Peptic ulcer
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Abstract

Objective: to present a current review about pathogenesis, pathophysiology, diagnosis, and treatment of peptic ulcer disease in children, based on the reviewed publications and the author personal experience.

Methods: we revised the most relevant articles about peptic ulcer in children, published from the last 20 years.

Results: the gastroduodenal peptic ulcer is very common in adults, mostly in the developing countries. Although it is less frequent in children, the optical fibroendoscopy has improved the number of diagnosed cases. The peptic ulcer is classified as its etiology in primary and secondary. The secondary peptic ulcer is related to a subjacent disease or use of drugs, while the primary ulcer happens in the absence of underlying systemic diseases The primary duodenal ulcer is the most common presentation, and there are strong evidences of the H. pylori association in the etiology. Clinical presentation changes with age and ulcer type. Secondary ulcers are mostly acute and sometimes dramatic, while the primary ones have a chronic evolution mostly similar to patients with functional recurrent abdominal pain, but the presence of epigastric pain, feeding-related pain, vomiting, bleeding, familiar history for peptic ulcer, nocturnal pain, and male gender are strongly related to peptic ulcer. The acid antisecretory agents have great efficacy on relieving symptoms and solving ulcerate lesion, although the H. pylori eradication itself prevents primary duodenal ulcer recurrence.

Conclusions: the primary peptic ulcer involve many factors in Its etiopathogenesis, being H. pylori the most important of them Although there isn t yet a ideal therapeutic course. The antibiotics play an important role in peptic ulcer and the H. pylori research must be done for an accurate diagnosis and treatment.


Introduction

Peptic ulcer is the circumscribed loss of tissue that occurs in portions of the digestive tract exposed to chlorhydro-peptic secretion: inferior third of esophagus, stomach, proximal duodenum and Meckel diverticulum with gastric ectopic mucosa. In this article, we will talk only about the gastroduodenal peptic ulcer.

Gastroduodenal peptic ulcer is a heterogenic disease, with multiple factors involved in its genesis and being one of the most chronic diseases among adults, occurring in 5% to 10% of the population. In pediatrics, an increase in the number of diagnosed cases has been observed, because of the availability of secure endoscopic techniques for this age group. However, the real incidence of the disease among children is unknown, considering that there are few works in literature with a substantial number of cases, where the diagnosis was performed through endoscopy, which defines the presence or absence of lesion. The estimation is of 1:2,500 hospital admissions3 (little frequent). The prevalence of the disease in large pediatric centers is of 4 to 7 new cases a year.1-5 In Pediatric Gastroenterology Service, at Hospital

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Peptic ulcer is classified by its location (gastric and/or duodenal) and by its probable cause (primary or secondary). This division is important due to the differences in both types regarding presentation and evolution. Primary ulcer occurs in the absence of subjacent systemic diseases, while secondary ulcer is associated with acute diseases, such as sepsis, cranoencephalic lesions or trauma, extensive burn, acidosis, hypoglycemia, shock, respiratory insufficiency and with the use of drugs such as acetylsalicylic acid, nonsteroidal anti-inflammatory drugs and corticosteroids. Some systemic diseases may also be associated with secondary peptic ulcer, such as cystic fibrosis, diabetes mellitus, Crohn’s disease, drepanocytosis and systemic lupus erythematosus. One rare and special type of secondary peptic ulcer is the Zollinger-Ellison Syndrome, in which the basic cause is a gastrin productor tumor, located primarily in the pancreas or duodenum, with metastases in other places, such as the liver. Multiple ulcers occur in the stomach, duodenum and jejunum and, sometimes, also in the esophagus, being liable to present concomitance with aqueous diarrhea.

In gastroenterologic practice, the greatest experience is associated with primary peptic ulcers. Concerning the secondary ones, the handling is more intimately related to professionals from the urgency services and from intensive care units.

Secondary ulcers have a more acute clinical presentation and are more frequent during the neonatal period, among infants and children younger than 6 years old. They are located in the stomach or duodenum, depending on the subjacent condition, and the ones associated with acetylsalicylic acid affect mainly the stomach. Primary ulcers are 4 to 7 times more frequent in the duodenal bulb than in the stomach. In this location, they affect mainly children older than 10 years of age, and generally have a chronic clinical course.

Concerning sex, there is a clear predominance of the masculine over the feminine sex, for both primary duodenal and primary gastric ulcers.

Etiopathogeny and pathophysiology

In spite of the great advances regarding knowledge about peptic ulcerous disease, its etiology is not totally known yet. The basic pathophysiologic concept is that peptic ulcer results from the rupture of the equilibrium between aggressive factors (acid and pepsin) and protector factors from the gastroduodenal mucosa.

Chloridric acid and pepsinogen I are secreted by the mucosa of the gastric body and fundus, and by the parietal and principal cells, respectively. Acid secretion is controlled by the action of three potent stimulants: histamine, acetylcholine and gastrin. They act through an outflow of events that lead to the activation of H+–K+ ATPase pump, which secretes hydrogen ions in exchange with potassium. Pepsin is a proteolytic enzyme that is secreted principally through cholinergic stimulation, under the form of pepsinogen I and II, which are converted to active pepsin by gastric acidity.

Several defense factors are involved in the protection of the gastroduodenal mucosa against the activity of acid and pepsin, such as mucosa, bicarbonate, hydrophobic layer, prostaglandins, cellular replication and resistance, and mucous sanguineous flow. The mucosa-bicarbonate layer covers the stomach and duodenum surface, being probable that the mucosa retards the diffusion of H+ ions from the lumen to the epithelial cells, and that the bicarbonate neutralizes ions that have diffused into the mucous layer.

Prostaglandins increase mucous resistance through an increased blood flow and through the stimulus of mucosa and bicarbonate secretion, decreasing acid secretion.

Among the factors that inhibit or reduce mucosa and bicarbonate secretion are the acetylsalicylic acid, biliary acids, nonsteroidal anti-inflammatories, corticosteroids, alcohol and nicotine. This action may be in great part mediated by the inhibition of prostaglandin synthesis.

Traditionally, it is considered that primary duodenal ulcer is more related to the increase of mucosa aggressive factors. Primary gastric and secondary duodenal ulcers, for their turn, tend to occur as a result of alterations in defense mechanisms.

The most probable hypotheses regarding the etiopathogenesis of ulcerous disease refer to genetic factors, pathophysiologic disturbs and environmental factors.

Genetic factors

The role of heredity has been proved by several studies. Homozygous twins have a concordance rate of 50% for ulcerous disease, which is three times higher than the rate observed among dizygous twins.

Positive familial history of peptic ulcer is significantly more frequent among children with duodenal ulcer than in non-ulcerous children, what does not occur in relation to those with gastric ulcer. In literature, up to 75% of children with duodenal ulcer have a first relative affected.

The incidence of type O, and HLA-B8 and B12 carriers is higher in patients with chronic peptic ulcer than in the general population.

Pepsinogen I is also a subclinical marker of peptic ulcer. Serum levels of pepsinogen I are higher in a significant percentage of children with duodenal ulcer. In these studies, hyperpepsinogenemia has also occurred in most of parents (with or without ulcer) of patients with elevated pepsinogen I. However, children of fathers with elevated
Acetylsalicylic acid and other nonsteroidal anti-inflammatories and corticosteroids over the peptic ulcer genesis has been investigated among adults. However, there is only a probable correlation with the last four items.14,17 Smokers present lower percentages of cicatrization and higher percentages of peptic ulcer recidivism. Acetylsalicylic acid and nonsteroidal anti-inflammatories are associated with acute lesions of the gastric mucous, while corticosteroids are more related to some cases of duodenal ulcer. The effects of these agents seem to arise from the negative action over the gastroduodenal mucosa defensive factors.

Another environmental factor is *Helicobacter pylori*. There are strong evidences that this bacterium is the most important causative factor regarding peptic ulcer. Over 90% of adults with duodenal ulcer and 70% to 90% of those with gastric ulcer are infected.15 When the cases of ulcer related to anti-inflammatory drugs are excluded, *H. pylori* is detected in almost all the ulcerous patients. 55% to 100% of children with duodenal ulcer and about 40% of those with gastric ulcer are infected.8,19-21 Out of 76 children with duodenal ulcer investigated by us, 69 had primary duodenal ulcer, and, among them, 83% and 91%, respectively, were positive *H. pylori*. These findings show that the bacterium is the most frequent factor among the ones described in the duodenal ulcer etiopathogeny. However, the definite evidence of its participation as an etiologic factor is that the treatment with antimicrobial solutions alters significantly the disease evolution, with recidivism rates of ulcerous duodenal lesion approaching zero among those in which the microorganism was eradicated.19,20,22 *H. pylori* seems not to have essential participation in children gastric ulcer pathogenesis, though, presenting infection rates similar to nonulcerous patients. It is possible that the relationship is less consistent because most gastric ulcers are associated with other specific causes.

It is estimated that around 50% of worldly population is infected by *H. pylori*. However, only 10% of the adults infected have peptic ulcer, and only a small percentage of individuals will develop adenocarcinoma or gastric MALT lymphomas (lymphoid tissue associated with mucosa), diseases also related to the bacterium. Probably the interaction of bacterial factors, the host and other environmental factors contributes to the development of several pathologies associated with the infection. Duodenal ulcerous patients are more frequently infected by strains that carry vacA A1 and cagA genes than the nonulcerous ones.23,24 These strains are associated with a higher degree of gastric inflammation. Some physiological alterations of the duodenal ulcerous patient may be secondary to the infection. Children colonized by *H. pylori* have increased serum levels of gastrin and pepsinogen I and increased levels of gastrin content in the antral mucosa than the noninfected ones - these levels decrease after the eradication.25,26 The infection by *H. pylori* is also accompanied by an increased level of acid in the duodenum, caused by an increased production of acid by the stomach and a lower production of bicarbonate by the duodenum, which is reverted with the eradication. The increased duodenal acidity predisposes to gastric metaplasia in the duodenum. The hypothesis is that the bacterium, previously restricted to the duodenum, will colonize gastric metaplasia areas in the duodenum, and as a result, chronic duodenitis.
will occur, which eases the retrodiffusion of hydrogen ions, and subsequently, the formation of ulceration.

The predominance of peptic ulcer in male sex cannot be explained by H. pylori infection, though, once the bacterium is equally distributed in both sexes.\textsuperscript{27}

**Clinical status**

Peptic ulcer symptomatology varies according to the type (primary or secondary) and to the age.

**Secondary peptic ulcer**

Secondary ulcers usually have an acute clinical course, being habitually manifested by high digestive hemorrhage, which may be accompanied by noncharacteristic abdominal pain, diffuse or located at the superior part of the abdomen, and by nonsanguineous vomits.\textsuperscript{1,3} Gravity and prognosis depend on the base disease and on the depth and extension of the lesions. More extensive and deep lesions result in voluminous bleeding and increased possibility of perforation, events that determine the increased rate of mortality and the need of surgical intervention. In case of cure, they do not recidivate if the provoking factor is ceased.

**Primary peptic ulcer**

Primary peptic ulcer is accompanied by substantial morbidity, but, in the age of acid secretion inhibitors, mortality among pediatric patients is not usually observed.\textsuperscript{1,5-7} Habitually, the clinical course is chronic with symptomatic periods lasting hours up to days, intercalated with periods of calm lasting days up to months. Main clinical manifestations are abdominal pain, high digestive hemorrhage, expressed as hematemesis and/or melena, and vomit. Hemorrhage in this cases is more commonly lower than in secondary ulcer cases, and, in most cases, does not require surgery.

In primary gastric ulcer, vomiting is the most frequent symptom, but either vomit, abdominal pain, hematemesis and/or melena may be the presentation symptom. Vomit may be postprandial or not, and may be associated with pain and bleeding. Abdominal pain may be located at superior abdomen, be periumbilical or, more rarely, diffuse. Concerning the type, it is commonly noncharacteristic, being liable to be manifested as colic or burning, and, more commonly, noncharacteristic. Most times, pain does not have any relation with feeding, and may occur at any time of the day/night. The probable reason for symptoms of primary gastric peptic ulcer to be so unspecific is the fact that it affects mainly children younger than 6 years of age, which have problems to express their complaints.

Among patients with primary duodenal ulcer younger than 7 years, the clinical manifestation is similar to the one regarding patients with gastric ulcer, having been observed abdominal pain, vomit and bleeding in equal percentages. Among patients older than 7 years of age, the main symptom is abdominal pain, which is significantly associated with vomit and hemorrhage cases. Sometimes, though, these symptoms may be the only manifestation. Vomits may many times improve the dolorous symptomatology. The abdominal pain characterization is habitually from weak to moderate intensity, leading to suspicion of perforated ulcer when the dolorous status is too intense. In these cases, there will also be signs of peritonism and abdominal distention. In the age group from 7 to 12 years, pain has epigastric location in two-thirds of children, and periumbilical location, on the right and left hypochondria or on the right flank, in the rest of the cases. In only one-third of the patients, it is manifested as burning, being liable to be presented also as colic, sticking, gnawing, hunger pain or noncharacteristic. In this age group, two-thirds of the patients report improvement of pain after alimentation and pain that awakes them at night. Among patients older than 12 years of age, pain is almost always epigastric, and burning or other characteristics are indifferent. Most patients get better with alimentation, and, in half cases, it is also manifested at night.

Other associated symptoms are nausea, heartburn, pyrosis, ptyalism, overloading, abdominal distention, eructation, and emaciation. Rarely, the clinical presentation may be iron deficiency anemia, caused by occult bleeding in feces.

Perforation and obstruction became rare events after the advent of acid secretion inhibitors. Nowadays, they are practically the only indications of surgical treatment, for the untreatability of uncontrollable symptoms and hemorrhages are not part of primary peptic ulcer clinical spectrum anymore.\textsuperscript{1,3-5}

Recurrent functional abdominal pain, so frequent in pediatrics, may present characteristics similar to those among children with peptic ulcer. A work has investigated 160 patients from 6 to 15 years of age, which were submitted to high digestive endoscopy for suspicion of peptic ulcer. The authors analyzed signs and symptoms of patients both with and without ulceration, and verified that the presence of epigastric pain, alimentation-related pain, vomit, hematemesis and/or melena, and positive familial history for peptic ulcer is what differentiates children with peptic ulcer.\textsuperscript{28} The presence of nocturnal pain presented high specificity, but low sensitivity, and sex was not analyzed in this work.

Recidivism after cure is not usually observed among children with peptic ulcer. However, among children with duodenal ulcer, 1,20 the estimated annual rate is at 56%.\textsuperscript{1,20}

**Diagnosis**

**Diagnosis of the ulcerated lesion**

Endoscopy is no doubt the chosen method for diagnosis of primary peptic ulcer. It permits to check the lesion characterization, if it is cicatrized or in activity, the presence
of bleeding and the application of endoscopic techniques for the control of massive hemorrhages, in addition to the collection of biopsies for the diagnosis of *H. pylori* and histopathologic study. Usually, among children who evolve in an asymptomatic way, the repetition of endoscopy to validate of cicatrization after treatment is not necessary, expect for special cases, such as giant, very deep and recidivous primary ulcers, or those which perforated or which were accompanied by important hemorrhage. In these situations, the confirmation not only of endoscopic cure, but also of eradication of *H. pylori* are necessary before antisecretory medication is suspended. Among patients that present subjacent conditions, which justify the diagnosis of secondary ulcer, it is not always necessary to carry out the endoscopy, except for doubtful cases, those that need therapeutic endoscopy for hemorrhage control and/or in the repetition of symptoms when potential ulcerogenic factors are absent.

In a child, contrasted x-ray presents a high risk of false positive and false negative diagnosis.

**Diagnosis of specific types of ulceration and complications**

Facing a patient with multiple or atypically located ulcerations, or, still, facing ulcers in patients not infected by *H. pylori* and refractory to treatment with proton pump inhibitors, the possibility of Zollinger-Ellison Syndrome should be removed by serum gastrin dosage.

In suspicion of perforation, simple x-ray of abdomen will demonstrate free air in the peritoneum.

**Diagnosis of infection by *H. pylori***

There are several methods, invasive or not, for detecting the infection. Invasive tests include urease test, culture, histology, and polymerase chain reaction (PCR), which are carried out in fragments of gastric biopsies collected by endoscopy. Culture is the gold standard; it permits typing of strains and performance of antibiograms. However, it is expensive and available only in research centers. Its sensitivity varies according to the culture medium used and to the experience of each laboratory with a determined medium. Urease test is based on the bacterium potent ureasic activity. It uses as substrate agar, urea, and phenol red (pH indicator). If the biopsy fragment immersed in the medium contains the microorganism, then hydrolysis of urea into ammonia and carbon dioxide will take place, with an increase in pH and consequent change of the agar yellowish color to rose, within 24 hours at the most. Urease test has high sensitivity and specificity, and it is the most widely method used in the ambit of endoscopy. Histologic research may be carried out with several stainings, and it has a good diagnostic accuracy, which will depend on the laboratory experience with a determined staining. It permits, in addition to research about the bacterium, histopathologic study.

PCR may be carried out with gastric biopsy material, with gastric juice, saliva, and feces for direct detection of the bacterium, but it is expensive, and not used in clinical practice.

The main noninvasive methods are serology and respiratory test with urea marked by carbon (13C or 14C).

Serologic tests commercially available, although presenting excellent accuracy in the diagnosis of infection among patients older than 12 years of age, do not have the necessary sensitivity and specificity among children younger than 12 years. Serology is the most common technique employed in epidemiological studies, but it is not indicated to the diagnosis of infection in a single patient, neither before nor after antimicrobial treatment. The reduction of antibody levels is done very slowly, after the bacterium eradication; they may persist for over a year.

Respiratory test with urea marked with 13C or 14C is based on the same principle as the urease test. In children, only 13C is used, for being nonradioactive. Samples of expired air are collected 30 minutes before and after the ingestion of marked urea, and the difference of CO₂ excretion in both samples is determined. The cutoff to be considered as positive will depend on the spectrometer used. For infrared spectrometer, the delta considered as positive is higher than 4 per thousand. Respiratory test is highly specific and sensitive, being the chosen one for the eradication control. Any test that is done with this purpose, except for serology, should be carried out with an interval of at least 4 weeks after the antimicrobial treatment.

**Treatment**

As the gastroduodenal peptic ulcer is much less prevalent in children than in adults, treatment studies for the disease are rare and, in general, noncontrolled, what may be taken into consideration at the interpretation of its results. The objective of the treatment is to relieve symptoms, cicatrize the lesion and prevent recidivism. The first two are easily reachable with antisecretor and acid neutralizer medication. However, prevention of recidivism in duodenal ulcer have been achieved successfully only with the eradication of *H. pylori* among infected individuals. Recidivism rate regarding duodenal ulcer goes from 0% up to 12.5% among those who keep long-term negative *H. pylori*. It is important to remember that there is a substantial percentage of recidivism/recurdescence of the infection among children, which may be accompanied by reactivation of the ulcerous disease.

**Histamine H2-receptor antagonists**

Histamine H2-receptor antagonists present good efficacy in the cure of peptic ulcer. Cimetidine, taken twice orally, at a dosage of 20 to 30 mg/kg/day, cures the lesions in 80% to 90% of cases after 8 weeks. Ranitidine, also taken
twice orally, at a dosage of 5 to 10 mg/kg/day, reaches, in 8 weeks, 80% to 100% of cicatrization. In daily practice, these drugs are used in one (at night) or two (in the morning and at night) daily dosages, for an average period of 8 weeks when it is not associated with antimicrobial treatment. Few data are available concerning famotidine and nizatidine, but they may be used orally at dosages of 1 to 2 mg/kg/day and 5 to 10 mg/kg/day, respectively. In cases where maintenance treatment is necessary after the cure of ulceration as recidivous ulcer, half dose is used at night for a prolonged period.

**Proton pump inhibitors**

Proton pump inhibitors are slightly more efficacious than histamine H2-receptor antagonists in the cure of uncomplicated peptic ulcer among children. Due to their high cost, they should be reserved for histamine H2-receptor antagonist-refractory cases, giant ulcers, perforations, important hemorrhages, and the Zollinger-Ellison Syndrome. Omeprazole in a single matutinal dosage of 0.5 to 0.7 mg/kg/day for 6 weeks cures up to 100% of ulcers that are refractory to histamine H2-receptor antagonist. Other proton pump inhibitors, such as lansoprazole and pantoprazole, may also be used among children, but there are no consistent reports regarding this aspect yet. Initial dosages to be used are of 30 to 40 mg/1.73 m² body surface for lansoprazole and pantoprazole, respectively. Proton pump inhibitors are administrated in a single matutinal dosage, 30 minutes before the first meal of the day, preferentially with intact capsule. For children that are not able to swallow capsules, these capsules may be open, and the granules may be ingested in an acid medium (yogurt, citric juices).

**Antacids**

Antacids are as efficacious as cimetidine in the cure of duodenal ulcer among children when used in high dosages. However, there is no definition of the adequate dosage for pediatric patients. Usually, 5 to 10 ml per dosage are used in the most potent formulations, depending on the age. They are taken four times a day, 1 hour after each of the three main meals and before going to bed. The great number of dosages and the unpleasant flavor, in addition to the side effects (diarrhea or constipation), make treatment adhesion difficult, making these drugs unpractical for routine use.

**Treatment of infection by H. pylori**

In 1997, during the European *Helicobacter pylori* Study Group meeting, in Portugal, treatment of the bacterium in all child infected by peptic ulcer was defined, independently on its active or cicatrized state. As most antimicrobial schemes are associated with side effects, if the patient is too symptomatic, it is preferable to prescribe first an acid secretion inhibitor and start with antimicrobials as soon as there is a clinical improvement, what occurs on average after 7 days with histamine H2-receptor antagonist, and after 3 days with proton pump inhibitor.

There is no ideal therapeutic scheme yet, but the recommendation is that only those that achieve eradication rates higher than 80% are used. It seems to be necessary, for therapeutic success, the inclusion of a drug with salivary and/or gastric secretion (metronidazole, clarithromycin) associated with drugs of luminal action (bismuth, amoxicillin, tetracycline, furazolidone, clarithromycin). The percentage of strains that are resistant to metronidazole and clarithromycin determines the success of a determined treatment. As microbial sensitivity varies according to the location, race and early use of these medicaments, the efficacy of a therapeutic scheme in a population does not permit the generalization of results. The ideal would be to base the treatment on studies about sensitivity or at least on the knowledge of the microorganism resistance indexes in the community, what, at the moment, is impossible in most Brazilian centers. In Belo Horizonte, the percentage of *H. pylori* strains isolated in children at Hospital das Clínicas da UFMG that are resistant to metronidazole and to clarithromycin is at about 40% and 5%, respectively (unpublished data). We have to keep in mind that, with the increased use of clarithromycin, a higher percentage of strains resistant to this drug may occur. Another point to be considered is that in vitro activity does not correspond, necessarily, to in vivo activity.

The schemes most used nowadays among children consist of the association of three drugs: a proton pump inhibitor with two antimicrobials (clarithromycin associated with amoxicillin or metronidazole) or bismuth with two antimicrobials (metronidazole associated with amoxicillin or clarithromycin).

The association of omeprazole (0.7 to 1.2 mg/kg/day, max. 40 mg/day, u.i.d or b.i.d.) with clarithromycin (15 mg to 30 mg/kg/day, max. 1000 mg/day, b.i.d.), plus amoxicillin (60 mg/kg/day, max. 2000 mg/day, b.i.d.) or metronidazole (20 to 30 mg/kg/day, max. 1000 mg/day, b.i.d.), used for 2 weeks, provided eradication rates of over 90% among children in Canada and Japan. When there is association with amoxicillin, clarithromycin should be used at the dosage of 30 mg/kg/day, and, when associated with metronidazole, it may be used at the dosage of 15 mg/kg/day, max. 500 mg/day.

The use of bismuth (480 mg/1.73 m² body surface/day, q.i.d.), associated with metronidazole (20 to 40 mg/kg/day, max. 1000 mg/day, t.i.d. or q.i.d.) and amoxicillin (20 to 40 mg/kg/day, max. 1000 mg/day, q.i.d.) or clarithromycin (15 mg/kg/day, max. 500 mg/day, b.i.d.) has achieved, in 1 or 2 weeks, eradication rates of 96% among children from Taiwan and Ireland. The scheme with bismuth was accompanied by an increased percentage of side effects than the previous scheme, but most times did not impede the continuity of the treatment.
In Belo Horizonte, we initially used amoxicillin (50 mg/kg/day, max. 1500 mg/day, metronidazole (20 to 30 mg/kg/day, max. 750 mg/day) and furazolidone (6 to 8 mg/kg/day, max. 300 mg/day), in three daily dosages for a week, with eradication of 84% among patients with early antimicrobial course.\textsuperscript{22} The percentage of side effects was significant, but most times did not motivate the suspension of medication, and the association with a proton pump inhibitor could decrease its occurrence. Although it has been reported that the association of a proton pump inhibitor with an antimicrobial scheme among adults increases the eradication percentage, we did not observe such result while associating omeprazole with the scheme described above. This may have occurred due to a small number of cases in which proton pump inhibitor was used. In noneradicated cases, or in those in which infection recidivism occurred, we used an association of proton pump inhibitor (omeprazole 1.2 mg/kg/day, max. 40 mg/day, b.i.d.), bismuth (7 to 8 mg/kg/day, max. 480 mg/day, q.i.d.), tetracycline (50 mg/kg/day, max. 2g/day, q.i.d.), and furazolidone (6 to 8 mg/kg/day, max. 300 mg/day, t.i.d.) for 1 or 2 weeks, with success in most cases. It is important to remember that tetracycline should only be used in children older than 8 years of age. The scheme with bismuth plus two other antimicrobials has been recommended for adults as a second-line treatment to be used for 14 days. Treatment time may be reduced to 7 days when used in association with a proton pump inhibitor. In first-world countries, where there is no furazolidone, it is substituted by metronidazole.\textsuperscript{40}

Amoxicillin (50 mg/kg/day) and tinidazole (20 mg/kg/day) in two daily dosages for 2 weeks eradicated the bacterium in 81% of Italian children\textsuperscript{39}. However, this scheme has not been tested in other countries.

Not considering financial cost, the scheme with a proton pump inhibitor (1-1.2 mg/kg/day, max. 40 mg/day, b.i.d.) associated with clarithromycin (30 mg/kg/day, max. 1000 mg/day, b.i.d.) and amoxicillin (50 mg/kg/day, max. 2000 mg/day, b.i.d.) for 1 or 2 weeks is maybe the first-line treatment, at the moment, for Brazilian children, due to the high percentage of strains resistant to metronidazole that are present in our environment. Amoxicillin may be substituted by furazolidone, but we do not have, up to the moment, knowledge about the eradication rates with the use of a proton pump inhibitor associated with clarithromycin and furazolidone among children.

As second-line treatments, any of the following schemes may be used:
- amoxicillin + metronidazole + furazolidone, preferably associated with a proton pump inhibitor, for 7 to 14 days;
- proton pump inhibitor + clarithromycin + furazolidone, for 7 to 14 days;
- proton pump inhibitor + clarithromycin + metronidazole, for 7 to 14 days;
- bismuth + tetracycline (or clarithromycin)+ furazolidone (or metronidazole), for 14 days;
- proton pump inhibitor + bismuth + tetracycline (or clarithromycin) + furazolidone (or metronidazole), for 7 to 14 days.

Up to the moment, there is no retreatment proposal among children in case of noneradication. Based on adult studies, it is recommended to use a scheme of proton pump inhibitor plus three antimicrobials, preferably bismuth, tetracycline and metronidazole, which in our environment may be substituted by furazolidone, for 7 to 14 days. Another option would be a triple scheme, with a proton pump inhibitor plus two antimicrobials, except for the bismuth, and not repeating clarithromycin and/or metronidazole if they had been used on the first treatment. When two therapeutic courses failed to eradicate the infection, the ideal is to perform culture with antibiogram for next treatment definition.

In addition to the fact that eradication of \textit{H. pylori} cures ulcerous lesion, it is recommended, among patients with active ulcer, to complement the antimicrobial treatment with the traditional treatment, with acid secretion inhibitors, for it is impossible to know previously what patients will remain infected. We have done this for more than 4 weeks if the patient is asymptomatic.

References


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