

Gastroesophageal reflux (pediatrics)

Gastroesophageal reflux (GER) or **esophageal reflux** is defined as the return of gastric contents to the esophagus. It is a physiological process that occurs throughout the day in individuals of all ages. If it causes symptoms, it is a disease of gastroesophageal reflux disease (GERD).

Risk factors in childhood:

- chronic respiratory diseases: cystic fibrosis , bronchial asthma , primary ciliary dyskinesia
- obesity , constipation
- psychomotor retardation ^[1]

Etiopathogenesis

Transient relaxation of the lower esophageal sphincter is considered to be the main etiopathogenetic mechanism.^[1]

Impaired motility causes prolonged exposure to the acidic content of the stomach in the lumen of the esophagus. The main causes include a decrease in the tone of the lower esophageal sphincter, antral hypomotility, and possibly duodenogastric reflux. The disease is affected by an imbalance of aggressive and protective mechanisms. Protective factors include the antireflux barrier (lower esophageal sphincter), luminal esophageal cleansing, and tissue resistance (epithelial integrity). Aggressive factors include gastroesophageal and duodenogastric reflux, HCl, pepsin, bile salts, lysolecithin and pancreatic enzymes.^[2]

Esophagitis is caused by a reflux of acidic stomach contents. Its severity ranges from the finding of isolated injected blood vessels with reddening of the mucosa to the finding of deep ulcers, which lead to the formation of scar strictures, brachyesophagus or intestinal metaplasia (Barrett's esophagus). ^[3]

Clinical picture

- **Gastrointestinal** (from esophagitis, strictures):
 - heartburn , retrosternal pain;
 - feeling of acidity in the mouth
 - recurrent vomiting with failure;
 - restlessness, irritability, intermittent sleep;
 - foetor ex ore , dysphagia , odynophagia , refusal to eat;
 - hematemesis , melena , anemia.
- **Extragastrintestinal** :
 - aspiration pneumonia , chronic bronchitis , bronchial asthma , irritating cough, wheezing, recurrent inflammation of the larynx, middle ear, sinuses;
 - apnea, life-threatening event (ALTE), SIDS ;
 - Sandifer – Sutcliffe syndrome (torticollis , torso dystonia).^[1]

Sandifer syndrome

- rare GER complication;
- includes extraesophageal manifestations of GER, especially neurological: atypical positions and movements of the head, torso, upper limbs and pathological eye symptoms;
- increased irritability or paroxysmal dystonic movements reminiscent of convulsions;
- it can also mimic torticollis and as a result lead to hypertonic neck extension of the character of opisthotonus;
- pathophysiology unclear (vagal reflex ?, reflex ncl. tractus solitari?);
- most often between 3 and 4 months of age;
- difficult feeding, refusal of oral intake, the need for repeated drinking breaks;
- the difficulties gradually diminish with the maturation of the lower sphincter and thus the decrease in the number of regurgitations. ^[4]

GERD diagnostics

- **History** , physical examination:
 - no therapy is required for thriving infants with repeated blinking
 - in older children with heartburn it is sufficient to perform a therapeutic test with proton pump inhibitors (eg omeprazole)
- **Sonography**
 - is not a method suitable for the search for reflux disease in children
- **24-hour esophageal pHmetry or esophageal pHmetry**
 - gold standard GERD examination
 - in children it is recommended to evaluate only the pH time below 4 and the relationship between symptom and acid reflux episodes

- description of the examination: insertion of a thin tube through the nose into the esophagus; connecting the probe to a device that can record the pH in the esophagus; within 24 hours the patient performs normal activities, eats a normal diet, then the probe is removed and the record is evaluated
- **Multichannel intraluminal impedance**
 - has a higher sensitivity and specificity in the search for an association between a symptom and a reflux episode because it is able to detect even non-acidic or mildly acidic reflux episodes
- **Esophageal endoscopy with biopsy**
 - for evidence of reflux oesophagitis and complications (Barrett's esophagus)
 - macroscopically and histologically normal findings do not rule out histopathological esophagitis
 - invasive examination with the need for general anesthesia in young children
- **Esophageal X-ray (esophagogram)**
 - is neither sensitive nor specific for the diagnosis of GER
 - useful to rule out anatomical abnormalities of the upper gastrointestinal tract (malrotation, annular pancreas, esophageal stenosis / stricture, hiatal hernia, achalasia)
- **Esophageal manometry**
 - provides information on pressure conditions in the lower esophageal sphincter, does not diagnose GER; suitable to rule out achalasia
 - description of the examination: a measuring probe is inserted through the nose into the esophagus and then into the area of the lower esophageal sphincter; the course of the swallowing act is measured when "empty" is swallowed and 10 ml of water is swallowed; it is performed on an empty stomach
 - sometimes manometry is combined with multichannel intraluminal impedance (detection of cough episodes, most accurate probe insertion)
- Further examination - for extragastrintestinal symptoms
 - **scintigraphy** with ^{99m}Tc - labeled diet (milk) (non-invasive examination with low radiation exposure, allows quantification of reflux, including alkaline reflux), bronchoscopy with bronchoalveolar lavage (BAL) with detection of lipophages can be used to demonstrate aspirations.

Non-pharmacological treatment

- Infants
 - elevated position
 - thickening of formulas (rice decoction), antireflux formulas (AR) - does not reduce the number of reflux episodes (expressed as%, when the pH in the esophagus is below 4 of the total duration of pHmetry), but reduces the number of visible episodes of blinking
 - some sources state that thickening of the diet is no longer recommended because the thickened diet continues to enter the esophagus at reflux for its higher viscosity and thus prolongs the contact time with the esophageal mucosa epithelium
 - more frequent portions of smaller volume
 - in case of suspected cow's milk protein allergy / intolerance 1-2 weeks treatment trial with hypoallergenic formula
 - in case of insufficient caloric intake, increase in caloric density of formulas
 - interesting: pHmetric studies show fewer episodes of GER in the tummy position, but in this position there is a higher incidence of sudden infant death syndrome (SIDS)
- Older children
 - some older measures have not been shown to be successful in older children
 - similar recommendations can be applied to adolescents as to adults
 - above all, weight reduction can be recommended for obese people, do not smoke, do not eat shortly before falling asleep, ev. adjust your sleeping position (pronation or left side).

Pharmacological treatment

- proton pump inhibitors are the method of choice in children with GERD ^[1]

Proton pump inhibitors (IPP)

- effect: irreversible inhibition of the $\text{H}^+ / \text{K}^+ \text{ATPase}$ enzymatic system of the gastric mucosal parietal cell (so-called proton pump), and thus inactivation of the secretory enzymatic mechanism of the gastric parietal cell; HCl secretion inhibited, pepsin secretion is not affected
- IPPs are more effective than H_2 -blockers
- representatives: **omeprazole** (*Helicid®*), **loseprazole** (*Lanzul®*), **pantoprazole** (*Controloc®*), **esomeprazole** (*Emanera®*), **rabeprazole** (*Zulbex®*)

Prokinetics

- the use of prokinetics due to their low effect and high risk is not recommended in children
- effect: selective stimulation of smooth muscle in the digestive tract (especially its proximal parts)
- dopamine D₂ receptor antagonists and acetylcholinesterase inhibitors
 - representative: **itopride** (*Ganaton®*)
- 5-HT₄ serotonin receptor agonists
 - necessary prudent indication for possible emergency room: severe cardiac arrhythmias (from QT prolongation)

- regime of use of an unregistered medicinal product (under the personal responsibility of the prescribing doctor, informed consent required, report each prescription to SÚKL)
- representative: **cisapride** (*Prepulsid®*) - no longer registered in the Czech Republic, it can be procured in the form of Individual Import
- effect: antidopaminergic and serotonergic
 - representative: **metoclopramide** (*Cerucal®, Degan®*)
 - prokinetic and antiemetic

H2 -blockers

- effect: competitive antagonism of histamine H₂ -receptors in the parietal cell, by this mechanism they inhibit basal and stimulated secretion of hydrochloric acid (hydrochloric acid) in the stomach, reduce the volume and content of H⁺ + gastric juice and also reduce the production of pepsin
- representative: **ranitidine** (*Ranital®*), **famotidine** (*Famosan®*)
- not recommended for long-term treatment

Antacid

- effect: neutralization of stomach acid
- antacids are not suitable for long-term therapy in children due to their side effects.
- not recommended for long-term treatment

Sucralfate

- effect: topical mucoprotectant, binds pepsin and bile acids
- use: with marked signs of oesophagitis, duodenogastric reflux.
- not recommended for long-term treatment

Surgical treatment

- Nissen fundoplication (Nissen-Rossetti fundoplication) performed with laparotomy or more often today laparoscopically (possibly endoscopically)
- only in exceptional cases in case of failure of conservative treatment
- there is only limited information on the results of funduplications in children
- Treatment complications are relatively common

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