GASTROESOPHAGEAL REFLUX IN NEWBORNS AND INFANTS (II)

Valeriu V. Lupu, Ancuta Ignat, Gabriela Paduraru, Marin Burlea
Pediatrics Department, "Gr. T. Popa" University of Medicine and Pharmacy, Iasi

ABSTRACT

Gastroesophageal reflux in newborns and infants is particularized by pathogeny, diagnosis and therapeutical approach, functional immaturity of the digestive tract, the anatomic immaturity of the Hiss lower esophageal sphincter and lower gastric acidity. In infants, the low compliance with the laborious procedures such as pH-metry, impedance – pH-metry and digestive endoscopy is also considered. The border between regurgitations, physiological gastroesophageal reflux and the reflux disease is sometimes hard to establish. Changing the lifestyle of infants (feeding and position changes) based on the mother's compliance with the medical recommendations is a first step in the treatment of GER, followed in non-responsive cases by pharmacological therapy and surgery.

Keywords: gastroesophageal reflux, newborn, infant

GERD TREATMENT

The treatment options in physiological GER (gastroesophageal reflux) and in GERD (gastroesophageal reflux disease) include: life style changes, pharmacological therapy and surgery.

Life style changes in infants with physiological GER include feeding and positional changes. Parents' education, guides and moral support are always necessary and usually enough for infants with physiological GER symptoms. In young infants with functional GER, regurgitations and vomits spontaneously disappear until the age of 1 year old. Parents have to be informed of the physiological nature of the condition and of the distinction between physiological and pathological reflux. Parents need to be listened to and comforted. We have the obligation to understand their anxiety, and tell them about the natural history of the disease. Parents have to be informed completely and to the point because most procedures will be performed by the parents.

Diet-related measures

Approximately 50% of the healthy infants aged 3 to 4 months have at least one regurgitation a day (26).

Both breastfed infants and formula-fed infants have a similar frequency of physiological reflux, but the length of the reflux episodes established by the pH monitoring can be shorter in breastfed infants (27,28).

A study done on infants showed that feeding a large amount of milk caused regurgitation, probably due to the increase in the frequency of the transient LES relaxation and a reduced volume of milk decreased the reflux frequency (29). The severe reduction of the food amount for a long time can deprive the newborn of the necessary caloric energy and can affect weight gain. Infants with inappropriate weight due to the losses caused by regurgitations can benefit from the caloric energy increase by means of special formulas when the volume or frequency of feeding is lower as part of the therapy (21).

Products that thicken meals or thickened formulas (Gelopectose 3-5%, Gumilk 2%) and anti-reflux milks lead to the decrease in the number of regurgitations; similarly, rich foods for infants such as cereal formula seem to reduce GER. They increase viscosity and form a fine flocculate easy to evacuate from the stomach, remaining as a suspension in the gastric fluid (30).

Corresponding author:
Ancuta Ignat, "Gr. T. Popa" University of Medicine and Pharmacy 16 Universitatii Street, Iasi
E-mail: anca_ign@yahoo.com

Lunches thickened with rice cereal are associated with a decrease in the number of vomiting episodes, but the reflux index is not improved (31). There are studies reporting that thickened formulas can reduce the frequency of regurgitations and the total volume per vomit. Furthermore, they can reduce the child's crying time and increase the sleeping time (32). Other studies show that thickening lunches can aggravate cough episodes and/or other postprandial respiratory symptoms (33). The rice cereals used increase the caloric density of the formula and can cause constipation. Milk thickening is associated with a higher risk for necrotic enterocolitis among premature infants.

In addition, milk formulas that are evacuated faster from the stomach are used. The richer the milk formulas are in casein, the slower is their evacuation. Casein flocculates in the acid gastric environment (30).

The tobacco environment will be supressed as it decreases the LES pressure. Moreover, all sources of abdomen compression must be avoided: wrapping the infant or clothes that are too tight, inappropriate anti-herniation bandage or sudden handling that can cause regurgitations or vomits (30).

Consequently, in formula-fed infants with frequent regurgitation, the following approach is recommended: the feeding history is established, the meal amount is reduced only if they are excessive for the child's weight, smaller and more frequent lunches are provided (at the same time maintaining the same amount of daily milk) except if lunches are already small and frequent, then thickened formulas are added (for example, the ones containing rice starch, corn starch or carob flour) (18).

In breastfed infants who continue to manifest regurgitations despite evaluation and counselling, alginate therapy is considered for 1 to 2 weeks. If the alginate therapy is beneficial, it is maintained, but it is suspended at certain intervals to check if the infant has recovered (18).

In formula-fed infants, if this approach is not successful, the thickened milk formulas are removed from feeding and an alginate therapy is administered for 1 to 2 weeks. Similar to the breastfed infants, if the alginate therapy is beneficial, it is maintained, but it is suspended at certain intervals to check if the infant has recovered (18).

Medication supressing acidity such as proton-pump inhibitors (PPI), H2 receptor antagonists is not administered to treat infants with regurgitations as isolated symptoms (18).

Postural recommendations

Originally, it was noticed that positioning the baby in ventral decubitus with the head higher leads to less frequent and shorter reflux episodes, but without significant effects on the duration of the reflux (34). Subsequently, the possibility of sudden death in this position reduced enthusiasm. In many countries a campaign against ventral positioning of infants was even launched due to the sudden death risk. This positioning can be useful when the infant is awake. This way, placing the awake infant in ventral position with the head on one side, inclined at 30-45^{o} is efficient in controlling regurgitations and/or vomits and implicitly reflux (35).

pH-metry helped prove that the ventral position decreases exposure of the esophagus to the acid refluxate in comparison to the dorsal position (36).

The supine position and the semi-sitting position are to be avoided, placing the infant in the car seat or in any sitting position after meals is to be avoided, as it can exacerbate the GER, by increasing intraabdominal pressure.

Consequently, the postural therapy is a therapeutic manner useful in small children, by placing them on a plane inclined at 35-40^{o} in dorsal decubitus under surveillance.

Pharmacological treatment

The purpose of the pharmacological therapy in GERD is: to improve the reflux symptoms, to prevent major complications and surgery, to prevent the recurrence of the disease. Pharmacotherapy is indicated in pathologic GER or when the conservative treatment (postural therapy and diet) did not have the expected result.

Therapy with PPI or H2 receptor antagonists is not recommended for the treatment of infants with regurgitations as an isolated symptom.

A 4-week treatment with PPI or H2 receptor antagonists is considered for patients who cannot account their symptoms (infants), with numerous regurgitations and difficult feeding (for example, in infants refusing food or with suffocating episodes), unusual behaviour or growth difficulties.

If the symptoms do not disappear or reappear after the treatment with PPI or H2 receptor antagonists is stopped, an upper digestive endoscopy is considered.

When the PPI or the H2 receptor antagonists are chosen, their availability for the age in question, the parents' preference and the purchase price are taken into account.

PPI is the most efficient treatment that suppresses hydrochloric acid, binds covalently and deacti-

vates the proton pumps in the parietal cells (pumps H+/K+ - ATPase). Due to their anti-secretory effect, they are the preferred medication in the treatment of GER, as they entail the disappearance of the reflux symptoms in over 90% of the cases (37). This empirical treatment is maintained during 4 to 8 weeks and is a true diagnosis test that is simple and cost-efficient, including for those with extra-digestive symptoms (38). Maximum efficiency is obtained when they are administered ½ hour before breakfast so that the peak of plasma concentration may coincide with the meal; if the treatment is administered in two daily intakes, the second dose is administered ½ hour before the evening meal. PPI are represented by benzimidazoles: Omeprazole, Pantoprazole, Lansoprazole, Esomeprazole, Rabeprazole. French authors reported high toxicity for PPI: headache, vertigo, sleepiness, cutaneous reactions, mental confusion, haematological changes, hepatitis (possibly in fulminant form), digestive and electrolytic disorders, medication interactions (39). The basic indication of the PPI treatment remains the severe esophageal lesion (erosion and esophageal ulceration) or Barrett's esophagus. The administration of PPI to those with non-acid reflux does not influence the volume and frequency of the reflux episodes in comparison to those with acid reflux. The emergence during the PPI treatment of nocturnal "acid leaks" (i.e. nighttime reflux episode) is controlled by doubling the PPI dose or by associating a H2 receptor blocker intermittently, to prevent tachyphylaxis, which develops quickly under continuous administration.

H2 receptor antagonists reduce the acid secretion by inhibiting the H2 histamine receptors in the gastric parietal cells. In a study on infants, ranitidine (2 mg/kg/dose) reduced the time in which the pH was < 4 by 44% when they were administered twice a day and by 90% when they were administered three times a day (40). Among the members of the series (Cimetidine, Ranitidine, Famotidine, Nizatidine), the most studied and used in paediatrics are Ranitidine and Nizatidine (41). H2 receptor blockers are still used as first-line therapy in mild and medium esophagitis, for 6 to 8 weeks in mild esophagitis and for 3 to 4 weeks for moderate forms of esophagitis. H2 receptor antagonists therapy is efficient, but it should not be used on a long term. They can cause tachyphylaxis in six weeks' time and can increase the risk of liver disease and gynecomastia.

Metoclopramide, domperidon and erythromycin are not administered to treat GER or GERD, considering their potential in side effects (18).

Prokinetics can reduce the symptoms of GERD by improving the contractility of the esophageal body, increasing the LES pressure and increasing the gastric emptying rate. Despite this, the benefits of these agents cannot overcome negative effects such as: sleepiness, agitation and extrapyramidal reactions. There is no sufficient proof to support the routine use of prokinetics in GERD in children.

Surgical treatment

For the surgical treatment (fundoplication), an upper digestive endoscopy is performed for biopsy purposes. pH-metry or impedance – pH-metry can also be performed before surgery.

After the GERD diagnosis is confirmed, surgical therapy is considered for patients:

- For whom medical management was not successful (severe regurgitations uncontrolled by treatment or important side effects following the treatment);
- For whom surgery is an option despite the efficient treatment (life quality, the administration of medication during the patient's entire life, the cost of medication are taken into consideration);
- Who develop GERD complications (Barrett's esophagus, peptic stenosis) (42,43);
- Who show extra-digestive manifestations (dysphonia, chronic cough, aspiration pneumonia) (44,45,46).

In addition, in infants with severe GERD, fundoplication is performed when the diet-related measures have proved inefficient, in case feeding thickened formulas by nasogastric tube continues for a long time (18).

The Nissen fundoplication is the preferred method, being very effective in controlling vomits. It is performed in classic surgery, and lately more and more centres choose to do the intervention laparoscopically, which is superior to the classic techniques, due to better visibility and its less invasive and aggressive character.

Generally, anti-reflux surgery has been more attentively evaluated in adults than in children. Among the children who had surgery, those with neurological disorders suffered from complications twice more often, morbidity was three times higher, and a second surgery was necessary 4 times more often than in those without neurologic disorders (47,48).

Fundoplication in early childhood has a rate of failure higher than fundoplication performed later in childhood (49).

EVOLUTION OF GERD IN NEWBORNS AND INFANTS

The consequences of reflux can become obvious from the very neonatal and small infant period. At this age, the emetic form, the hemorrhagic form and respiratory forms or forms of neurologic expression settle into shape.

Hematemesis emerges before the age of 10 days of life (through esophagitis often associated with gastroduodenitis) and is the main cause for haemorrhage at this age, being aggravated by hypovitaminosis K; thus prophylaxis with vitamin K administered systematically during the first hours of life becomes useful, and in some countries it is maintained until the age of 3 months (for example in Italy).

Moreover, a pathologic GER can generate paroxysmal attacks, which often have a dramatic course, with cyanosis and hypotonia, respiratory distress, laryngeal dyspnea or apnea crises, needing reanimation (sometimes marks sudden death); manifestations are hard to correlate with reflux, but the positive answer to anti-reflux therapy and the pH-metry tests confirm the cause.

In addition, at the same age, other consequences of reflux are not negligible either, such as the respiratory ones: repeated bronchiolitis or pneumopathies, nocturnal cough and wheezing episodes, which – in evolution – turn into chronic respiratory disease, and nutritional consequences: weight stagnation, hypochromic anemia.

PROGNOSTIC IN GERD

The prognostic for infants with a history of physiological or functional GER is very good, even with spontaneous and full healing.

GERD raises problems where the manner of treatment, the response to therapy and time play a decisive role.

The following can deemed unfavourable prognosis factors:

- Delayed diagnosis, in the phase of severe esophagitis, esophageal stenosis or Barrett's esophagus;
- Encephalopathic children or children with other associated neurologic disorders or behavioural disorders; considering that infants with psychomotor retardation are affected by GER in over one third of the cases. These develop extended esophagitis lesions generating short-term anemia, and long-term esophageal stenosis lesions;
- Other associated diseases such as: scleroderma, mucoviscidosis;
- Incorrect treatment, with discordance between the lesion type and the type of treatment used;
- The patients' or parents' lack of compliance;
- Resistance to treatment (for example, non-responsive to the PPI treatment).

In conclusion, GERD is a condition with a good prognostic, the therapeutic results reported by all the data in literature are favourable. Every case must and needs to be individualized.

CONCLUSIONS

It is important to establish accurately the physiological or pathological character of gastroesophageal reflux to know the subsequent therapeutic approach.

Reduced compliance to laborious procedures (pH-metry, impedance – pH-metry and upper digestive endoscopy) makes the clinical examination and parents' accounts sufficient to diagnose reflux.

In the case of newborns and infants, it is important to apply the diet-related and postural measures necessary when regurgitations and vomits appear.

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