



# From Newborn to Teenage: Gastroesophageal Reflux

Nafiye Urgancı, Merve Usta

Clinic of Pediatrics, Şişli Hamidiye Etfal Training and Research Hospital, İstanbul, Turkey

## ABSTRACT

Gastroesophageal reflux (GER) is characterized by the involuntary passage of gastric contents into the esophagus. GER disease is defined as a persistent or intermittent passage of gastric contents into the esophagus, which often results in overt clinical signs and symptoms and affects the quality of life. GER is a common disorder in childhood and has a good prognosis. GER in infancy begins within the first month of life, peaks at the 4<sup>th</sup> month, and after the first year, it steadily decreases and finally resolves at the age of 2 years. GER physiologically occurs due to the relaxation of the lower esophageal sphincter, independent of swallowing. The mechanisms against GER include the following; 1. Lower esophageal sphincter dysfunction, 2. Clearance effect of esophagus, 3. Esophageal mucosal integrity, and 4. Gastric emptying, which prevent the development of GER disease. Although the physiopathology of GER is still not clearly established, proposed factors are genetic, environmental, anatomic, hormonal, and neurogenic. The most responsible factor is lower esophageal sphincter relaxations. The clinical signs of GER varies with age but commonly appear with gastrointestinal and respiratory symptoms. The diagnosis of GER disease is based on history, physical examination, esophageal pH monitoring, multichannel intraluminal impedance and esophageal manometry, motility examinations, endoscopy, biopsy, examinations with barium, and nuclear scintigraphy. Treatment of GER includes non-pharmacological and pharmacological therapies, such as prokinetic agents and acid suppressors. Surgical treatment indications are relatively limited. (*JAREM 2016; 6: 67-73*)

**Keywords:** Gastroesophageal reflux, gastroesophageal reflux disease, children

## INTRODUCTION

Although gastroesophageal reflux (GER) is a common childhood problem with a good prognosis, its incidence in all age groups gradually increases in proportion to socioeconomic conditions, modern urban life, and fast food consumption. It may especially present with esophageal and extra esophageal symptoms, such as chronic cough, sore throat, and hoarseness. The variety of symptoms and complications of GER disease changes with age in children.

## DEFINITIONS

### GASTROESOPHAGEAL REFLUX (GER)

GER is the leakage of the stomach content into the esophagus with or without regurgitation or without vomiting. GER is a physiological condition that occurs frequently during the day in newborns, infants, and in childhood and adulthood. Many of the attacks of GER in healthy individuals are short-term and they present without symptoms or a few may have mild symptoms. It is a clinical condition that is encountered in more than two-thirds of healthy children and a quarter of infants brought to the 6<sup>th</sup> month controls to pediatricists (1, 2).

### GASTROESOPHAGEAL REFLUX DISEASE (GERD)

GERD is a widespread condition affecting almost 3% of the general population. In GERD, the stomach content leaks into the esophagus intermittently or continuously, causing clinical symptoms and findings, such as pain and dysphagia, and complications, such as a reduced quality of life and even growth retardation, nutrition or sleep problems, chronic respiratory disease, esophagitis, bleeding, and apnea (1).

## REGURGITATION (SPITTING-UP)

Regurgitation is the bringing up of the stomach content to the pharynx or mouth or sometimes outside without effort or in a non-projectile way. It is mainly physiological and occurs after meals in infants but usually resolves after the child reaches 12–18 months of age (1, 3).

## RUMINATION

Rumination is characterized by effortless regurgitation attacks, resulting in bringing up newly swallowed foods to the mouth without any difficulty, chewing again and swallowing or ejecting through the mouth. Although it is rare in childhood, it is seen in infants between 3–12-month-old or in children with mental retardation (3).

## EPIDEMIOLOGY

Reflux in infancy appears from the 1st month of life. While its incidence peaks approximately at the 4<sup>th</sup> month, it gradually decreases after 1 year of age and almost all children recover at 2 years of age. Regurgitation, which is highly seen in 70–85% of healthy infants, especially those younger than 3 months old, heals spontaneously at 12–14 months of age at a rate of 95% (1, 4). GER in older children tends to become chronic and has a similar clinical picture to reflux in adults (5). In the literature, while the frequency of regurgitation in healthy infants is 50% at 0–3 months old, it is 23–67% at most at 4–6 months old, and drops to 21% at 7–9 months old, and then it is reported to be below 5% at 10–12 months old (6, 7). Although a reflux of >4 times/day is seen less, it is suggested that the regurgitation rate of >4

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Address for Correspondence: Dr. Nafiye Urgancı,  
E-mail: nafiyeurganci@yahoo.com

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times/day in infants up to 3 months old is 20%, while it is 23% at 4–6 months old, 3% at 7–9 months old, and 2% at 12 months old (7). The incidence of gastroesophageal reflux in children differs by ethnicity and geography. Its incidence is reported to rise from Western to Eastern countries and is related with age. It was detected in a study conducted in Australia that GER attacks that occur at a rate of 41% in 3–4-month-old infants dropped below 5% at 13–14 months old, and then recovered at the 19<sup>th</sup> month (7). Gastroesophageal reflux-related symptoms in children are more frequently seen in GERD. It is reported that 5–8.2% of children aged between 10 and 17 years old in the US had at least once had GERD symptoms, while a GERD diagnosis was made in 10.9/1000 patients in the UK. Furthermore, in adult studies, GERD symptoms in Asian countries were below 5%, while they were 10–20% in North America and Western European countries (8). It is reported that the GERD incidence in infants is 12.3% in North America and below 1% in older children (9). The frequency of GERD was –reported to be 20–25% in adults and was seen to be between 5% and 15% in childhood. It is known that complaints of reflux, which fairly decrease in the final period of infancy, have a weak relationship with GERD, which tends to occur in later periods of life. Additionally, for children whose mothers (not fathers) also had a GERD history and who had frequent regurgitation histories in their infancy, this is another factor increasing the risk of occurrence of symptoms associated with reflux in their later ages (3, 5). In the literature, it is reported that children having regurgitation more frequent than 90 days display adult type reflux symptoms more often around 9 years of age, while children having GERD symptoms in their early childhood continue to have them in adolescence and adulthood (10, 11).

It is reported that gastroesophageal reflux disease is more common in females than in males (7, 8).

## **PATHOPHYSIOLOGY**

Gastroesophageal reflux physiologically occurs frequently as a result of transient lower esophageal sphincter relaxation (TLESR), independent of swallowing in daily life. When food enters the stomach, mechanoreceptors in the gastric mucosa are activated in response to little pressure increases in the stomach, and fundus dilation takes place, with circular muscle relaxation and nitric oxide emission. Stretching of the fundus leads to TLESR, stimulating the vagosympathetic reflex. Transient lower esophageal sphincter relaxations are triggered by a right-side lying position, the presence of a nasogastric tube, and bloating after meals (1, 7, 8). Four major mechanisms prevent the occurrence of GER in physiological conditions.

1. Lower esophageal sphincter incompetence, 2. The cleaning function of the esophagus, 3. Mucosal continuity, 4. Gastric emptying. Disorders of these mechanisms are responsible for the disease, most importantly, low pressure lower esophageal sphincter (LES) and transient relaxation of the LES. The antireflux barrier is formed from the lower esophagus sphincter (LES), diaphragm crus, and His angle. While the upper esophageal sphincter resting pressure is 15–70 mmHg in adults, it varies between 10 and 40 mmHg (20 mmHg on average) in children. The lower esophageal sphincter is not a simple anatomic valve, rather it is a physiological sphincter formed of smooth muscle cells, which are 3–7 cm in

adults and a few millimeters in infants, having a pressure area of 20 mmHg on average (10–40 mmHg). Both sphincters are shorter than those of adults. The crus of diaphragm is the part of the esophagus in the stomach that strengthens the sphincter function by wrapping the LES with the right crus. As the diaphragmatic crus in infants is almost 2 cm above the diaphragm in the first six months of life, it is insufficient for wrapping the LES (till the abdominal cavity). Therefore, intraabdominal pressure increases in cases of deep inspiration or stretching and leads to the occurrence of GER. 82% of reflux episodes in premature infants is linked to spontaneous transient LES (12).

The angle of His is the wide angle between the esophageal body and fundus of stomach, and it is not yet formed in children. As they grow up, it sharpens and becomes a protective obstacle to GER.

The anatomic shape of the stomach in adults is vertical and in the shape of letter J, while on the contrary, it is horizontal and in the shape of a flat bottle in children. Saliva, bicarbonate secretion of esophagus, and primary and secondary peristalsis in the esophagus are important for cleaning the esophagus. Motility failure (primary peristalsis beginning with swallowing and esophageal body motility failure sending back milk to the stomach that has come from the stomach by secondary or tertiary peristalsis); a small volume of stomach; the life style of infants (lying or in a horizontal position most of the time in a day); the nutrition styles of infants and prematures (frequent, more liquid, and large volume nutrition) who have not yet developed sucking, swallowing, retching reflexes, and esophageal motility; a short esophagus and its low capacity; and long-lasting gastric emptying are responsible for the occurrence of GER.

Apart from these, many anatomical, environmental, genetic, and neurogenic factors of changes of the physiological reflux mechanisms, such as the esophageal mucosal barrier, the frequency of reflux, gastric acidity, gastric emptying time, visceral hypersensitivity, standing, and hiatal hernia, are responsible for GERD occurrence.

The reasons increasing the intraabdominal pressure, such as cough; constipation; intraabdominal mass; convulsion; tightly dressing; distention; functional and anatomical reasons, such as neuromuscular disorder, obesity, some genetic syndromes; esophageal atresia operation; scoliosis; chronic pulmonary infection; and preterm labor history increase the risk of GERD compared to in healthy children (1, 8, 12).

While overeating; eating late at night; consuming fizzy drinks; and fatty, salty, and spicy food intake in older children increase reflux; caffeine, nicotine, some drugs (nitrates, theophylline,  $\beta$  adrenergic agonists,  $\alpha$  adrenergic agonists, dopamine, calcium canal blockers), and feeding with cow milk in infants cause reflux by decreasing LES pressure (1).

Moreover, a genetic predisposition is also held responsible for GERD. It is reported that its incidence in monozygotic twins is 19–31%, while it is 4–13% in dizygotic twins (10). It is considered that environmental factors are also effective besides genetics in cases with intermittent and frequent GERD. In particular, there is a problem in the 13q14 gene locus of the 13<sup>th</sup> chromosome in

pediatric cases in whom respiratory system symptoms of GERD are dominant (10, 13).

### CLINICAL FEATURES

The symptoms of gastroesophageal reflux disease vary with age. Infants eating well and not having unrest even though they have frequent regurgitation are called "happy spitters". There is no need for a special application for these infants. Convincing and training families form the basis of treatment. However, GERD has to be considered since symptoms such as unrest, apnea, cyanosis, recurrent attacks of vomiting, failure to thrive or weight loss, inappetence, the bodies' stretching like a bow during eating, stridor, sleep disorders, and observation of swallowing like movements during sleep are observed in children younger than 2 years of age, while recurrent attacks of vomiting, failure to thrive or weight loss, inappetence, refusal of food, chronic cough, Sandifer's syndrome (the form of reflux posture seen in older children), and stomachache in children older than 2 years of age are frequent symptoms. While intermittent regurgitation in preschoolers is frequent, complaints of stomachache and chest pain in addition to dyspeptic complaints similar to those of adults, such as retrosternal pain, acid reflux, burp, and tooth disorders, attract attention (1, 6-8).

Respiratory system complaints related with gastroesophageal reflux also vary with age: GER disease may accompany, for instance, obstructive apnea, stridor, or lower respiratory diseases in infants. Little children having persistent wheezing have to be evaluated also with regard to GER. Moreover, GERD has to be considered in cases of frequent attacks of otitis media, sinusitis, rhinitis, pharyngotonsillitis and lymphoid hyperplasia, muffled voice, vocal cord nodules, and laryngeal edema. Particularly, globus sensation and throat clearing movements in older children are important with respect to regurgitation. Respiratory system symptoms related with gastroesophageal reflux may often be related with diseases such as asthma or laryngitis and sinusitis (1, 6, 8). The coexistence of asthma and GER has been known for many years. GER may trigger asthma. It was detected in studies that GER played a role in triggering asthma in 25–75% of children. It is suggested that this coexistence is observed more apparently in cases when both pathologies are advanced (14, 15). Although the etiologic role of GER in asthma is not definite, it is suggested that asthma exacerbates GER. The possible mechanism of gastroesophageal reflux triggering asthma is by direct airway inflammation, aspiration of the gastric content, the passage of even a little acid to the lower respiratory airways, vagal stimulation, and bronchial and laryngeal spasm and inflammation (15). It was observed in some cases that asthma healed with the effective treatment of GER. However, which patients will respond to this treatment cannot be predicted (14, 15). Chronic cough, hoarseness, sinusitis, chronic otitis media, erythema in the larynx, a cobblestone appearance, reaching of the reflux content to hypopharynx, the release of cytokines and associated with this laryngeal symptoms, such as mucosal inflammation, edema, erythema, and stridor appear. Moreover, it is suggested that nasopharyngeal inflammation leads to an increase in otitis media by causing obstruction in the Eustachian tube (16-18).

In people having a habit of eating before bedtime, the relationship between obstructive sleep apnea and GERD causes apnea

through a protective mechanism during sleep while the gastric content is aspirated to the trachea and with the relaxation of the LES through a transdiaphragmatic pressure change, which in turn leads to GER again (19).

There is also a relationship between dental erosions and GERD. Acidic and sweet drinks and foods either directly cause erosion or decay with acid reflux by passing to the mouth or proximal esophagus or indirectly by leading to reflux attack (20).

### DIAGNOSIS

**Anamnesis and Physical Examination:** There is no reflux finding in newborns, infants, and children at the ages of 2–3 years old; however, there may be complaints and physical examination findings similar to adults in children older than 3 years old and in adolescents. Feeding history and the way of feeding, feeding frequency, quantity, position, behavior during feeding (rejection, feeling like drowning after feeding, coughing, throwing head back) and frequency, quantity and the way of vomiting, whether there is blood during vomiting, and unrest should be questioned (1, 2).

**Esophageal pH Monitoring:** This is used for evaluating the contact duration and frequency of acid with the esophagus. Acid reflux episodes take place in asymptomatic infants, young children, adolescents, and adults. The reflux index (RI), which is the ratio of time the esophageal pH is below 4 compared to the total time, is assessed generally as the most valuable measurement for indicating esophageal acid exposure. In infants, above 7% is abnormal, while between 3% and 7% is suspicious. The upper limit of RI in studies conducted with adults and older children is taken as 4–7%. The consideration of GERD is recommended in cases where the reflux index is >10% in infants and >5% in children. Additionally, the relationship between RI and clinical symptoms and the response to the disease or treatment is weak and the pH may be normal. It is also not related with the severity of the disease. It may even be normal in cases with defined esophagitis (1). Its sensitivity and specificity is above 94%. Its sensitivity is 30% and specificity 20%, approximately, in the diagnosis of GERD. Food intake during the operation, position, activity, the probes used, the location of probe, and the recording device may affect the results. Moreover, it is expensive and invasive. Also, it may not detect particularly nonacid postprandial refluxes. Prokinetics have to be cut at least 2 days, H<sub>2</sub> receptor blockers (H<sub>2</sub>RA) 3 days and proton pump inhibitors 5–7 days before the operation (1, 2).

**Multichannel Intraluminal Impedance (MII) and pH Monitoring:** This is a method that complements pH monitoring. It can detect acid in the esophagus, as well as weak acid and alkaline refluxes. It is appropriate in the evaluation of patients continuously feeding with a tube. It also indicates low level reflux and gas reflux. Non-acidic GER is often seen during feeding or within 1 h afterwards. It is more frequent in infants. 54% of GER episodes in 2–3-month-old infants and 45% in 8–11-month-old infants are not acidic. Therefore it is superior to pH monitoring alone. It was indicated that 45–78% of GER especially leading to respiratory symptoms were cases of non-acidic reflux. It can display the progress of the gastroesophageal reflux to specific parts of the esophagus. However, it is costly and its use is limited, and furthermore, there is no evidence-based data about the interpreta-

tion of data and it is unclear whether it can be used in evaluating the response to the treatment for children (1, 2, 21, 22).

**Motility Studies:** Motility studies place in diagnosis is restricted. They do not have enough sensitivity and specificity in gastroesophageal reflux disease but they are quite useful in the diagnosis of achalasia and motor disorders of esophagus (1). They are not a method used in the primary diagnosis of gastroesophageal reflux disease. Furthermore, their application in the childhood age group, particularly children under 6–7 years old is difficult since manometric assessment necessitates patient–physician collaboration (1, 2).

**Endoscopic Examination and Biopsy:** These are considerably valuable with regard to both examining the esophagus mucosa and in histopathological evaluation by conducting a biopsy. They are quite useful in displaying mucosal injury in the lower esophagus, reflux esophagitis, and stricture. Erythema in mucosa, its paleness, increased or decreased vascular appearance, or mucosa may be seen as normal. Eosinophilia, hyperplasia in basal membranes and an increase in the intercellular distances can be detected histopathologically. However, the absence of findings does not rule out esophagitis. Endoscopy is considerably important in following other reasons of esophagitis and for the control of Barrett's esophagus and its complications (1, 2, 7, 8).

**Barium Examination:** This is not useful in the diagnosis of gastroesophageal reflux disease. However, it is helpful in displaying anatomical abnormalities of the upper gastrointestinal system, such as pharyngeal, laryngeal, or upper esophageal abnormalities, having similar symptoms to GERD, GERD-associated complications, such as stricture and pyloric stenosis, the reasons causing obstruction, such as malrotation with intermittent volvulus, and motility disorders, such as achalasia. Approximately, its sensitivity is 30% and specificity is 20% (1, 2).

**Nuclear Scintigraphy:** This is a non-invasive, accessible, and inexpensive diagnostic method. When compared with the esophageal pH study, it determines the reflux of non-acidic stomach content and the rate of gastric emptying. However, its specificity (83–100%) and sensitivity (15–59%) are low due to crying, coughing, not staying firm during the procedure, and the shortness of examination when compared with pH monitoring. Therefore, while it has a limited place in the diagnosis of gastroesophageal reflux disease in the literature, it can be helpful for the diagnosis of pulmonary aspiration in cases having chronic and resistant cough. It can also be used for indicating the gastric emptying time. Nuclear scintigraphy is not used routinely for GERD diagnosis in child patients (1, 2).

**Esophageal and Gastric Ultrasonography:** This is not used routinely for the evaluation of GERD diagnosis in children (1). However, short liquid movements may be observed during the USG examination of the gastroesophageal junction and non-acidic refluxes can be recognized.

**Ear, Lung, and Esophageal Liquid Examinations:** It is suggested that pepsin, lactose, glucose, or lipid laden macrophage in the middle ear or bronchoalveolar fluid indicates reflux-related aspirations in the middle ear, sinus, and pulmonary diseases. However, there are no controlled studies indicating that this case

is specific to only reflux or if the detection of reflux material in the lungs is the main reason leading to the disease (1, 23-25).

**Bilirubin Monitoring in the Esophagus:** It is suggested that this is significant to indicate duodenogastroesophageal reflux. Routine use in children is not recommended (1). Empiric treatment involves: 4 weeks of PPI treatment applied in older children and adults having clinical findings of gastroesophageal reflux disease. However, because reflux complaints in infants and children are non-specific, there is no data supporting acid suppressive therapy (1).

## TREATMENT

1. Lifestyle Change
2. Pharmacological Treatment
3. Surgical Treatment

### Lifestyle Change

Family training, recommendations, and supportive care are necessary for children having symptoms similar to increased physiological reflux complaints. Avoiding high volume nutrition should be recommended. Cow's milk protein sensitivity may sometimes lead to unexplained crying or vomiting in infants. Therefore, cow's milk allergy should be considered in children having intermittent vomiting attacks while feeding and an observation of feeding with hydrolyzed formula for 2–4 weeks should be evaluated (1, 26). Thickeners may decrease visible reflux but do not reduce the frequency of esophageal reflux. Although feeding with formulas with thickeners containing rice, rice starch, corn starch, carob, and potato starch achieve good results, since they increase caloric intake, families should be informed about excessive weight gain (1, 27, 28).

Babies' lying prone before they are 1 year old decreases esophageal reflux frequency more compared to them lying on their back. In a study conducted on premature infants, it was reported that a left lateral position was effective in decreasing acidic GER that occurred especially 1.5 hours after feeding, while the prone position was effective in decreasing acidic GER seen at a later time after feeding (28). However, as it is known that the frequency of sudden infant death increases in prone and lateral position, it is recommended that infants up to 12 months old lie on their backs. It is reported that nipple use in premature infants accelerates stomach emptying, decreases reflux, and swallowing and increases esophageal clearance (29).

Lifestyle changes in children and adolescents; there is no data that support eliminating some routine foods from older children's diet. Obesity, high volume feeding, caffeine, products with cacao, such as chocolate, spicy and fatty foods, fizzy drinks, use of alcohol, smoking, and eating at night have been shown to be related with GERD complaints. Lying prone, right lateral lying, and/or lying head up are recommended. Moreover, it is reported that chewing after eating decreases reflux (1, 2, 7).

### Pharmacological Treatment

The main drugs used are gastric acid buffers, mucosal surface barriers, and preventers of gastric secretion. Prokinetic agents are less preferred. The purpose of the treatment is to provide



healing through decreasing the symptoms by reducing acid reflux in the esophagus and respiratory tract, the prevention of complications, and by enabling remission.

### Drugs Preventing Acid

**Histamine Receptor Antagonist:** Histamine receptor antagonist is most frequently used in infants younger than 1 year old. This decreases acid secretion through inhibiting histamine 2 receptors on parietal cells of the stomach. It is reported that time for the stomach to be at pH <4 decreases 44% when ranitidine 4 mg/kg/day is given at 2 doses, while it decreases 90% when ranitidine 6 mg/kg/day is given, and it can be used safely at up to 10 mg/kg a day (3x1).

It was shown that tachyphylaxis developed with intravenous use after 6 weeks; therefore, it cannot be used for a long period of time. It does not have a postprandial acid suppression effect. According to PPI, it is used against GERD symptoms, although it is weaker both with regard to the regression of symptoms and the recovery of esophagitis. Side effects such as irritability, hitting the head, headache, and somnolence can occur (1, 2, 7, 8).

**Proton Pump Inhibitors:** Proton pump inhibitors inhibit acid secretion by the selective and irreversible blockage of Na-K-ATPase in the final common path of parietal cell acid secretion. It protects intragastric pH  $\leq 4$  for a long time (12–17 h). They provide faster and better recovery compared to histamine 2 receptor antagonists; however, contrary to H2RA, their effect does not decrease with chronic use. They decrease the 24 h intragastric volume with their potent acid secretion suppressive effects, whereby gastric emptying increases and they lead to a reduction in volume reflux. The use of omeprazole, lansoprazole, and esomeprazole in North America and omeprazole and esomeprazole in Europe for children has been approved. None of their use was approved for infants younger than 1 year of age (1). In Turkey, omeprazole, lansoprazole, and pantoprazole have been licensed.

They are received as a single dose before breakfast, whereby their effects increase when the stomach is empty but decrease when food is given. A 95% recovery was provided in erosive esophagitis with a use of 12 weeks and longer. They are superior for the recovery of GERD symptoms compared to H2RA. Acid suppression for a long time is not recommended. The lowest dose should be recommended when necessary. A single dose in a day is used routinely.

Although the side effects vary among PPIs, the frequency of side effects in children has been reported as 14%. Major side effects include idiosyncratic reactions (1–9%), headache, stomachache, constipation, diarrhea, nausea, feeling of dizziness, skin eruption, hypergastrinemia, fundic gland polyps, parietal cell hyperplasia, enterochromaffin cell hyperplasia, hypochlorhydria, community-acquired pneumonia, gastroenteritis, candida infection, and an increase in the risk of necrotizing enterocolitis in prematures is seen (1, 2, 8, 9, 30, 31). It is reported that they may be used for up to 11 year olds safely (32). As there is not a syrup form in Turkey, there are difficulties in the use with little children. The capsule can be opened and divided into micropellet granules without crushing for the desired doses and can then be given with weak acidic food and drinks like with a spoonful of yogurt and apple juice.

**Prokinetic Agents:** Metoclopramide and domperidone increase gastric emptying through regulating LES pressure, esophageal cleaning or peristalsism, and intestinal peristalsism. They are used as an additional therapy besides the basic recommendations. They also have an antiemetic effect by dopamine receptor blockage. Though not significant, they cause a decrease in the symptoms in RI with pH meter measures; however, they cannot make it completely normal (1). They are not widely used for infants due to the side effects of the nervous system, such as metoclopramide, lethargy, irritability, gynecomasty, and tardive dyskinesia, and due to their short duration of effect (33). Domperidone is more frequently used due to its less central effects (34). There is a placebo-controlled trial in the literature indicating the recovery of esophagitis (1).

Erythromycin is the dopamine receptor antagonist and it increases gastric emptying; however, its effect could not be evaluated in GER and GERD.

Bethanechol has a direct cholinergic effect but its effectiveness is not clear. Baclofen decreases the frequency of the temporary relaxation of the lower esophageal sphincter; however, there is not a controlled study about its use with children in GERD treatment (1).

Cisapride increases the release of acetylcholine in the myenteric plexus and synapses and, being a serotonergic agent, it increases saliva release and gastric emptying and regulates esophageal and bowel peristalsism. However, it is not used as it leads to a sudden death risk due to long QTc and cardiac arrhythmia (1).

### Other Drugs

**Antacids:** Antacids decrease retrosternal burning by buffering gastric content directly and they enable recovery in esophagitis. They are effective in improving nonacid reflux symptoms in adults. High dose antacid therapy can be beneficial since esophagitis frequency due to GER is high in diseases such as esophageal atresia, chronic muscular disease, chronic pulmonary disease, and diaphragmatic hiatal hernia. It is necessary to be careful with regard to aluminum intoxication when they are used in infants for a long time (1).

Aluminum compounds may cause osteopenia, rickets, microcytic anemia, and neurotoxicity, while a high dose intake of calcium carbonate compounds may lead to milk-alkali syndrome, hypercalcemia, alkalosis, and renal failure. Therefore, they should be used carefully in infants and small children (1).

Alginate or sucralfate may be used as a surface protection agent.

**Sodium Alginates:** These are surface protection agents. They are natural products derived from moss and have a polysaccharide structure. Their powder forms for infants differ from the liquid forms for adults and they have no hyponatremia risk. They are used for the treatment of GER in infants and children. In the presence of gastric acid, they accumulate as a viscous gel with low density, and sodium in the compound transforms into sodium bicarbonate carbon dioxide, which is kept in the gel layer and forms a foam that floats like a raft in the gastric content and this layer passes into the esophagus in place of the gastric content during GER. It does not destroy the gastric

acid barrier as it does not have an antacid efficacy. An effectiveness with condensation is provided that does not damage physiology. It may be added to formula. It is used after nutrition by dissolving in 15 cc water or breast milk for infants feeding with breast milk. It may be used safely in infants having excessive physiological reflux. It was displayed that it decreased the number of gastroesophageal reflux episodes, the quantity of acid reflux extending to the proximal, and the esophageal acid exposure. It was also indicated that it decreased the frequency of GER in older children (1).

**Sucralfate:** This is bound to the mucosa where there are peptic erosions by transforming to a gel in acidic medium composed of sucrose, sulfate, and aluminum. It reduces the symptoms in adults and speeds up recovery. Though there are few data about its use in infants and children, its effectiveness and safety have not been determined yet since it may cause aluminum intoxication in long-term GERD treatment (1). The use of the surface protectors alone is not recommended in GERD treatment (1).

The duration of medical therapy with PPI should be at least 12 weeks, then, its cessation should be tested as reducing within 2–3 months. It may cause rebound hyperacidity if it is ceased suddenly. An increase in the PPI dose is necessary if the symptoms do not improve. The drug is initiated again if the complaints repeat when PPI is ceased. It has been displayed that prolonged PPI treatment for 3–12 years is safe (7).

**Surgical Treatment:** This treatment called “fundoplication” is a method applied for the purpose of increasing LES pressure, reducing the number of TLESRs, and eliminating hiatus hernia if it is present. Moreover, it increases the pressure during relaxation when swallowing begins and the intraabdominal length of the esophagus and corrects the angle of His. At the same time as preventing physiological reflux, it does not recover the underlying esophageal cleaning mechanisms, gastric emptying, or other GI motility disorders (35). Although the response in some patients is good after the operation, reception of appropriate drugs, esophageal dilatation, and surgery repletion may be needed with complaints such as chest pain and heartburn. Surgical complications of excessive gas, distention, dysphagia, belching, and difficulty of vomiting in more than two-thirds of the operated patients have been reported (36). Antireflux surgery may be useful for children not responding to medical treatment sufficiently, having long-term medical treatment dependency, not being able to adapt to medical treatment, having complications due to GERD threatening life, and having chronic repetitive GERD. Advantages and disadvantages should not be ruled out when deciding surgical treatment, especially in older children.

Children with asthma related with gastroesophageal reflux disease or recurrent pulmonary aspiration benefit highly from anti-reflux treatment (1).

Consequently, because PH monitoring and endoscopy may not be so accessible, especially in developing countries, all physicians should know the pathophysiology, symptoms, diagnosis, and treatment very well and should be able to diagnose with simple questions, follow up for a long time, and administer the process in coordination with the child and family.

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