

Gastro esophageal reflux disease

Definitions

Gastro esophageal reflux (GER) is defined as the return of gastric content into the esophagus several times during a 24 hour period. These events could be considered normal in the regular population under circumstances in which these episodes are short in duration also the natural mechanisms for reflux defense are intact, and there is no subsequent inflammation or impaired calorie intake.

Regurgitation is the passage of gastric content into the mouth.

Spitting out is regurgitation which comes out effortlessly from the mouth.

Vomiting is the forceful expulsion of gastric content from the mouth.

Vomiting is a complex term where it is difficult to differentiate innocent GER from underlying disease because both conditions result in gastric contents coming out from the mouth.

Transient relaxation of the lower esophageal sphincter, a simple relaxation of the lower esophageal sphincter muscle or ring of muscles which is well recognize in healthy individuals, and increases in frequency after eating due to increased gastric pressure.

GER vs. GER disease (GERD)

GER occurs when pressure inside the stomach is higher than the pressure inside the esophagus. In normal GER it is important that the pressure inside the stomach is higher than normal after applying any external force such as sitting or mobile activity, or internal forces due to large volume ingestion.

GERD is distinguished from GER because it is associated with damage of the esophageal lining and evidence of inflammation as consequence of the release of gastric content. The gastric content has a low pH (gastric acid) and prolonged contact of any natural surface (in this case the mucosal lining of the esophagus) with the digestive enzymes that are present in gastric acid leads to tissue damage and inflammation. It is well known that the oral cavity, teeth, airways (upper and lower respiratory tract systems) and esophagus can be affected by the caustic effects of digestive enzymes and gastric acid if the natural anti-reflux mechanisms do not perform optimally or fail to function. Our anti-reflux mechanisms consist of a small ring of muscle known as the lower esophageal sphincter, esophageal clearance which is acid swiped back into the stomach, mucus, bicarbonate and saliva secretions from the mouth and esophagus lining. Additional mechanisms such as the upper esophageal sphincter, vocal cord reflex, and cough reflex help to protect the oral cavity and airways.

A combination of preventive mechanisms to prevent the development of GERD include (a) gravity force, which works better in upright comparing with lying down positions, (b) muscle function from moving the food down the gastrointestinal stream, in combination of with the maintenance of high muscle tone at sphincter areas, and (c) the neutralizing function of bicarbonate, mucous, and saliva secretion which buffer or balance the acidic pH preventing future damage. Other important mechanisms of reflux

protection such as apnea and coughing are located in the respiratory system and promote lung protection to avoid atypical GERD symptoms such as chronic cough, bronchospasm, or pneumonia.

Reflux from birth to walking

Reflux is so common in infancy that virtually all infants experience a certain degree of reflux. When it is very frequent and associated with medical symptoms and over half of infants will experience GERD. This frequent reflux improves after one year of age when infants begin to decrease the volume of food needed to grow, start eating more solids and master vertical positions both while seated or standing.

What are the risk factors for reflux?

Children are at increased risk for both GER and GERD, but in the children, adolescents or adults in who one or more of anti-reflux preventive mechanisms are not properly working will have higher risk of GER. In general, neurologically-impaired children when positioned away from vertical, or with poor muscle tone or coordination which will increase intra-gastric pressure, will have a higher risk of reflux. Poor intestinal motility also will increase intra-gastric pressure and induce reflux, as well as anatomic defects or surgical interventions such as esophageal atresias repaired, trachea-esophageal fistulas repaired, or the presence of hiatal (diaphragm hiatus) hernia. Obesity and chronic lung disease are frequently observed in children with a higher degree of reflux.

DIAGNOSTIC TESTING FOR GERD

The first thing to consider in GERD is whether symptoms are present and what type(s) of symptoms are present, their intensity, and additional nutrition status. Careful analysis of symptoms could give a clear diagnosis from the beginning.

Symptoms:

Regurgitation, vomiting, hematemesis (vomiting with blood)

Poor weight gain

Heartburn, chest pain, abdominal pain, irritability

Protective position adopted by the children to prevent the recurrent symptoms known as Sandifer's syndrome

Anemia

Asthma or wheezing, chronic cough

Acute life-threatening events such as apnea

Recurrent pneumonia

Feeding refusal

Sleep apneas

Hoarseness

Sinusitis

Otitis media

Dental erosions

Evaluating the amount of feeding and the speed of growth is critically important in children. The volume eaten in relation to child weight should be appropriate for prevent GERD and induce weight gain (0.5 to 0.6 oz per kg q 3 hours). Higher volume of feeding will induce increased intra-gastric pressure and vomiting. The normal speed of growth of infants is a doubling of birth weight by 6 months with few exceptions as very few infants double their birth weight at 4 months and still is considered normal, triple their weight by 12 months and quadruple their weight at 24 months, this will suggest overfeeding and increased risk of GERD if the speed of growth is faster than shown above.

Radiologic studies to assess anatomy

Upper gastrointestinal studies; the main role of this is to evaluate potential defects in the gastrointestinal system which could lead to a predisposition to GERD, such as hiatal hernia, dilated esophagus, or trachea-esophageal fistulas, sides of stomach and stomach position. This test could document GER but it will not be enough to diagnose this condition.

Esophageal pH monitoring; this allows the evaluation of the level of acidity in the esophagus. This test will calculate the number of episodes with an esophageal pH less than 4, and the duration of episodes of low pH during 24 hours in order to calculate a reflux index. This test is very sensitive and can associate reflux with esophagitis or significant reflux.

The downside of esophageal pH monitoring is that it cannot detect reflux episodes which are not acidic, and during the test anti-reflux medication needs to be withheld until the study is completed.

Esophageal electrical impedance monitoring; this technology measures the current generated by the lining of the esophageal mucosa when they are close to each other. The impedance change along the length of the mucosal lining allows doctors to see the direction of bolus movement if the bolus is up (reflux), or down (swallowing). This enables the diagnosis of reflux and the size of reflux with no need to measure changes of pH; in others words it is not limited to acidic reflux. Impedance technology along with pH monitoring is powerful tools to analyze acidic vs. not acidic reflux, the size of reflux and associated symptoms.

Upper endoscopy with biopsy; this technology allows the gastroenterologist to evaluate the degree of damage caused by reflux, and to distinguish reflux disease from other diseases. It also allows the

evaluation of additional risk factors for GERD, or complications from GERD such as Barrett's esophagus or strictures

Laryngoscopy; this is a direct or indirect visualization of the pharynx, and it is limited to situations in which there are upper respiratory symptoms such as hoarseness, recurrent sinusitis, cough, and pneumonia. The interpretation of observations is operator dependent

Bronchoscopy; this tool looks for evidence of gastric content located in the bronchus or lung and it is documented by the presence of lipid-laden macrophages

Scintigraphy or gastric emptying scan with 24 hours delayed pictures; after ingesting a radio labeled food, multiple pictures are taken every 20 minutes to detect the presence of food above the stomach. Delayed pictures are used to see if there is food in the lungs after sleeping overnight

Trial of anti-reflux therapy or empiric therapy; This approach can be used when clinical presentation is highly suggestive of GERD and a short therapy should be considered with close monitoring of the response of the symptoms to the anti-reflux medication.

Treatment of GER

Reflux disease treatment will upon the symptoms and degree of reflux. The reflux treatment is focused on decreasing symptoms, prevention of damage and avoidance of the complications of GER.

The first goal of reflux therapy should be to focus on feeding volume and to schedule feeding-time intervention. Infants should drink from 0.5 to 0.6 oz/kg (0.25 to 0.27 oz/pound) per feeding every 3 hours during the first 6 months then decrease to every 3.5 hours from the ages of 6 months to 12 months. It is important to appreciate that feeding every 3 hours gives a total of 8 feedings per day, which is a big difference from feeding every 2 hours which gives 12 feedings per day, and the ingestion of 15 to 20 % more than recommended. It is also important to ensure that all caregivers know and follow the scheduled recommendations.

Non-pharmacologic treatment

Non-pharmacologic options for GERD therapy in infants include:

Positioning changes; up to a 45° angle for 45 to 60 minutes after eating. Until today the American Academy of Pediatrics still recommends the supine position to sleep because this reduces the sudden infant death rate compared to other positions. Lateral position could be also used for sleeping, but never the prone position.

Formula changes; thickening the formula with rice cereal is appropriate after birth to control GERD. The concentration range from 1 tbs per 2 oz to 1 tbs per 1 should be appropriate. This is done by careful and minimal cutting of the tip of a bottle nipple in a cross. The use of hypoallergenic formulas has been documented to help with formula allergy, which can induce GERD, and also helps reduce the time that the formula stays inside the stomach. Further reduction of volume and increased concentration of

calories in a high calorie formula at 22 to 24 cal/oz is also appropriate. Increasing the volume of feeding should be done at a rate of no more than ¼ oz every 1 to 2 weeks. Breast feeding should take into consideration the level of maternal breast milk production and breast feeding to an average maximum of 10 to 15 minutes total and very close to every 3 hours.

Eating habits; In children and adolescents large amounts of food and frequent feeding could induce GERD. In addition, large volumes of drinks should be avoided as well as sugar and artificial sweeteners because they will induce pain and GERD. A good rule is for children aged 10 years and younger to limit themselves to 4.5 oz volume 5 times a day, and for children older than 10 years to 5 to 6 oz 5 times per day in addition to their regular diet.

Water breaks for sport participants should be limited to 3 to 4 oz of water every 20 to 30 minutes during the first hour of exercise and in subsequent hours the participants could alternate with sports drinks at the same amount and frequency.

Special note; it is important to avoid food items recognized to induce GERD such as fatty food, chocolate, peppermint, and carbonated drinks. Maintenance of a healthy weight is important in prevention and treatment of reflux. Also treatment of constipation is a well-known additional intervention.

Pharmacologic treatment

A number of pharmacologic approaches for GER are known, and these include:

Acid damage prevention; Oral antacids and Sucralfate are well-known therapies and are very effective to relieve the painful symptoms of GER. These should be used on an as needed basis due to their secondary effects that can occur with prolonged use. Antacids will buffer the excess gastric acid and Sucralfate will cover the mucosa to help with process of healing.

Agents that alter gastrointestinal motility; these agents, also known as prokinetic agents are controversial in terms of efficacy and side effects. These agents work by increasing mobility of food through the gastric system, which reduces the chances of reflux. Erythromycin is an antibiotic which has been well documented to improve motility and prevent reflux in specific circumstances.

Acid suppression; these agents act by inhibiting the secretion of excess acid in the stomach, reducing the damaging effects of reflux. Examples of these drugs include H₂-receptor antagonists (H₂RAs) act to decrease acid secretion by inhibiting the histamine-2 receptor on gastric parietal cells which are responsible for acid secretion in the stomach. H₂RA agents include Cimetidine, Ranitidine, Nizatidine, and Famotidine. Proton pump inhibitors (PPIs) covalently bind and deactivate the H⁺, K⁺ ATPase pumps in the stomach, providing more effective gastric acid suppression compared to H₂RAs. Omeprazole, Lansoprazole, Pantoprazole and Esomeprazole are examples of PPIs.

The best way to administer a PPI is ½ to 1 hour before breakfast in a single dose to maximize acid suppression after breakfast. Atypical GERD (respiratory symptoms), persistence of symptoms, or Barrett's esophagus will require a second PPI dose ½ to 1 hour before dinner time. In children

medication refusal could be improved by using a dissolvable dose or opening the capsule and diluting in 10 cc of apple juice or apple sauce.

Acid suppression it is an excellent therapy for GERD but using for prolonged periods leads to an increased risk of gastrointestinal and respiratory infections, vitamin B12 deficiency, and osteopenia with fractures.

Surgical Approaches

It is possible to perform anti-reflux surgery in selected groups of patients. Anti-reflux therapy should be focused on management of the non-medical, then medical option first, with surgery as the final option due to its associated complications. The Nissen fundoplication is the most commonly performed surgical procedure for GERD in which the upper part of the stomach is wrapped, or plicate, around the lower end of the esophagus and stitched in place, reinforcing the closing function of the lower esophageal sphincter. The Nissen fundoplication is an excellent surgery when properly indicated, however, this is not a complication free procedure and much more difficult to reverse once a complication is presented.

Nissen fundoplication complications arise from being too tight or too loose, nerve entrapment and subsequent dysmotility leads to slow gastric emptying, gas bloating syndrome leads to too fast gastric emptying (dumping syndrome), and anatomic modification of the gastric outlet while pulling the wrap induces gastric outlet obstruction.

Future technologies such as endoscopic surgery have yet to be proven effective.

CYCLIC VOMITING SYNDROME AND ABDOMINAL MIGRAINE SYNDROME

Cyclic vomiting syndrome is a very characteristic phenomenon in which patients present with recurrent episodes of vomiting, which are usually severe and occasionally incapacitating, preventing the patient performing his/her standard activities. This usually needs medical evaluation which usually results in a negative work up, the vomiting crisis recovers quickly and it is followed by a completely asymptomatic periods. The patients then appear completely healthy and able to perform their standard activities.

These patients are usually labeled by a series of wrong diagnoses as recurrent gastroenteritis, virus illness, recurrent strep throat, including psychiatric disorder as depression, bipolar disorder, and many others. The alternating pattern of illness and no illness can range from a few times a week to few times a year.

The symptomatic periods are very specific and usually called stereotyped:

In children the symptoms present suddenly with a lack of appetite, and change of behavior (irritability or sleepiness), change of skin color from pale face or around the mouth to facial flushing, occasionally increased of temperature few degrees or real fever, sweating, headache, abdominal pain from esophagus (behind the chest to any part of the abdomen), and recurrent and frequent retching and vomiting of food initially, which rapidly changes to yellow or green (bilious) with occasionally blood (hematemesis). The first few stools are soft, loose or mucous, and occasionally skin tingles with a feeling of ants moving over the skin or areas with hot or burning feeling. The symptomatic period follows its own course from a few minutes up to seven days.

After following this course, symptoms are suddenly resolved very quickly and the child can perform his regular activities.

Cyclic vomiting syndrome is most frequently seen in 5 to 15 year olds but early cases and older patients are also been diagnosed as well. Cyclic vomiting syndrome is a diagnosis of exclusion whose specific etiology or reason has not be elucidated yet. But it is clearly associated with neuron-intestinal dysfunction where there are multiple triggers for the symptoms. It is believed (by the author) that this dysfunction is triggered by serotonin which can give a cascade of symptoms from migraine, flush and smooth muscle contraction from small vascular vessels to intestinal wall or any other intra-abdominal viscera. This could have an end-product of poor blood flow to the bowel leading to spasms that induce severe pain, vomiting and change of behavior as described before.

Due to the severity of the symptoms, other important diagnoses need to be evaluated:

Brain: intracranial tumor, sinusitis, or any cranial infection (otitis media); gastrointestinal peptic ulcer disease, duodenal ulcers, intestinal malrotation or distal obstruction, pancreatitis including early appendicitis as well; metabolic amino acid disorder, mitochondrial defect, porphyria. In our

experience the most common diagnosis as secondary is after migraine, is sinusitis, duodenitis and infrequently follows inborn errors of metabolism.

Once the most important diagnoses are excluded and cyclic vomiting syndrome is considered, the most common trigger is stress in any kind, from very hot temperatures, to cold temperatures, school test, PE (physical education at school), big parties, holidays, and family problems. Specific food usually associated with migraine could trigger the symptoms, such as chocolate, Chinese food due to soy sauce component, cheese etc.

This evaluation of these children can usually point to migraine, recurrent abdominal pain with nausea or frequent episodes of dizziness and nausea (less degree of headache). They have a strong family history of headache and migraines and irritable bowel syndrome as well as current family members.

After recognizing these symptoms and excluding other important diagnoses, the therapy is focused to avoid triggers such as stress, and protect patients from weather changes.

Very useful pieces of advice are:

Follow a migraine diet or avoid food and environmental triggers.

Cyproheptadine medication to prevent migraine in children.

Other migraine prevention medications are Propranolol, Topamax, and Amitriptyline.

Acetaminophen at standard dose for body weight with a warm bath for 15 minutes.

Consider warm compress in the abdomen.

Antispasmodic medication could be considered.

If vomiting becomes severe Ondansetron (Zofran) is very useful in this condition.

Very often these children become dehydrated due to the lack of appetite and vomiting and need to be hospitalized very soon.

Prevention is followed by anti-migraine medication (Cyproheptadine), lifestyle changes; plenty of sleep and avoidance of long periods of starvation.

ABDOMINAL MIGRAINE

Abdominal migraine is similar to cyclic vomiting syndrome but with a much lesser degree of symptoms and for a shorter time. The major differences are: no severe and frequent vomiting, listless or sleepiness is less intense and the intensity of abdominal pain is lower, but the rest of symptoms could be present;

The symptom free period alternating with the symptomatic period, the stereotype group of symptoms: change of behavior from irritable to sleepy or listless, skin color from pale to flushed, nausea and occasionally vomiting, Headache or dizziness followed by symptom free periods.

The prophylaxis and therapy is usually the same but secondary etiology such as sinusitis, peptic ulcer disease, should be excluded.

Cyproheptadine, Propranolol and Topamax could be used as prophylactic therapy for migraine

Tylenol, ibuprofen or Excedrin could be used as abortive, stronger migraine medication as Sumatriptan should be use under medical supervision from neurologist.

Abortive migraine medication (Tylenol) and warm shower has been very useful as well as warm local abdominal compresses.

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