insufficient data to make conclusions for formula-fed infants with colic¹⁸.

3 EDUCATION ON FGIDs

FGIDs often lead to a **vicious cascade** of distressed infants, concerned parents, increased medical consultations, overprescribing and use of over-the-counter medication, resulting in escalating healthcare costs (Figure 3)⁷.

By providing complete and updated parental education, reassurance and nutritional advice, healthcare professionals can help to disrupt this cascade and optimize the management of FGIDs and related symptoms by reducing infants' distress, alleviating parental anxiety and improving the quality of life for the family while protecting healthcare budgets (Figure 3)7.



Recommendations

- 1. Observe for any warning signs and symptoms in the infant, the composition of the meal and the maternal-infant interaction.
- **2. Educate** and reassurance by providing information on the natural history of FGIDs, growth and nutritional advice.
- 3. Avoid overfeeding and extra-fluid to the infant, passive smoking, cow's milk protein in selective cases, and unnecessary tests, diet and drugs.

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