

Is gastro-oesophageal reflux associated with COPD exacerbations?

O refluxo gastroesofágico está associado a exacerbações da DPOC?

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COPD is an important long-term condition associated with considerable disability, with a large unmet need for novel therapeutic approaches. The course of COPD is characterized by episodes of respiratory symptom worsening termed exacerbations,⁽¹⁾ and these events are now known to affect health status and disease progression and to be a major factor in the need for hospital admission and readmission.⁽²⁾ These COPD exacerbations are costly to healthcare services worldwide, and, although a number of pharmacological therapies alone or in combination prevent COPD exacerbations, reductions in exacerbation rates of only about 25% have been observed.^(3,4) Thus, novel additional approaches targeting specific pathophysiological mechanisms are essential for COPD patients.

Although exacerbations generally increase in frequency with increasing disease severity, approximately 22% of the patients with moderate COPD in one observational study (FEV₁ = 50–80% of the predicted value) were found to be particularly susceptible to COPD exacerbations and have two or more treated events per year despite usual therapy.⁽⁵⁾ These frequent exacerbators have been shown to have a relatively stable exacerbation frequency phenotype, and the number of exacerbations in one year predicts the number of events that are likely to occur in subsequent years.

A number of studies have highlighted the importance of gastro-oesophageal reflux (GOR) as a co-morbidity in COPD.^(6–8) This is not unsurprising as GOR symptoms are common with increasing age in the population. That same observational study also showed that the presence of gastro-oesophageal reflux (GOR) was related to exacerbation frequency in COPD with the frequent exacerbators having a greater chance of developing GOR symptoms.⁽⁵⁾ In that study, the prevalence of self-reported GOR was at 27%, and this was similar to the prevalence in other studies in COPD. However, it is known that self-reported GOR may under-estimate the true prevalence as GOR may occur in the absence

of symptoms and validated questionnaires need to be used to assess GORD in COPD.

In the present issue of the Brazilian Journal of Pulmonology, Sakae and colleagues present an interesting paper in which they have performed a systematic review and meta-analysis on the relationships between GOR symptoms and exacerbation frequency.⁽⁹⁾ The review confirmed the association between exacerbations and GOR and showed that the risk of having a COPD exacerbation was seven times higher in GOR patients than in those without GOR. Furthermore, the authors also showed that patients with COPD have a significantly higher prevalence of GOR than those without COPD, emphasising that GOR is an important and common co-morbidity in COPD.

GOR is a complex condition and may involve both acid and non-acid reflux, including gaseous reflux. The various forms of reflux arise through transient relaxation of the lower oesophageal sphincter, delayed gastric emptying, and increased intra-abdominal pressure. These processes are more likely in COPD patients who are elderly and present with lung hyper-inflation, coughing, use of abdominal muscles, anticholinergic medication use, and altered autonomic tone. Patients with COPD have evidence of lower airway bacterial colonisation,⁽¹⁰⁾ which is now known to increase airway inflammation and affects exacerbation susceptibility. It is possible that airway reflux may increase airway bacterial load in the lower airways with an increase in airway inflammation and, thus, an increase in susceptibility to frequent exacerbations.

Anti-reflux therapy in pulmonary fibrosis has been shown to be independently associated with prolonged survival.⁽¹¹⁾ However, a study in asthma showed no significant effect of the proton-pump inhibitor esomeprazole on poorly controlled asthma, though there was evidence of considerable asymptomatic GOR in asthmatic patients⁽¹²⁾ and in COPD patients.

Sasaki and colleagues reported that the proton-pump inhibitor lansoprazole reduced

exacerbation frequency, though this was in a 12-month, single-blind randomised study involving only 100 patients.⁽¹³⁾ Thus, there is a need for further well-designed studies of the therapy for GOR in COPD that are adequately powered for exacerbation reduction and with an appropriate intervention targeting the various types of reflux.

We now know that COPD is associated with complex co-morbidities and that GOR is common in COPD and is associated with a higher exacerbation frequency. Thus, GOR symptoms need to be recognised in COPD, as these patients will be most at risk of future exacerbations and their consequences. Further studies are now required to evaluate what the best intervention is to reduce GOR in COPD patients so that we can more effectively prevent exacerbations in these patients and improve their quality of life.

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