

Eosinophilic esophagitis and proton pump inhibitors: is there a new link?

Morais MBM. Eosinophilic esophagitis and proton pump inhibitors: is there a new link? *Arq Gastroenterol.* 2017;54(4):269-7.

HEADINGS – Eosinophilic esophagitis. Omeprazole. Ranitidine. Gastroesophageal reflux. Infant. Child. Adolescent.

Two topics of importance for child and adolescent health are addressed in this number of *Arquivos de Gastroenterologia*: histologic diagnosis of eosinophilic esophagitis⁽¹⁾ and antisecretory treatment of the gastroesophageal reflux disease⁽⁸⁾.

The eosinophilic esophagitis is currently conceptualized as a chronic esophagus disease, characterized clinically by manifestations of esophageal dysfunction and histologically by predominant eosinophilic inflammation. Immunologic mechanisms are involved in the etiology of the disease^(4,7,9,11). The article of Carrasco et al.⁽¹⁾ highlights relevant topics on the histologic evaluation in pediatric patients with eosinophilic esophagitis, that is to say, the absence of visible abnormalities in the upper digestive endoscopy and the presence of eosinophilic infiltrate with focal distribution in a significant number of the patients. Therefore, from the practical point of view, it is important that multiple esophageal biopsies are performed even in the absence of classic abnormalities that may be seen in the esophagoscopy. From the histologic point of view, the eosinophilic infiltrate was more intense on the distal third of the esophagus. Individually, in 9 of the 34 specimens, the histological characteristics did not allow to establish the diagnosis of eosinophilic esophagitis. It was also observed that the thickness of the basal layer in the eosinophilic esophagitis is larger than in the esophagitis caused by gastroesophageal reflux disease. Thus, the authors warn for two prevailing relevant aspects in the eosinophilic esophagitis at the pediatric age, which means, normal esophageal mucosa in the endoscopy and focal eosinophilic infiltrate in significant number of the patients⁽¹⁾.

The classic treatment of the eosinophilic esophagitis involves corticosteroid therapy, mainly topical, and food elimination diets^(4,7,11). In the past years it was identified a group of patients, both children and adults, in which eosinophilic esophagitis responds to the treatment with proton pump inhibitors⁽⁹⁾. Previously, rejecting the hypothesis of gastroesophageal reflux disease, which also associates with eosinophils in the esophageal mucosa, was considered essential. For this purpose, esophageal pH-metry and/or therapeutic test with proton pump inhibitors was employed. The old paradigm was modified when it was confirmed that some patients with typical presentation of eosinophilic esophagitis and normal esophageal pH-metry showed clinical and histological recovery. In this context, about half of the patients show positive response when treating with the proton pump inhibitor⁽⁹⁾. It is suggested that the positive

response is due to an anti-inflammatory effect of the proton pump inhibitors. Therefore, a new therapeutic modality for eosinophilic esophagitis arises. It is worth highlighting that the therapy with proton pump inhibitors is easier to be performed than the topical treatment with corticosteroids and the traditional food elimination diets (amino acids formula as only source of food and diet with elimination of six foods⁽⁶⁾). Regarding the dietary treatment, it has been observed that the recovery can happen through elimination diet by eliminating only the cow milk protein. Thus, in the treatment of eosinophilic esophagitis, which is a recurrent chronic disease, two therapeutic options that may be useful for a share of the patients arise. It must be emphasized that the eosinophilic esophagitis treatment is individualized and the therapeutic option must be chosen along with the patient. Additional researches to identify predictive factors of good response with proton pump inhibitors or elimination diet of cow milk protein are still necessary.

The objective of the second article was to assess the role of the proton pump inhibitors and/or histamine H₂ receptor antagonists for the treatment of pediatric gastroesophageal reflux disease⁽⁸⁾. It is a systematic review that, by following the international recommendations, found 23 clinical trials on the theme. Taking into consideration that the gastroesophageal reflux disease may present a wide range of clinical manifestations, the results were interpreted according to types of clinical manifestation. It is worth highlighting that there is not a gold standard for the diagnosis of the gastroesophageal reflux disease. Another essential point is that the heterogeneity of the clinical trials did not allow a meta-analysis to be carried out. The evidence point out that both, the proton pump inhibitors and the histamine H₂ receptor antagonists, have efficacy for the treatment of the esophagitis. It was also observed that the proton pump inhibitors are more potent than the histamine H₂ receptor antagonists. They concluded that the proton pump inhibitors or histamine H₂ receptor antagonists may be used to treat children with gastroesophageal reflux disease, but not to treat asthma or unspecific symptoms⁽⁸⁾.

An aspect that must be enhanced is the role of the proton pump inhibitors among infants with excessive crying which is one of the unspecific symptoms assigned to the gastroesophageal reflux disease. It was found that there was a significant increase in the consumption of proton pump inhibitors among infants in the United States, 11 times from 2002 to 2009^(2,3).

One of the main indications are unspecific clinical manifestations such as excessive crying and irritability associated with regurgitation and vomit. Even in the absence of regurgitation and vomit the possibility of occult gastroesophageal reflux is considered. However, the metanalysis showed that there is no efficacy when using proton pump inhibitors to treat infants with irritability and/or excessive crying⁽⁵⁾. At this age group, in addition to gastroesophageal reflux, excessive crying and irritability may be caused by the maturation of the digestive system itself, functional gastrointestinal disorders such as infant colic and allergy to cow milk protein⁽¹⁰⁾. It is important to remind that some patients on exclusive breastfeeding may benefit from the

mother elimination diet excluding cow milk proteins. Another major aspect is that proton pump inhibitors may have negatives consequences on the health of the infant. Thus, it is concluded that the use of proton pump inhibitors among infants must be restricted to cases in which the presence of a peptic disease has been confirmed.

Thus, as well as in other medical scenarios, the effective therapeutics must be prescribed according to the defined individual needs based on the careful application of appropriate diagnostic criteria.

Mauro Batista de **MORAIS***

Morais MBM. Esofagite eosinofílica e inibidores de bomba de prótons: existe uma nova relação? *Arq Gastroenterol.* 2017;54(4):269-7.

DESCRITORES – Esofagite eosinofílica. Omeprazol. Ranitidina. Refluxo gastroesofágico. Lactente. Criança. Adolescente.

REFERENCES

1. Carrasco AEAB, Machado RS, Patricio FRS, Kawakami E. Histological features of eosinophilic esophagitis in children and adolescents. *Arq Gastroenterol.* 2017;54:281-5.
2. Chen IL, Gao WY, Johnson AP, Niak A, Troiani J, Korvick J, et al. Proton pump inhibitor use in infants: FDA reviewer experience. *J Pediatr Gastroenterol Nutr.* 2012;54:8-14.
3. Ferreira CT, Carvalho Ed, Sdepanian VL, Morais MB, Vieira MC, Silva LR. Gastroesophageal reflux disease: exaggerations, evidence and clinical practice. *J Pediatr (Rio J).* 2014;90:105-18.
4. Furuta GT, Liacouras CA, Collins MH, Gupta SK, Justinich C, Putnam PE, et al. Bonis P, Hassall E, Straumann A, Rothenberg ME; First International Gastrointestinal Eosinophil Research Symposium (FIGERS) Subcommittees. Eosinophilic esophagitis in children and adults: a systematic review and consensus recommendations for diagnosis and treatment. *Gastroenterology.* 2007;133:1342-63.
5. Gieruszczak-Białek D, Konarska Z, Skórka A, Vandenplas Y, Szajewska H. No effect of proton pump inhibitors on crying and irritability in infants: systematic review of randomized controlled trials. *J Pediatr.* 2015;166:767-70.
6. Kagalwalla AF, Sentongo TA, Ritz S, Hess T, Nelson SP, Emerik KM, et al. Effect of six-food elimination diet on clinical and histologic outcomes in eosinophilic esophagitis. *Clin Gastroenterol Hepatol.* 2006;4:1097-102.
7. Liacouras CA, Furuta GT, Hirano I, Atkins D, Attwood SE, Bonis PA, et al. Eosinophilic esophagitis: updated consensus recommendations for children and adults. *J Allergy Clin Immunol.* 2011;128:3-20.
8. Mattos AZ, Marchese GM, Fonseca BB, Kupski C, Machado MB. Antisecretory treatment for pediatric gastroesophageal reflux disease – a systematic review. *Arq Gastroenterol.* 2017;54:271-80.
9. Molina-Infante J, Bredenoord AJ, Cheng E, Dellon ES, Furuta GT, Gupta SK, Hirano I, Katzka DA, Moawad FJ, Rothenberg ME, Schoepfer A, Spechler SJ, Wen T, Straumann A, Lucendo AJ; PPI-REE Task Force of the European Society of Eosinophilic Oesophagitis (EUREOS). Proton pump inhibitor-responsive oesophageal eosinophilia: an entity challenging current diagnostic criteria for eosinophilic oesophagitis. *Gut.* 2016;65:524-31.
10. Morais MB. Signs and symptoms associated with digestive tract development. *J Pediatr (Rio J).* 2016;92(3 Suppl 1):S46-56.
11. Papadopoulou A, Koletzko S, Heuschkel R, Dias JA, Allen KJ, Murch SH, Chong S, Gottrand F, Husby S, Lionetti P, Mearin ML, Ruummele FM, Schäppi MG, Staiano A, Wilschanski M, Vandenplas Y; ESPGHAN Eosinophilic Esophagitis Working Group and the Gastroenterology Committee. Management guidelines of eosinophilic esophagitis in childhood. *J Pediatr Gastroenterol Nutr.* 2014;58:107-18.

* Disciplina de Gastroenterologia Pediátrica, Escola Paulista de Medicina, Universidade Federal de São Paulo, SP, Brasil.

Correspondence: Mauro Batista de Morais. Rua dos Otônios, 880, ap. 63. CEP: 04025-002 – São Paulo, SP, Brasil. E-mail: maurobmorais@gmail.com.br.