Editorial

Asthma and gastroesophageal reflux

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There is an association between asthma and gastroesophageal reflux disease (GERD). The prevalence of GERD is higher in asthma patients than in individuals without asthma. However, GERD is associated with asthma-related respiratory symptoms. In other words, asthma worsens GERD, and GERD worsens asthma.

One group of authors[1]studied the presence of classic GERD symptoms in individuals with asthma and noted that heartburn, reflux, and dysphagia were reported by 77, 55, and 24%, respectively, of those interviewed. The mechanisms associated with the high frequency of GERD symptoms in asthma patients are related to alterations linked to asthma and the effects of medications.[2] Dysfunction of the autonomous nervous system and an increase in the pressure gradient between the chest and abdomen, as well as changes in the position of the diaphragm, are seen in asthma patients and can play a role in the appearance of hiatal hernia and GERD. Another group of authors[3] noted that repeated doses of inhaled salbutamol resulted in a decrease in the basal pressure of the lower esophageal sphincter. Yet another group[4] observed that the use of 60 mg/day of prednisone, per oral, for seven days increased the contact time between gastric acid and the esophagus.

In the presence of GERD, there is an association between reflux episodes and respiratory symptoms in asthma patients. Some possible mechanisms have been proposed to explain that association. Microaspiration of gastric acid might result in bronchial inflammation and bronchoconstriction. Vagal reflexes originating in the receptors of the lower third of the esophagus could cause a cholinergic stimulus in the airways and the release of certain pro-inflammatory neuropeptides.[2] Either one of those mechanisms could result in an increase of pulmonary hyperresponsiveness. The results of some laboratory studies suggest that microaspiration plays an important role. Another group of authors[5] observed that the administration of a large quantity (10 mL) of 0.2 N hydrochloric acid in the lower third of the esophagus in cats resulted in a 1.5-times increase in pulmonary resistance, whereas the infusion of a small quantity (0.05 mL) in the trachea resulted in a 4.7-times increase in pulmonary resistance. We carried out an experimental study using guinea pigs with a model of allergic pulmonary inflammation and noted that a large quantity of acid infused into the esophagus (1 mL of 0.2 N HCl) resulted in only minimal increases in pulmonary resistance, whereas a small quantity (50 µL of 0.2 N HCl) resulted in significant increases in pulmonary resistance.[6] It is possible that in asthma patients there is more than one mechanism involved in the correlation between reflux and asthma. Other authors[7] studied the effect of acid infusion into the stomachs of 13 volunteers with stable moderate asthma and GERD. They noted that two patients presented a more than 10% decrease in forced expiratory volume in one second after esophageal tube insertion. That decrease persisted after saline infusion and became even more pronounced after acid infusion. The remaining 11 patients presented no alterations in forced expiratory volume in one second after acid infusion.

Despite all of the advances in our understanding of the correlation between asthma and GERD, it still has not been established whether the treatment of GERD influences the clinical and functional evolution of asthma. In a meta-analysis published in 1998,[8] it was noted that anti-reflux therapy in 326 asthma patients with GERD improved their asthma symptoms by 69% and reduced the use of asthma medications by 62%. However, in those same patients, peak expiratory flow improved by only 26%. A review of studies on the surgical treatment of GERD,[9] which included a combined total of 417 asthma patients having undergone surgery, presented similar results (reduction of asthma symptoms and the use of asthma medications as well as an improvement in pulmonary function in 79, 88, and 27% of the patients, respectively). However, in another review,[10] the randomized, placebo-controlled studies included in the Cochrane Collaboration registry were evaluated. The authors of that review concluded that treatment of GERD did not consistently improve pulmonary function, asthma symptoms, or nocturnal asthma symptoms; nor did it reduce the use of medications. Those researchers observed that longer-term studies with a larger number of patients should be carried out.

In this issue of the Brazilian Journal of Pulmonology there is a study by Santos *et al.*[11] in which asthma patients

with GERD received proton pump inhibitors (pantoprazole 40 mg, in a single daily dose). The study was prospective, randomized, double-blind and placebo-controlled, with 22 patients in each of the groups. The patients were monitored for 90 days. The authors evaluated patient quality of life, measured daily peak expiratory flow, and performed esophageal pHmetry at the study endpoint. It was noted that the patients who received treatment with pantoprazole obtained a better score for respiratory symptoms and quality of life but not for the respiratory function parameters.

In order to ascertain whether, with a longer treatment period, pulmonary function parameters improve in asthma patients who receive anti-reflux therapy, additional, longer-term studies of the effects of GERD treatment on the clinical and functional evolution of asthma are needed. Such studies should involve larger patient samples and longer treatment durations. Another avenue would be to profile asthma patients who show improvement after anti-reflux therapy and determine identify which characteristics set them apart from those who show no such improvement.

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