

Role of Sleep Apnea and Gastroesophageal Reflux in Severe Asthma



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KEYWORDS

- Asthma • Obstructive sleep apnea • Gastroesophageal reflux
- Continuous positive airway pressure • Comorbidity

KEY POINTS

- Treatment of gastroesophageal reflux (GER) with proton pump inhibitors (PPIs) has a limited impact on symptoms and lung function in patients with asthma and symptomatic GER.
- Treatment with PPI of GER identified by pH probe in the absence of GER symptoms does not improve asthma control.
- The impact of treatment of severe GER on asthma has not been fully explored in existing clinical trials.
- Multiple potential mechanisms suggest a relationship between obstructive sleep apnea syndrome (OSA) and asthma, but the directionality of cause and effect is unclear.
- Limited data suggest that treatment of OSA may improve asthma, but further exploration of clinical outcomes and mechanism of benefit are warranted.

INTRODUCTION

Historically, asthma guidelines recommend assessing and treating comorbid conditions in order to achieve asthma control. Recent guidelines from the European Respiratory Society/American Thoracic Society propose the term difficult to control asthma for those in whom treatment of comorbid conditions will presumably improve asthma control.¹ In this review, the author reviews evidence linking obstructive sleep apnea syndrome (OSA) and gastroesophageal reflux (GER) to “difficult to control” asthma and looks critically at the evidence base supporting that evaluation and treatment of these conditions impacts asthma control.

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IS THERE A LINK BETWEEN ASTHMA AND GASTROESOPHAGEAL REFLUX?

The prevalence of GER may be present at a higher rate in those with asthma than what would be expected based on general population prevalence of GER alone. Diagnosis of GER by pH probe in those with asthma with or without typical reflux symptoms has identified prevalence rates of 40% to 60%.²⁻⁴ Despite coexistence of these conditions, it is unclear whether GER impacts asthma control or whether asthma increases the likelihood of GER.

DOES GASTROESOPHAGEAL REFLUX IMPACT ASTHMA CONTROL OR DOES ASTHMA CONTRIBUTE TO GASTROESOPHAGEAL REFLUX?

A classic hypothesis linking asthma and GER involves the direct microaspiration of acidic gastric contents into the lower airways triggering epithelial damage, neurogenic inflammation, and bronchoconstriction.⁵⁻⁸ Because of shared embryologic origin and innervation of the esophagus and airways via the vagus nerve, reflux in the upper esophagus can trigger bronchoconstriction without direct aspiration. These two hypotheses have been referred to as *reflux theory* and *reflex theory* and are illustrated in Fig. 1. Nonacid reflux with bile acids and pepsin has been associated with GER symptoms, although a relationship with extraesophageal manifestations of GER is less clear.³ Findings suggestive of laryngopharyngeal reflux by laryngoscopy or bronchoscopy is common in refractory asthma and may potentially impact asthma via reflux or reflex pathways.⁹

Contrarians have argued that the presence of asthma impacts lower esophageal sphincter (LES) tone and, thus, promotes GER rather than GER triggering asthma.¹⁰ Swings in intrathoracic pressure and/or descent of the diaphragm due to hyperinflation may reverse the normal thoracoabdominal pressure gradient, drawing the LES into the chest and altering its barrier function. Asthma may lower LES tone and promote GER via direct effects of beta agonists and theophylline.¹¹

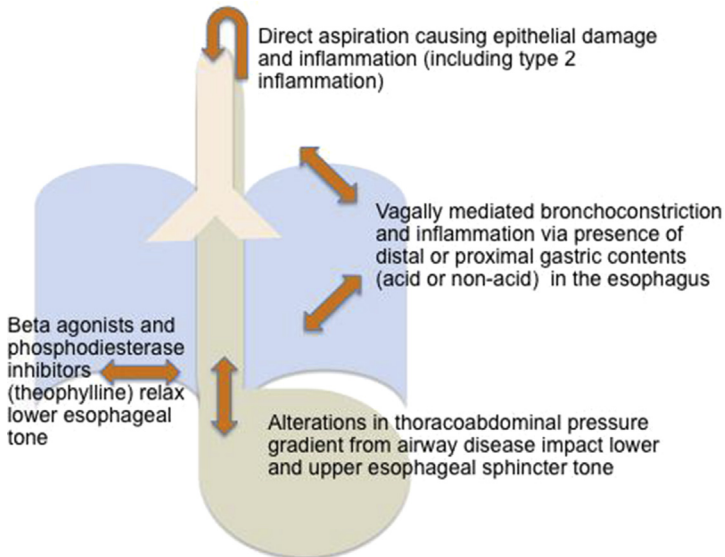


Fig. 1. Potential mechanisms explaining the interrelationship between GER and asthma.

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