National Prescribing Centre

MeReC Monthly

No. 26 May 2010

MeReC Publications

Cardiovascular safety of anticholinergics in COPD

A US cohort study in patients with COPD found an increased risk of cardiovascular (CV) events associated with the use of ipratropium within the past six months.[1] In contrast, a report from Boehringer Ingelheim's pooled safety database found tiotropium was associated with a statistically significant reduction in the risk of all-cause mortality, CV mortality and CV events.[2]

Action

CV safety concerns about ipratropium (and to a lesser extent tiotropium) come from observational studies and retrospective pooled analyses of data. These have inherent limitations and only flag up potential safety issues, not confirm them. The UPLIFT trial and the recent report from the tiotropium trial database[2] are somewhat reassuring about the safety of tiotropium. However, continued monitoring of both ipratropium and tiotropium is required.

Prescribers should continue to follow current NICE guidance on the management of patients with COPD, which is due to be updated in June 2010. When considering the use of an anticholinergic bronchodilator, choice in individual patients should take account of their response to a trial of the drug, the drug's side effects, patient preference and cost. These new safety data should feature in discussions, as well as the potential benefits from treatment. However, the optimal decision in individuals will probably depend more on how well they use the inhaler device, whether they can tolerate the medicine and how effective the medication is at controlling their symptoms. COPD is a heterogeneous disease that affects patients in different ways, and the management of an individual's disease should be guided, at least in part, by their symptoms and level of disability.

More details about the ipratropium study[1] and the tiotropium report,[2] and how they fit with what we already know about the safety of inhaled anticholinergics in COPD are available in MeReC Rapid Review Blog No. 1214. More information on COPD can be found on the COPD floor of NPCi and in MeReC Bulletin Volume 19, No. 4.

References

1. Ogale SS, et al. Cardiovascular events associated with ipratropium bromide in COPD. Chest 2010;137:13–19
2. Celli B, et al. Cardiovascular safety of tiotropium in patients with COPD. Chest 2010;137:20–30

Vitamin D alone may not prevent fractures

A meta-analysis found that daily calcium and vitamin D supplementation significantly reduced the overall risk of fracture across a wide age range of people, irrespective of sex or fracture history. In contrast, vitamin D alone in doses equivalent to 10 to 20 micrograms (400 to 800 units) per day did not prevent fractures.[1]

Action

Health professionals should follow the two NICE technology appraisals on the use of drugs for the primary and secondary prevention of osteoporotic fragility fractures in postmenopausal women with osteoporosis, and the NICE guideline on the assessment and prevention of falls in older people. The technology appraisals assume that women who receive drug treatment for osteoporotic fragility fractures have adequate calcium intake and are vitamin D replete. Unless clinicians are confident that women who receive treatment meet these criteria, calcium and/or vitamin D supplementation should be considered. There are a number of licensed preparations that supply the evidence-based doses of 1g per day for calcium (measured as elemental calcium) and around 20 micrograms (800 units) per day for vitamin D.

More details about this study, its implications and how it relates to other studies are available in MeReC Rapid Review Blog No. 1052. Information about the management of osteoporosis is available on NPCi.

Reference

1. The DIPART Group. Patient level pooled analysis of 68 500 patients from seven major vitamin D fracture trials in US and Europe. BMJ 2010;340:b5463

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

Does variation in blood pressure affect drug choice in hypertension?

We know already that raised blood pressure (BP) increases the risk of stroke. A recent study suggests that variation in BP is also an independent risk factor for stroke.[1] Two further studies suggest that thiazide (and thiazide-like) diuretics and calcium channel blockers (CCBs) may offer advantages over ACE inhibitors/ angiotensin-2 receptor antagonists (A2RAs) and beta-blockers for treating those with variable BP.[2,3]

Action

Health professionals should continue to follow NICE guidance on the management of hypertension. These studies should not change practice until the research has been considered by NICE and, if appropriate, alternative recommendations made for assessing BP (including assessment of variation) and/or drug treatments.

Reducing mean BP has an important role in reducing CV risk and this research does not challenge that. Clinicians should be aware, however, that wide variation in measurements from time to time or episodic high measurements might increase the risk of stroke, and that certain drugs might be more advantageous in this respect than others. Although the clinical significance of the differences over and above that achieved by BP reduction per se is not known, the studies suggest that diuretics and CCBs may be more effective than ACE inhibitors, A2RAs or beta-blockers in terms of their relative effects on BP variation.

The NICE guideline recommendation that thiazide-type diuretics or CCBs should be used first-line for most people (those over the age of 55 or black patients of any age) with uncomplicated hypertension remains appropriate. As we said in MeReC Bulletin Volume 17 No. 1, given that a choice has to be made, prescribers may decide to use diuretics preferentially in view of their lower acquisition costs, unless there are good reasons to do otherwise. NICE currently recommends ACE inhibitors (or A2RAs where not tolerated) for first-line treatment of patients under the age of 55 years. Beta-blockers, unless otherwise indicated (i.e. for conditions such as angina), are not appropriate first- or second-line antihypertensive choices.

For further information, including details of the studies[1,2,3] and their limitations see MeReC Rapid Review Blog No. 1149. See also the hypertension floor of NPCi.

References

1. Rothwell PM, et al. Prognostic significance of visit-to-visit variability, maximum systolic blood pressure, and episodic hypertension. Lancet 2010;375:895–905
2. Webb AJS, et al. Effects of antihypertensive-drug class on interindividual variation in blood pressure and risk of stroke: a systematic review and meta-analysis. Lancet 2010; 375:906–15
3. Rothwell PM, et al. Effects of β blockers and calcium-channel blockers on within-individual variability in blood pressure and risk of stroke. Lancet Neurol 2010;9:469–80

Uncomplicated UTI: don't routinely send urine for culture

A randomised controlled trial found that there was no advantage in routinely obtaining urine bacteriology to inform the treatment of acute uncomplicated urinary tract infections (UTIs) in adult, non-pregnant women. Using delayed antibiotics (to be taken after 48 hours if symptoms do not improve) or targeting antibiotics by dipstick results with delayed antibiotics as back-up were both effective in controlling symptoms overall compared to immediate antibiotics, and also reduced antibiotic use.[1]

Action

In accordance with advice from the Health Protection Agency (HPA), routine urine culture (midstream urine, MSU) is unnecessary in acute uncomplicated lower UTI. If a bacterial infection is likely (no vaginal discharge or irritation plus three or more symptoms of dysuria, urgency, frequency, polyuria, suprapubic tenderness or haematuria) then a strategy of immediate or delayed antibiotics (depending on patient preference) seems reasonable. The HPA recommends a three-day course of trimethoprim or nitrofurantoin for acute uncomplicated UTI in women, unless contraindicated.

If the diagnosis is in doubt, using dipsticks to guide treatment (including an option of back-up delayed antibiotics) can be helpful. It is important that women are offered explanation and reassurance, especially if a delayed antibiotic strategy is offered. Pyelonephritis, UTIs in men, the elderly, children or pregnant women, or recurrent UTIs require different management from acute uncomplicated UTIs in women.

For more details of this study[1] and three associated studies (an economic study, a qualitative study of women's attitudes and an observational study) see MeReC Rapid Review Blog No. 1118. More information on the management of acute uncomplicated UTI is available on NPCi.

Reference

1. Little P, et al. Effectiveness of five different approaches in management of urinary tract infection: randomised controlled trial. BMJ 2010;340:c199

The National Institute for Health and Clinical Excellence (NICE) is associated with MeReC Publications published by the NPC through a funding contract. This arrangement provides NICE with the ability to secure value for money in the use of NHS funds invested in its work and enables it to influence topic selection, methodology and dissemination practice. NICE considers the work of this organisation to be of value to the NHS in England and Wales and recommends that it be used to inform decisions on service organisation and delivery. This publication represents the views of the authors and not necessarily those of the Institute.

National Prescribing Centre, Ground Floor, Building 2000, Vortex Court, Enterprise Way, Wavertree Technology Park, Liverpool, L13 1FB
Tel: 0151 295 8691 Fax: 0151 220 4334 www.npc.co.uk www.npci.org.uk