Gastroesophageal reflux disease in special groups

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Abstract

Gastroesophageal reflux disease (GERD) has particularities in special populations such as infants and children, pregnant women and the elderly. This article presents the main characteristics and variations in the physiology and pathophysiology of GERD, the typical or atypical clinical presentations, the indications for diagnostic support studies, as well as the different types of treatment for each age.

Keywords: Reflux. Pregnancy. Children. Elderly. Special groups.

Enfermedad por reflujo gastroesofágico en poblaciones especiales

Resumen

La enfermedad por reflujo gastroesofágico (ERGE) tiene particularidades en poblaciones especiales, como los lactantes y niños, las mujeres embarazadas y las personas de la tercera edad. En este artículo se presentan las características principals y las variaciones en la fisiología y la fisiopatología de la ERGE, las presentaciones clínicas típicas y atípicas, las indicaciones para realizar estudios de apoyo diagnóstico y los diferentes tipos de tratamiento para cada edad.

Palabras clave: Reflujo. Embarazo. Niños. Ancianos. Poblaciones especiales.

Gastroesophageal reflux disease in pregnancy

It is well known that pregnancy, by itself, is a condition that predisposes women to gastroesophageal reflux disease (GERD). Hormonal changes decrease lower esophageal sphincter pressure and affect gastric and intestinal motility, and there is also an increase in intra-abdominal pressure due to uterine growth and weight gain with the progression of gestation[1]. Its prevalence is reported between 30 and 50%, but can reach up to 80%[2], with regurgitation (47%), a sour taste in the mouth (43.7%), and heartburn (38.5%) being the most frequently reported symptoms[3]. Extraesophageal symptoms present an unexpectedly low prevalence[4].

GERD significantly affects the quality of life of pregnant women, with sleep disorders, weakness, and alterations in social and work performance being the most frequently reported. An important fact to consider is that GERD during pregnancy predisposes up to 20% of women to postpartum GERD.

Risk factors

Risk factors for presenting GERD during pregnancy are:
– Family history of GERD during pregnancy.
– Not being able to objectively establish whether it depends on environmental or genetic factors.
– Number of previous pregnancies with the presence of GERD.
– If there is a history of heartburn during any pregnancy, the risk is 17.7%, and with more than two pregnancies with a history of heartburn it rises to 36.1%, regardless of age and obesity[5].
– Pregnancy progression. Prevalence increases from 26.1-36.1% in the first trimester to 52.1% in the second and third trimesters[6].

Age, body mass index, consumption of alcoholic beverages, and smoking show contradictory and non-significant results to be considered as independent risk factors.

Diagnosis

Generally, there is no need to perform diagnostic support studies, such as esophagogastroduodenal series, endoscopy, or pH-metry, given the short duration of symptoms and their evident origin. However, in cases with complications, such as hemorrhage or dysphagia, endoscopy may be indicated.

Treatment

The first line of treatment is hygiene-dietary measures, and here we will list those with more scientific support; for obvious reasons, weight loss is not recommended. One can start with dietary adjustments, decreasing consumption of acidic foods, heavily spiced foods, citrus fruits, wine, coffee, and especially foods with high fat content, as these take longer to leave the stomach and facilitate the return of content toward the esophagus. It is advisable to eat meals in small portions and divide schedules into four or five intakes, leaving at least 2 hours between the end of a meal and going to bed, and if there is a need to do so, raise the head of the bed 10 cm and prefer left lateral decubitus[7,8].

If these measures do not work, medications should be used as a second line of treatment, with antacids being the most recommended. Thirty to 50% of pregnant women can control their symptoms with these products and do not need to add more medications[9]. The most commonly used presentations are mixtures of aluminum and magnesium hydroxide, simethicone, calcium carbonate, sucralfate, and alginate.

In a double-blind, controlled study of 156 pregnant women with heartburn, the mixture of aluminum and magnesium hydroxide plus dimethicone achieved partial or complete control of heartburn in 93%, versus 66% with placebo (p < 0.01)[10]. Alginates are safe and effective in controlling heartburn; several studies report efficacy greater than 90% for heartburn control[11,12]. Sucralfate has slow absorption, which confers greater safety during pregnancy and lactation, with efficacy for controlling heartburn and regurgitation of 90% versus 43% with placebo (p < 0.05)[13]. In women at high risk of complications, it is recommended to use antacids containing calcium, due to the benefit they have shown in preventing hypertension and preeclampsia[14].

If symptoms persist despite the use of antacids, gastric acid blockers can be used. This should be considered as the third line of treatment. In these patients, histamine H2 receptor antagonists have been used. Cimetidine is not used due to the reduction in testicular size and antiandrogen effect in animal models. Ranitidine was withdrawn from the market in 2020 due to elevated levels of N-nitrosodimethylamine. Famotidine and nizatidine have never been studied for heartburn control in pregnancy[7].

Proton pump inhibitors (PPIs) are recommended at standard doses for the control of GERD in pregnancy[8] despite not having prospective, randomized, controlled

studies, being an expert recommendation, especially for intractable cases. This represents the fourth line of treatment. Regarding the safety of their use in pregnancy, the Food and Drug Administration classifies omeprazole as class C due to its potential fetal toxicity, while other PPIs are classified as class B. The use of these medications during the first trimester of pregnancy was not related to a significant increase in major birth defects in newborns in a cohort of 840,000 cases[15].

Conclusions

Typical symptoms of GERD in pregnancy, heartburn and regurgitation, should be treated initially with hygiene-dietary measures. If control is not achieved, antacids in different presentations or PPIs can be used, assessing risk-benefit in each patient.

Gastroesophageal reflux disease in infants

Introduction

The passage of gastric contents into the esophagus, that is, gastroesophageal reflux (GER), is a normal physiological process that occurs in infants, children, and healthy adults. Most episodes are brief and do not cause symptoms or lead to other complications. In contrast, GERD occurs when reflux episodes are associated with complications such as esophagitis or poor weight gain. Symptoms and complications of GERD in children vary with age.

Pathophysiology

Physiologically, GER is secondary to transient lower esophageal sphincter relaxation. This is the most relevant mechanism of GER in infants[16-18]. Reflux can be liquid, solid, gaseous, or a combination of these. It can also be acidic, weakly acidic, or non-acidic. The degree of acidity of reflux has not been associated with symptom severity[18].

Risk factors

Various risk factors contribute to a higher prevalence of GER during infancy. Abnormal aerodigestive reflexes and esophageal motility disorders, either in isolation or secondary to other conditions, such as neurological disorders, can also lead to an increased frequency of GER events[19].

The following conditions are associated with increased risk of GERD: hiatal hernia (including congenital diaphragmatic hernia), neurodevelopmental disorders, cystic fibrosis, epilepsy, congenital esophageal disorders, asthma, and prematurity. Obesity and parental history of reflux may also be risk factors for GERD in children[19].

Diagnosis

Complete medical history and thorough physical examination are fundamental to distinguish between GER and GERD. The diagnosis of GERD should be based primarily on clinical suspicion, although it can be strengthened with some diagnostic methods that qualify the degree or intensity of GERD. It is necessary to differentiate between typical and atypical signs and symptoms, as they may vary according to age (Table 1), and always identify possible alarm signs (Table 2).

It is important to be alert to alarm signs that may suggest other pathologies or complications of GERD. There is no pathognomonic sign or symptom for suspected GERD, but it is well known that typical symptoms are vomiting and regurgitation, although both can be present in both GER and GERD[20].

In children 0 to 12 months of age who frequently vomit or regurgitate, in the absence of alarm data, diagnostic tests are not required[20-22]. The Consensus of the Mexican Association of Gastroenterology (AMG) on the diagnosis and treatment of GER and GERD does not recommend the use of the esophagogastroduodenal series due to its low specificity and sensitivity; it is only recommended in selected cases when anatomical alterations are suspected[22]. The use of scintigraphy or ultrasound is not systematically recommended for the diagnosis of GERD in childhood, because they are not useful tools for diagnosis[22].

Esophagogastroduodenoscopy with biopsies may be beneficial in children who do not respond to treatment, and it is also useful to rule out complications (esophagitis, stenosis, Barrett's esophagus) and for differential diagnosis (eosinophilic esophagitis, infectious esophagitis, hiatal hernia). In the absence of erosive esophagitis, microscopic esophagitis is not sufficient to diagnose the presence of GERD[21,22]. However, GERD can exist even with normal appearance of the esophageal mucosa and without histological abnormalities[22].

The use of esophageal manometry in children is reserved for those with suspected esophageal motility disorders (rumination, achalasia) that can simulate GERD. In the vast majority of children with GERD, it

Table 1. Signs and symptoms probably associated with gastroesophageal reflux in children 0 to 18 years old

Symptoms	Signs

General
  Irritability
  Poor weight gain
  Sandifer syndrome
	Dental erosion
	Anemia

Gastrointestinal
  Recurrent regurgitation with or without vomiting
  Heartburn or chest pain
  Epigastric pain
  Hematemesis
  Dysphagia or odynophagia
	Esophagitis
	
	Esophageal stenosis
	Barrett's esophagus

Respiratory
  Wheezing
  Stridor
  Cough
 	
  Hoarseness
	Apnea periods
	Asthma
	Recurrent aspiration pneumonia
	Recurrent otitis media

Adapted from the ESPGHAN/NASPGHAN GERD guidelines (2018)[2].

Table 2. Alarm signs and symptoms ("red flags") suggesting other disorders

General
  Weight loss
  Lethargy
  Fever
  Excessive irritability or pain
  Dysuria
  Vomiting or regurgitation starting after 6 months of age or increasing or persisting beyond 12-18 months of age

Neurological
  Bulging fontanelle or rapid increase in head circumference
  Seizures
  Macro- or microcephaly

Gastrointestinal
  Persistent vomiting (projectile)
  Nocturnal vomiting
  Bilious vomiting
  Hematemesis
  Chronic diarrhea
  Rectal bleeding
  Abdominal distension

Adapted from the ESPGHAN/NASPGHAN GERD guidelines (2018)[2].

will not be necessary to perform pH-metry to establish the diagnosis; only in children with symptoms suggestive of GERD and unfavorable evolution despite treatment, as well as to establish the relationship between GERD and extradigestive symptoms, and as control of medical treatment or prior to surgical treatment[22]. The main disadvantage of pH-metry is that it does not detect non-acidic reflux, which can occur in more than half of infants, nor is it possible to determine the correlation of symptoms with non-acidic reflux episodes. Despite these limitations, it may be useful in special, infrequent cases, such as infants with discrete episodes of severe symptoms (apnea, bradycardia, cough, or desaturation). In this context, it is used together with monitoring of respiration, heart rate, or oxygen saturation to determine if there is a temporal relationship between reflux episodes and these events[21,22].

Multichannel intraluminal impedance associated with pH-metry is not recommended as the sole tool for diagnosing GERD in infants. When esophageal reflux monitoring is carried out, the ideal technique is to measure both esophageal pH and impedance in a single device and record for 24 hours. pH-metry with impedance detects reflux events regardless of pH, while pH monitoring detects only acidic reflux[22,23].

pH-metry with impedance is currently considered the reference method for the evaluation of GERD with symptoms[22,23]. Its indications are the same as those for esophageal pH-metry, with the addition of providing information on non-acidic reflux[23,24].

The therapeutic trial with PPIs is not recommended as a diagnostic method[20,22]. GERD is diagnosed primarily based on symptoms, and only in older children or adolescents can the diagnostic trial with PPIs be justified, which can help support, although not confirm, the diagnosis of GERD. There are limitations to performing the PPI test to diagnose GERD[25]: it does not control for placebo effect, spontaneous resolution of symptoms, the possibility that other conditions may improve symptoms, and it does not distinguish between healing of esophagitis and GERD symptoms. A negative test with PPIs does not exclude GERD as a diagnostic possibility[2]. The use of this test in infants and young children is not justified because symptoms are less specific in this age group[20-22,26].

Treatment

The management of GERD is based on the combination of non-pharmacological measures (lifestyle and dietary modification) and pharmacological treatment, and rarely surgery. When there is clinical suspicion of GERD and the patient presents alarm symptoms, they should not be treated, but rather investigated. Patients without alarm symptoms should be treated conservatively. The most important aspect of treatment is education and support of parents or caregivers[20,22]. They should be informed about the benign natural course of GER in infants. In breastfed children, breastfeeding

should be promoted and not discontinued, the feeding technique should be verified and improved, and the mother should be taught to identify hunger and satiety signals to avoid overfeeding[22].

In formula-fed children, thickened preparations can be used to decrease visible regurgitation. Current guidelines for GERD recommend the use of thickeners as a first-line option to treat infants and children with GERD[20,22], as they increase the density of the food so that it remains in the stomach longer and decrease regurgitation events. Different anti-regurgitation formulas containing pregelatinized rice starch, tapioca, potato and corn, carob bean flour, or xanthan gum, among others, are available in Mexico. To date, there are no clinical trials comparing one thickener against another. The use of special formulas, such as extensively hydrolyzed or amino acid-based formulas, for the management of GERD should be reserved for patients with a suspected diagnosis of cow's milk protein allergy; their use is not systematically recommended[22]. In children with physiological regurgitation, there is no justification for carrying out this approach.

During the last two decades, body position therapy has been explored as a possible non-pharmacological strategy for the treatment of GERD in infants[20-22]. While the use of head elevation or left lateral position has been suggested for the treatment of GERD symptoms in children under 1 year of age, recent NASPGHAN/ESPGHAN recommendations suggest that positional therapies should not be used to treat sleeping babies[20-22]. Current standards of the American Academy of Pediatrics, as well as the AMG Consensus recommendation, are that babies sleep in supine position[13,16,20-22,27-29].

Prokinetic agents currently have a minimal role in the treatment of GERD in pediatric patients. Systematic reviews on metoclopramide, domperidone, and cisapride have not found solid evidence of their efficacy[20-22,29,30], and international guidelines do not recommend their systematic use. These drugs have potentially serious side effects; metoclopramide has been associated with extrapyramidal neurological symptoms, and cisapride and domperidone with cardiac arrhythmias. Therefore, adding a drug with questionable efficacy and possible side effects is debatable, and the risk of adverse effects outweighs the benefit[30].

PPIs and histamine H2 receptor antagonists are not recommended for healthy infants who present crying or irritability with or without regurgitation[31,32]. PPIs are the first line of treatment in reflux related to erosive esophagitis[33,34].

Surgical treatment

Surgical intervention is reserved for patients with refractory symptoms or life-threatening complications, as well as for chronic conditions with a significant risk of GERD-associated complications despite optimal medical treatment.

Nissen fundoplication is the surgical technique of choice in most patients, generally by a laparoscopic approach. However, some pediatric centers promote better medical treatment, non-invasive feeding methods, or other surgical interventions, such as gastrostomy without fundoplication or gastrojejunal feeding, as alternative strategies[35].

In patients with feeding problems due to altered swallowing mechanics, poor weight gain, and GERD, placement of a percutaneous endoscopic or surgical gastrostomy may be indicated. However, the systematic practice of adding fundoplication to these patients is no longer recommended because it increases the risk of complications and does not improve reflux-related outcomes[36,37].

According to the recommendations of the AMG Consensus, children with GERD should be referred to the pediatric gastroenterologist if there are alarm signs and symptoms suggestive of underlying gastrointestinal disease, in case of no response to optimal treatment, and when they depend on pharmacological treatment after 6-12 months.

Conclusions

GER in infancy is a common, physiological, and self-limited phenomenon, which is distinguished from GERD by the presence of organic complications or bothersome symptomatology.

The diagnosis of GERD in infants is based almost exclusively on medical history and physical examination; the role of invasive tests and empirical therapeutic trials should be individualized.

In the evaluation of pediatric patients with vomiting and regurgitation, alarm signals should be sought, and they should not be attributed to GER or GERD without adequate medical history.

The management of GERD should follow a stepwise approach that uses non-pharmacological options initially when possible and pharmacological interventions only when necessary. Surgical therapy is reserved as a last option before exhausting all diagnostic and therapeutic strategies.

Gastroesophageal reflux disease in older adults

Typical symptoms of GERD in older adults may be mild, but histological damage may be greater than in younger populations. In fact, in the United States of America, the incidence of Barrett's esophagus and esophageal adenocarcinoma has increased in older adults by 600% in the last four decades[38].

The prevalence of GERD in these groups is higher. In traditionally long-lived populations, such as China, it is reported at 17.3%, and in Japan at 17.5%. In the United States of America, up to 17% is reported. Heartburn can occur in up to 52% and regurgitation in 42% of older adults; figures lower than those reported in those under 60 years[39]. However, since symptoms are milder, they are often not taken into account by patients, so the figures may not be entirely accurate.

Risk factors

Rather than talking about risk factors, it is necessary to consider the physiological and pathophysiological changes that occur with the passage of years. The most frequent are:
– Decreased or ineffective peristalsis[40].
– Decrease in quantity and quality of saliva[41].
– Presence of hiatal hernia; in those over 50 years, an OR of 2.71 is reported, and 69% of those over 60 years have it.
– Consumption of medications that decrease the lower esophageal sphincter resting pressure.
– Concomitant diseases, such as Parkinson's disease (60-80% of patients have GERD symptoms)[42], diabetes mellitus, and anxiety (44.3% versus 34.8% in patients with GERD who do not have anxiety).

Age, body mass index, consumption of alcoholic beverages, and smoking show contradictory and non-significant results to be considered as independent risk factors.

Diagnosis

The prevalence of moderate to severe erosive esophagitis in those over 70 years has been reported at 37%, versus 12% in those under 21 years[43]. In the same study, the prevalence of severe heartburn was 34% in those over 70 years and 82% in those under 21 years. The intensity of symptoms does not predict the severity of histological damage in older adults[43].

The most frequent atypical symptoms in older adults, as well as alarm symptoms, are globus, pharyngeal burning, chronic cough, laryngopharyngeal reflux, asthma, otitis and sinusitis, dysphagia, epigastric pain, and chest pain, which must be carefully analyzed to rule out ischemic heart disease. In patients in whom this latter condition has been objectively ruled out, it is reported that in 40% to 70%, GERD is the origin of chest pain. Given the poor correlation between GERD symptoms and possible histological damage, in these patients it is necessary to perform upper digestive tract endoscopy. In some selected cases, esophageal manometry may be indicated to rule out primary motor disorders[44].

Treatment

The initial management of these patients is similar to that of younger patients. Hygiene-dietary measures, such as raising the head of the bed, sleeping in left lateral decubitus, leaving 2-3 hours between the end of a meal and going to bed, and avoiding consumption of carbonated beverages, alcohol, and smoking, are those with the most supporting evidence in controlled studies. If these measures do not work, it is necessary to start drugs that block acid production in the stomach, since this secretion does not decrease with age. PPIs are the most used due to their excellent safety profile and efficacy in managing heartburn, regurgitation, and even many of the atypical symptoms of GERD. Possible interactions with other drugs that are frequently used by these patients should always be considered.

Once PPIs are withdrawn, up to 90% of patients return to them, so it is preferable to institute a maintenance or on-demand strategy, depending on the intensity of symptoms or histological damage in the esophagus.

Recently, new potassium-competitive acid blockers (P-CAB) have demonstrated efficacy comparable to that of PPIs, with the advantage that they do not need acid-mediated gastric activation and their intake does not depend on food intake, which facilitates treatment adherence[45]. In some patients with clinical evidence of delayed gastric emptying, prokinetics can increase therapeutic response to PPIs and P-CABs.

Endoscopic management of reflux in these patients should be reserved for those with mild symptoms and hiatal hernias no larger than 2 cm with good response to acid blockers. Techniques such as radiofrequency and transoral fundoplication are those with more support. In patients with large hiatal hernias, Los Angeles classification grade C or D esophagitis, dependence on PPI or P-CAB use, or refractory reflux, surgical management should be considered, especially with the laparoscopic

technique. Surgical management is safe and effective, but should be performed by expert surgeons. One study demonstrated that there is no difference between patients over 65 years and those under that age in terms of improvement of reflux symptoms (90% vs. 90%; p > 0.05) and postoperative dysphagia (3% vs. 3%; p > 0.05), nor in the incidence of early satiety, abdominal distension, and chest pain[46].

Conclusions

GERD in people over 60 years is similar to that occurring in those under that age. However, symptoms may be mild and present more histological damage due to the physiological and pathophysiological changes that occur with the passage of years.

Endoscopy is mandatory in those patients with recent onset symptoms or clear alarm signs. Treatment should be carefully personalized, taking into account concomitant diseases, polypharmacy, obesity, and cognitive status, and is based on PPIs, P-CABs, or anti-reflux surgery.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical considerations

Protection of people and animals. The authors declare that no experiments were performed on humans or animals for this research.

Confidentiality, informed consent, and ethical approval. The study does not involve personal patient data nor require ethical approval. SAGER guidelines do not apply.

Declaration on the use of artificial intelligence. The authors declare that they did not use any type of generative artificial intelligence for the writing of this manuscript.

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