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MeReC Publications

Inhaled corticosteroids more effective than oral montelukast in reducing asthma exacerbations in children

A 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.

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 of RCTs compared the efficacy of ICSs versus montelukast alone and montelukast added to an ICS in school children and adolescents with mild-moderate persistent asthma. It found that school children and adolescents taking ICSs (200–400 micrograms per day of beclometasone diproprionate or equivalent) had fewer asthma exacerbations requiring systemic corticosteroids compared with those taking montelukast (usually 5–10mg per day) (21.3% vs. 25.6%, respectively, number needed to treat to avoid one extra asthma exacerbation requiring systemic corticosteroids 24, 95% confidence interval [CI] 13 to 110; relative risk [RR] 0.83, 95%CI 0.72 to 0.96, P=0.01). Children taking ICSs also had better lung function and asthma control than children taking montelukast.

There was no significant difference in the number of patients experiencing exacerbations requiring systemic corticosteroids between the ICS group and the montelukast plus ICS group (RR 0.53, 95%CI 0.10 to 2.74, P=0.45). However, this result was based on only two studies, which had evidence of statistical heterogeneity.

See *MeReC Rapid Review No. 1862* and the asthma floor of NPCi for more details.

Reference

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

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.

All information was correct at the time of publication (November 2010)

For an overview of the recommendations see the quick reference guide, and for more detailed information see the guideline. To accompany the guideline, NICE has produced clinical case scenarios and a free on-line learning module in collaboration with BMJ Learning, particularly focused at primary care. More information on heart failure can also be found on the heart failure floor of NPCi, which will be updated in 2011.

Management of COPD

Updated NICE guidance was published in June 2010 (CG101). There are significant changes from the previous 2004 guidance on:

- Diagnosis, with the introduction of post-bronchodilator spirometry
- Assessment of severity: NICE classification now follows the GOLD classification, and the guidance now includes the use of the BODE index
- Inhaled therapy: this is substantially different from the previous guidance (see quick reference guide).

There are also additions and modifications to the guidance on oral therapy and pulmonary rehabilitation. For more detail of the recommendations see the guideline. We are reviewing our materials on the COPD floor of NPCi; these will be updated early in 2011.

References

1. NICE. Chronic heart failure: management of chronic heart failure in adults in primary and secondary care. Clinical guideline No. 108. August 2010
2. NICE. Chronic obstructive pulmonary disease: management of chronic obstructive pulmonary disease in adults in primary and secondary care (partial update). Clinical guideline No. 101. June 2010

Are oral bisphosphonates associated with an increased risk of oesophageal cancer?

A UK case-control study[1] 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 1,000 people aged 60–79 years who have taken bisphosphonates for five years. However, in view of the limitations of the study and evidence from other studies, the findings are not strong enough to suggest a definite association between oral bisphosphonates and oesophageal cancer.

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.

Reference

1. Green J, et al. Oral bisphosphonates and risk of cancer of oesophagus, stomach, and colorectum: case-control analysis within a UK primary care cohort. BMJ 2010; 341:c4444

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