Inhaled therapies for chronic obstructive pulmonary disease and hospital admissions

An English retrospective cohort study suggests that increases in prescribing rates of inhaled long-acting muscarinic antagonists and combined inhaled long-acting beta-2 agonist and corticosteroid medicines are associated with an increase hospital admission rates in people with chronic obstructive pulmonary disease.

Overview: Chronic obstructive pulmonary disease (COPD) is characterised by airflow obstruction, which is usually progressive and not fully reversible (NICE 2010). It is predominantly caused by smoking. About 900,000 people in the UK have diagnosed COPD and an estimated 2 million people have COPD that remains undiagnosed. COPD produces symptoms, disability and impaired quality of life, which may respond to pharmacological and other therapies that have limited or no impact on their airflow obstruction. Exacerbations often occur, during which there is a rapid and sustained worsening of symptoms beyond normal day-to-day variations.

A meta-analysis by Van den Bruel at al. (2010) found that inhaled long-acting muscarinic antagonists (LAMAs) reduce COPD exacerbations, but it is less clear whether they reduce exacerbation-related hospital admissions. Similarly, a Cochrane review (Nannini et al. 2012) compared the combination of long-acting beta-2 agonist (LABA) and an inhaled corticosteroid (ICS) with a LABA alone and found that the combination reduces COPD exacerbations but not admissions. However, few studies have looked at how these findings translate to patients found in everyday practice who are not selected for trials.

Current advice: The NICE guideline on COPD advises that all people who are still smoking should be encouraged to stop, and offered help to do so, at every opportunity. Recommendations on inhaled treatments are summarised in the NICE Pathway on COPD. The key points are:

- Short-acting bronchodilators, as necessary, should be the initial empirical treatment for the relief of breathlessness and exercise limitation.
- A LAMA is an option for people with stable COPD who remain breathless or have exacerbations despite using short-acting bronchodilators as needed and in whom a decision has been made to commence regular maintenance bronchodilator therapy with a muscarinic antagonist.
- Either a LAMA or a combination inhaler containing a LABA+ICS should be offered if the person's forced expired volume in 1 second (FEV1) is less than 50% predicted.
- A LABA+ICS may also be considered in people with stable COPD and an FEV1 of 50% predicted or more who remain breathless or have exacerbations despite maintenance therapy with a LABA.
- A LAMA may be used with a LABA if an ICS (plus LABA) is declined or not tolerated.
New evidence: A retrospective cohort study by Harries et al. (2014) aimed to determine whether increasing rates of use of LAMA and LABA+ICS inhaled therapies in general practice in England were reflected in reduced rates of admissions for COPD.

Prescribing data were obtained from the NHS Business Services Authority (NHS BSA) to determine costs of dispensed prescriptions for LAMA and LABA+ICS inhaled therapies. The study investigators considered prescribing costs to be the best available estimate of prescribing volume. For LABA+ICS, prescribing volume would be affected by the actual item prescribed because costs of individual products vary. Information on hospital admissions for COPD was obtained from the NHS Information Centre Hospital Episodes Statistics database. The relationship between LAMA and LABA+ICS prescription costs per practice patient and the rate of people with COPD admitted per 10,000 practice patients was examined for the years 2007 to 2010.

Data were included from 806 practices (5.26 million patients) in 15 primary care trusts. The annual prescribing cost per practice patient for LAMAs increased by 60% from a mean of £1.81 in 2007 to £2.90 in 2010, while for LABA+ICSs costs increased by 26% from a mean of £7.87 in 2007 to £9.89 in 2010. The annual rate of people with COPD admitted to hospital increased by 17% from a mean of 15.7 per 10,000 practice patients in 2001 to 18.3 per 10,000 practice patients in 2010.

After adjusting for potential confounders including COPD prevalence, deprivation, Quality and Outcomes Framework (QOF) points and practice size, higher practice prescribing volumes of LAMAs and LABA+ICSs were found to be associated with higher practice admission rates for COPD.

Limitations to the study include analysis of data at practice rather than patient level, which meant individual patient factors such as disease severity could not be accounted for. In addition, data relate to prescriptions dispensed, and it is not known whether patients actually used their medicines. NHS BSA prescribing data cannot provide information on the indication for which inhaled therapies are being prescribed; therefore it is possible in some practices that the increasing rate of prescribing of LABA+ICSs could have been attributable to patients with asthma, not COPD.

Commentary: “This is a useful ‘real world’ study that attempts to examine what happens in real life patients rather than idealised study patients, who are carefully selected. The overall message is that despite increased prescribing of LAMAs and LABA+ICS combinations in primary care, the rate of COPD hospitalisations of patients from practices that are high prescribers of these medications has not reduced. The study was not designed to look at other potential beneficial outcomes such as quality of life or exacerbations that did not result in hospital admissions.

“LAMAs and LABA+ICS combinations are expensive medications, and currently a LABA+ICS combination and a LAMA are included in the top 5 most costly medications to the NHS (NHS BSA: personal communication 2014). In COPD, these medications have been shown to reduce exacerbations but not necessarily hospitalisations.

“The study is confounded by the fact that LABA+ICS combinations are also widely used in asthma. It is also possible that the high COPD admission rate seen in practices in the study that were high volume prescribers of LAMAs and LABA+ICSs was because these practices had a higher prevalence of people with more severe COPD who might be expected to experience more exacerbations.

“Until there is more evidence of real world efficacy, prescribers should continue to follow NICE guidance but individualise treatment according to the needs of the patient, with regular review of response to treatments.” – Dr Vincent Mak, Consultant Physician in Respiratory Integrated Care, Imperial College Healthcare and Central London Community Healthcare NHS Trusts; Clinical Director, Outer North West London Integrated Care Programme; and Member of NHS England (London Region) Respiratory Clinical Leadership Group – Lead in Medicines Management. Dr Mak has received honoraria for lecturing fees from AstraZeneca, GSK, Novartis and Almiral, and help with travel, accommodation, food and conference fees for international conferences from AstraZeneca, Boehringer Ingelheim and Almiral

Eyes on Evidence September 2014 2
Study sponsorship: No study funding declared.

About this article: This article appeared in the September 2014 issue of the Eyes on Evidence e-bulletin. This free monthly e-bulletin from NICE Evidence outlines interesting new evidence and what it means for current practice. They do not constitute formal NICE guidance. The opinions of contributors do not necessarily reflect the views of NICE.

To receive the Eyes on Evidence e-bulletin, please complete the online registration form.

Visit Evidence Search

Copyright © 2014 National Institute for Health and Care Excellence. All Rights Reserved.