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MeReC Publications

Ezetimibe: room for review?

A recent editorial[1] in the Drug and Therapeutics Bulletin questions whether adding ezetimibe to simvastatin provides good value for money. It also asks whether the increasing spend on ezetimibe (about £85million in primary care in England in the year to June 2010) is a rational use of NHS resources.

Action

Prescribers should review, and where appropriate, revise prescribing of ezetimibe to ensure it is in line with NICE guidance.

NICE guidance on lipid modification recommends use of simvastatin 40mg/day for secondary prevention of cardiovascular (CV) events and for primary prevention in adults who have a 20% or greater 10-year risk of developing CV disease. For secondary prevention, in patients without acute coronary syndrome (ACS), prescribers **should consider** increasing the dose of simvastatin to 80mg/day (or a drug of similar efficacy and acquisition cost) **only** in patients whose total cholesterol is greater than or equal to 4mmol/L **and also** whose LDL-cholesterol is greater than or equal to 2mmol/L. For a review of NICE lipid guidance, and the role of simvastatin 80mg in the light of recent MHRA advice, see *MeReC Rapid Review No. 1423*.

Ezetimibe has a limited role and is recommended as an option by NICE only for the treatment of adults with primary (heterozygous-familial or non-familial) hypercholesterolaemia and only in the following circumstances:

- where statins are contraindicated or not tolerated
- in conjunction with a statin where serum total or LDL-cholesterol is not appropriately controlled by initial statin therapy (after appropriate dose titration or because dose titration is limited by intolerance) and when consideration is being given to changing the initial statin therapy to an alternative statin.

Addition of ezetimibe to simvastatin 40mg increases the acquisition cost considerably over simvastatin 40mg and has not been demonstrated to improve patient-oriented outcomes. Evidence for efficacy of ezetimibe is based on surrogate outcomes (i.e. cholesterol lowering). There is no evidence to suggest its addition to simvastatin 40mg offers any improved tolerability over simvastatin 80mg or alternative NICE-recommended statins. See *MeReC Stop Press No. 1722*. More information on the management of lipids can be found on the cardiovascular disease – lipids floor of NPCi.

Reference

1. Anon. Money, money, money. DTB 2010;48:73

Calcium supplements without vitamin D may increase the risk of MI

A meta-analysis[1] found that calcium supplements without vitamin D increased the risk of myocardial infarction (MI) versus control by about 30% in relative terms, but did not find a statistically significant effect on risk of stroke or death. The analysis did not include studies of calcium plus vitamin D versus control; UK practice is usually to prescribe calcium with vitamin D, which limits the relevance of these new data.

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

Action

It is likely that the regulatory authorities will be considering this safety study. Until any advice is published, health professionals may wish to consider their prescribing of calcium alone taking into account:

- The safety concern from this study regarding calcium alone possibly increasing CV risk.
- The absence of information from this study about any increased CV risk from calcium plus vitamin D combinations, and the limited evidence that

suggests that addition of vitamin D may negate, or at least lessen, any harmful effects of calcium supplementation alone.
- The evidence that the combination of calcium 1000mg/day or greater plus vitamin D 800 units/day or greater is more effective than calcium alone in reducing the risk of falls and fracture.

The evidence and rationale supporting these points are discussed in *MeReC Rapid Review No. 1772*. In accordance with NICE guidance on primary and secondary prevention of osteoporosis, unless prescribers are confident that women who receive treatment (e.g. with bisphosphonates) have an adequate calcium intake and are vitamin D replete, they should consider calcium and/or vitamin D supplementation. More information on osteoporosis can be found on the relevant floor of NPCi.

Reference
1. Bolland MJ, et al. Effect of calcium supplements on risk of myocardial infarction and cardiovascular events: meta-analysis. BMJ 2010;341:c3691

First and second generation antipsychotics in early psychosis

A meta-analysis[1] found no significant differences between first generation (typical) antipsychotics (FGAs) and second generation (atypical) antipsychotics (SGAs) with regard to their effects on symptoms or discontinuation rates, when used to treat early psychosis. Patients taking SGAs gained more weight than those taking FGAs, whereas FGAs were associated with more extrapyramidal side effects than SGAs.

Action

Practitioners should follow NICE guidance on schizophrenia, which does not give preference to FGAs or SGAs in people with newly diagnosed schizophrenia. Rather, NICE advises that the antipsychotic should be chosen in partnership with the person (and carer if appropriate) taking into account the relative potential of individual antipsychotics to cause extrapyramidal side effects, metabolic side effects (such as weight gain), and other side effects.

A patient decision aid is available on the schizophrenia floor of NPCi, which includes a chart showing the relative side effect profiles of different antipsychotics. This may be helpful when considering which antipsychotic is most appropriate for a person to try first. In view of the substantial differences in acquisition costs of FGAs and SGAs, prescribers and prescribing managers may need to review their use of SGAs carefully and ensure that it is in line with NICE guidance. See *MeReC Rapid Review No. 1804*.

Reference
1. Crossley NA, et al. Efficacy of atypical v. typical antipsychotics in the treatment of early psychosis: meta-analysis. Br J Psychiatry 2010;196:434–9

HPA updates guidance on management of infections in primary care

The Health Protection Agency has updated its guidance[1] on management of common infections in primary care. The recommendations are in agreement with other guidance, including that from NICE, SIGN and CKS.

Action

This is a valuable guide to prescribers and is worth comparing with local policies and practice. Prescribing managers, microbiologists, local laboratories and other stakeholders should review this guidance and make any necessary adaptations to local policies.

All the recommendations are fully referenced and graded, and there are hyperlinks to further resources if more detail is needed. In addition, the rationale behind the recommendations and comments on the references are given, making this a very robust, evidence-based resource in this important area. See *MeReC Stop Press Blog No. 1796*. More information on antibiotic prescribing can be found on the common infections floors of NPCi.

Reference
1. Health Protection Agency. Management of infection guidance for primary care. For consultation & local adaptation. Latest Review March–July 2010

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