

INTRODUCTION

Gastroesophageal reflux disease (GERD) is one of the most common diseases affecting upper gastrointestinal tract. It is a chronic disease, with steadily growing incidence and prevalence in west countries during last 30 years. GERD is caused by pathologic gastroesophageal reflux (GER). GERD includes endoscopically positive, endoscopically negative and extraesophageal reflux disease. Extraesophageal symptoms of GERD have been of a growing attention and discussion during last few years. The most discussed topics are the relation of GERD and bronchial asthma (BA), chronic cough and symptomatology from ear, nose and throat (ENT) regions, but also non-cardial chest pain and many others (*Matyasova et al., 2005*).

Asthma is an inflammatory disease of the airways characterized by increased airway reactivity with airflow obstruction. It is exacerbated by multiple triggers, and one common, often overlooked, trigger is gastro esophageal reflux. A connection between GER disease (GERD) and asthma was first appreciated in 1960s-1970s with reports of asthma patients being cured of asthma following surgery for hiatus hernia or GERD. Additional research has continued to validate that reflux may cause or trigger asthma symptoms. Recent data suggest that treatment of GERD in selected asthmatics not only improves asthma symptoms and pulmonary function but may also decrease steroid medication usage (*Paterson, 2001*).

The prevalence of GERD in asthmatics is estimated at between 34% and 80%. On endoscopic studies alone, 43% of asthmatics have evidence of esophagitis; while on 24-hour esophageal-pH testing, up to 82% of patients have abnormal amounts of acid reflux. Up to 24% of

asthmatics may have silent GER without the classic reflux symptoms of heartburn, regurgitation, or dysphagia. The prevalence of gastroesophageal reflux in childhood asthmatics is reported to be as high as 61% (*Cinquetti et al., 2002*).

There are 2 proposed mechanisms whereby acid refluxing into the esophagus induces or exacerbates airflow obstruction in asthmatics. These mechanisms include:

1. Vagally mediated reflex bronchospasm; and
2. Microaspiration of gastric acid resulting in bronchoconstriction.

(1) Vagally mediated reflex bronchospasm:

Stimulation of esophageal mucosal receptors giving rise to vagally mediated reflex bronchospasm has emerged as the leading hypothesis. Prolonged reflux-clearance-time often causes symptomatic esophageal disease and esophagitis. The epithelial layer of the mucosa becomes eroded, exposing vagal nerve endings. Consequently, esophageal receptors become increasingly sensitive to refluxed material. Once stimulated, the receptors transmit a signal that results in constriction of the bronchioles (*Everett et al., 2004*).

(2) Microaspiration of gastric acid resulting in bronchoconstriction:

Micro-or macroaspiration of gastric contents into the lungs causing a chemical pneumonitis. This is the other proposed mechanism by which GER can cause or exacerbate asthma. This theory was based on the observation that refluxes associated with asthma occurred most commonly in patients with nocturnal asthma. It was hypothesized that supine position of sleep increased the incidence of aspiration of acid material into the airways (*Pisegna, 2001*).

The proof that GER may be the cause and not the effect of asthma is lacking, but studies that demonstrate improvement or even cessation of asthma symptoms after medical or surgical antireflux treatment provide the strongest evidence of GER acting as the cause rather than effect of asthma. In the study of **Harding and colleagues**, 73% of asthmatics with GERD responded to medical antireflux therapy (*Harding et al., 1996*).

Sontag and Colleagues performed antireflux surgery in 13 patients with GERD and asthma and found that 6 patients were completely cured of asthma. These cases must be those asthmatics in which GER was the cause of asthma. Others who did not respond could have other or multiple trigger factors for their symptoms (*Sontag et al., 2004*).

Also, four hundred patients with bronchial asthma (BA) were questioned. Complex clinical and instrumental examination of 60 patients with BA and endoscopic-positive gastroesophageal reflux disease was carried out; the control groups included 30 patients with BA alone and 30 patients with GERD alone. Clinical symptoms of GERD were revealed in 58% of BA patients; endoscopic-positive GERD was diagnosed in 48.6% of BA patients. The study proved the connection between the degree of respiratory disturbances, on the one hand, and the degree of esophagitis and the level of intraesophageal pH, on the other, in patients with BA plus GERD. The study also established the role of esophageal and gastric epitheliocytes, producing endothelin-1, melatonin, NO-synthase, and calretinin, in the occurrence of mutual exacerbation syndrome (*Kozlova et al., 2006*).

Supraesophageal manifestations of GERD including bronchial asthma and chronic laryngitis have received much attention particularly with regard to therapy with potent acid suppression. In a recent study, they showed a positive response to treatment with PPI in patients with GERD and difficult to control (DTC) asthma (*Goh, 2007*).