

COPD - is one exacerbation enough?

Chronic obstructive pulmonary disease (COPD) remains one of the most prevalent pulmonary diseases worldwide, causing significant morbidity and mortality. The recent GOLD guidelines have changed the classification of COPD from the previous ABCD system to an ABE classification, with the E category representing those with one severe exacerbation, or two or more moderate exacerbations.^[1] This is a clinically important threshold, as patients with category E disease are commonly given inhaled corticosteroid (ICS) therapy, while it is often withheld from category A and B patients. With the goal of examining the validity of this threshold, Vanfleteren and colleagues^[2] have recently published a nationwide cohort study based on over 45 000 patients in the Swedish National Airway Register. They divided the patients into the GOLD groups and added a 0 or a 1 for category A and B patients, with a 1 indicating that a patient had a prior moderate exacerbation and 0, none. The groups were followed up and exacerbation rates, hospitalisation, and mortality compared.

Perhaps predictably, hazard ratios for all these adverse events increased with increasing symptoms and exacerbations. These were only slightly attenuated when adjusted for age, sex, smoking status and FEV1. Notably, group A1 had a risk of moderate exacerbation that exceeded that of group B0, and compared with group A0, group A1 had a risk for a moderate exacerbation that was more than three-fold higher.

These findings suggest that moderate exacerbations in COPD have greater clinical importance than has hitherto been ascribed to them. Based on this data, it does appear that even a moderate exacerbation would warrant the initiation of ICS therapy. The benefits of triple therapy over dual therapy in reducing exacerbations in this population have been validated in two recent studies performed by Singh *et al.*^[3], and Halpin *et al.*^[4]

This recommendation gains strength as triple therapy has been shown not only to improve lung function and patient reported outcomes, but two recent randomised controlled trials (IMPACT- InforMing the Pathway of COPD Treatment and ETHOS- Efficacy and Safety of Triple Therapy in Obstructive Lung Disease) have shown a reduction in mortality, when compared with dual bronchodilators.^[5,6]

The use of ICS has always garnered some controversy especially with regards to the risk of pneumonia. However, confounding factors such as smoking, an altered respiratory microbiome, age and oral corticosteroids are seldom considered; hence, one must consider the attributable risk for pneumonia with ICS. In a reanalysis of clinical trials, this risk appears to be negligible: 0 - 3%.^[7] In the South African context, the risk of mycobacterial disease with concomitant ICS therapy also has to be considered. This appears to be low, but if there are leading symptoms, TB should be excluded.

It should be remembered that the benefits of ICS therapy both in terms of symptom control and mortality are likely greater in those with more severe disease. This study^[2] therefore, probably heralds a change in our thinking about the use of ICS in COPD patients with exacerbations, regardless of their GOLD grouping.

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