Action

Health professionals should follow the BTS/SIGN guideline on the management of asthma. For patients not adequately controlled on a short-acting beta2-agonist when required (step 1), inhaled corticosteroids (ICSs) are the first-choice regular preventer therapy (step 2). A leukotriene receptor antagonist (LTRA, e.g. montelukast) may be considered in children younger than five years if an ICS cannot be used. A proportion of patients with asthma may not be adequately controlled on an ICS alone at step 2. For adults and children aged 5 to 12 years, the addition of a long-acting beta2-agonist (LABA, e.g. salmeterol or formoterol) to an ICS should be considered next (step 3). For children younger than five years, the first-choice add-on therapy to an ICS is a LTRA. However, before adding or changing treatment, practitioners should check adherence with existing therapy, check the patient’s inhaler technique and eliminate trigger factors.

What does this study claim?

This meta-analysis\(^1\) has found that inhaled corticosteroids are more effective than oral montelukast at preventing asthma exacerbations requiring systemic corticosteroids in school children and adolescents with mild to moderate asthma.

New guidance from NICE on heart failure and on COPD

NICE has updated its clinical guidelines for chronic heart failure\(^1\) and chronic obstructive pulmonary disease (COPD).\(^2\)

**Chronic heart failure**

This guidance (CG108) was published in August 2010. There are significant changes from the previous 2003 guidance in relation to:

- Diagnosis, including referral of people with suspected heart failure and previous myocardial infarction (MI) for transthoracic Doppler echocardiography, and measurement of serum natriuretic peptides in people without previous MI
- Pharmacological management of heart failure

The guideline recommends that both ACE inhibitors and beta-blockers licensed for heart failure should be considered as first-line treatments for patients with heart failure due to left ventricular systolic dysfunction, using clinical judgement to decide which drug to start first. The guidance also advises switching stable patients who are already taking a beta-blocker for a co-morbidity (for example, angina or hypertension) to one which is licensed for heart failure. There are also changes to the guidance on second-line drug therapy, which should be started only after specialist advice.

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\(^1\) Castro-Rodriguez JA, Rodrigo GJ. The role of inhaled corticosteroids and montelukast in children with mild-moderate asthma: results of a systematic review with meta-analysis. Arch Dis Child 2010;95:365–70

\(^2\) All information was correct at the time of publication (November 2010)
Are oral bisphosphonates associated with an increased risk of oesophageal cancer?

A UK case-control study suggests a small increased risk of oesophageal cancer (but not stomach or colorectal cancer) in people previously prescribed oral bisphosphonates. The increased risk equates to about one extra case of oesophageal cancer for every 2 cases per 1,000 population over a period of five years (0.5 cases per 1,000 women and 1.5 cases per 1,000 men). If these study results are true, these rates would be approximately doubled in users of bisphosphonates to 2 cases per 1,000 population aged 60–79 years over a period of five years (1 case per 1,000 women and 3 cases per 1,000 men).

Action

On the basis of this study, there is no need to change prescribing practice; the MHRA has issued detailed guidance. It is important that patients who are prescribed bisphosphonates are advised to follow carefully the instructions in the Patient Information Leaflet on how to take the medicine. Tablets should be taken on an empty stomach and swallowed whole with at least 200ml water immediately after getting up in the morning. Patients should remain fully upright for at least 30 or 60 minutes (depending on the particular preparation) after taking the tablet and before taking any food, drink or other medicine. Patients should be advised to report to their doctor any signs of oesophageal irritation such as difficulties or pain on swallowing, chest pain or heartburn. The safety of all bisphosphonates will continue to be monitored closely by the MHRA.

What does this study claim?

Following post-marketing reports of oesophageal cancer in association with oral bisphosphonate use, the MHRA, in conjunction with the Cancer Epidemiology Unit at the University of Oxford, conducted this nested case control study using a large cohort from the UK General Practice Research Database (GPRD).

Taking into account a number of confounding factors, the study identified a statistically significantly increased risk of oesophageal cancer (but not stomach or colorectal cancers) in individuals with prior prescriptions for oral bisphosphonates compared with those who had not been prescribed bisphosphonates (RR 1.30, 95%CI 1.02 to 1.66; P=0.02). The risk was significantly higher for those patients who used bisphosphonates for more than 3 years (on average about 5 years; RR 2.24, 95%CI 1.47 to 3.43 compared with no use) and for those who had 10 or more prescriptions for bisphosphonates. The incidence of oesophageal cancer in Europe and North America in people aged 60–79 years is about 1 case per 1,000 population over a period of five years (0.5 cases per 1,000 women and 1.5 cases per 1,000 men). If these study results are true, these rates would be approximately doubled in users of bisphosphonates to 2 cases per 1,000 population aged 60–79 years over a period of five years (1 case per 1,000 women and 3 cases per 1,000 men).

So what?

This study has a number of limitations which are discussed in MeReC Rapid Review No. 1880. In view of these, and the absence of supporting evidence from other studies, the MHRA considers that there is insufficient evidence to suggest a definite association between oral bisphosphonates and oesophageal cancer. The benefits of bisphosphonates are still considered to outweigh the risks, although as with all medicines, the safety of bisphosphonates will continue to be monitored. See the MHRA webpage for details.