LOTHIAN PRESCRIBING BULLETIN

Supporting prescribing excellence - informing colleagues in primary and secondary care

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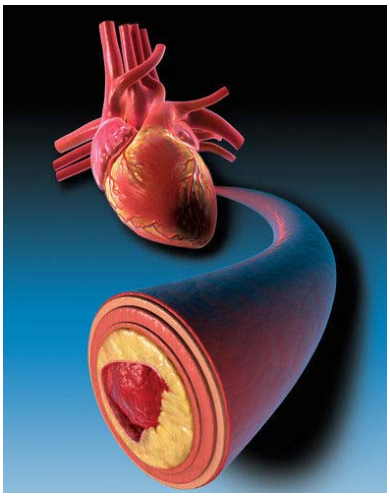
In this issue …

Ezetimibe on trial

Ezetimibe, a cholesterol absorption inhibitor, reduces levels of low-density lipoprotein when added to statin treatment. Despite this unique pharmacological effect ezetimibe clinical trials have demonstrated that it has no positive effect on patient outcomes.



The **ENHANCE**[1] trial, published in 2008, looked at the effect on carotid artery intimal thickness of adding ezetimibe to simvastatin. Participants with familial hypercholesterolaemia were randomised to simvastatin 80mg or simvastatin 80mg plus ezetimibe 10mg. There was no statistically significant difference in intimal thickness between the two groups after 24 months. Despite this, NICE 67[2] recommends considering the use of ezetimibe in patients with primary hypercholesterolaemia in line with NICE TA 132[3].

Also published in 2008, the **SEAS**[4] trial looked at whether a combination of ezetimibe 10mg and simvastatin 40mg prevented major cardiovascular events in patients with mild to moderate aortic stenosis when compared to placebo. The results showed no difference between the two groups in terms of incidence of major cardiovascular events (primary end-point) (confidence interval [CI] 0.83 to 1.12; p=0.59) or progression of aortic stenosis (secondary end-point) (CI 0.84 to 1.18; p=0.97).

The **SHARP**[5] trial was published in 2011. In this five-year trial patients with chronic kidney disease and no evidence of coronary heart disease were randomised to placebo or simvastatin 20mg plus ezetimibe 10mg. Within the treatment arm there was a reduction in major cardiovascular event compared with placebo (CI 0.74 to 0.94; p=0.0021). It is widely interpreted that this effect could have been due to the simvastatin alone.

The **IMPROVE-IT** trial is due to be published in June 2013. This phase three trial is looking at the effect of simvastatin 40mg plus ezetimibe 10mg compared with simvastatin 40mg in patients with stabilised acute coronary syndrome. Clinical benefit will be identified by a composite reduction in major cardiovascular event and mortality.

Lothian currently spends approximately £900,000 per annum on ezetimibe, although expenditure has gradually decreased over the last year, most likely driven by the Quality and Productivity prescribing Quality Outcomes Framework.

The Lothian Joint Formulary currently recommends that ezetimibe may be considered where a patient is intolerant of statins. It should not be used in combination with a statin.

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NO antibiotic for self-limiting respiratory tract infections

This third article on antimicrobial stewardship focuses on the management of self-limiting respiratory tract infections. For the majority of patients '*no antibiotic*' is the preferred treatment.

Acute sore throat

This illness lasts on average seven days and antibiotics reduce symptoms (pain) by 16 hours[1]. The Centor criteria are well recognised in identifying when a patient should be considered for an antibiotic:

- anterior lymphadenopathy
- absence of cough
- history of fever
- pustular exudate.

A score of three or more means that antibiotics are more likely to be beneficial and that Group A beta-haemolytic streptococci are more likely to be present (40% chance). Some clinicians may consider treating acute sore throats to prevent complications such as peritonsillar abscess (quinsy). The evidence suggests that there is little merit to this approach (number needed to treat (NNT) >4,000). However it is important to be aware that there is a small subgroup of patients at particular risk of quinsy, namely male smokers, aged between 21 and 40 years[2]. Using antibiotics has no effect on the incidence of glomerulonephritis[3] or the risk of developing rheumatic fever[4].

Acute rhinosinusitis

This illness may last up to three weeks, although 80% of people are better after 14 days with no antibiotics[5,6]. There is no benefit in giving antibiotics during the first week of the illness. If antibiotics are prescribed in the second week then there is a benefit, but only marginal. Unlike the other self-limiting conditions there are no clearly identifiable subgroups where antibiotics are more likely to be beneficial. Subgroup analysis does imply that those with purulent nasal discharge are more likely to benefit from antibiotics.

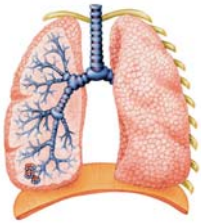
Acute otitis media

For 66% of children this illness lasts 24 hours. The majority will be better after four days. The use of antibiotics in these patients has a mild effect on reducing the duration of pain and does not prevent deafness. However, as with acute sore throat there is a subgroup of patients who are more likely to benefit from antibiotics[7]:

- Children under the age of two years with bilateral symptoms (NNT4)
- Children of any age with purulent discharge (NNT3).

Acute cough / bronchitis

This condition may last up to three weeks and antibiotics only have a minimal effect of reducing symptoms by one day[8]. For most patients it is a true self-limiting respiratory condition. However, for the over 65s there is an increased risk of complications such as community acquired pneumonia. There are no clear diagnostic criteria for identifying those of *over 65 years* with acute cough who are most likely to benefit from antibiotics, but the following modified **CRB-65** score[9] can be used:



- **C**onfusion (new)
- **R**espiratory rate >30/min
- **B**P systolic <90mmHg
- age > **65** years

Those scoring greater than one should be considered for admission to hospital and those scoring one should receive immediate antibiotics of optimal dose and duration.

NO antibiotic, continued …

Immediate antibiotics or hospital admission must be considered for the following conditions:

- √ **systemically very unwell**
- √ **serious diagnosis (pneumonia, mastoiditis, quinsy, intraorbital or intracerebral complications)**
- √ **co-morbidities (heart, lung, kidney, liver or neuromuscular disease)**
- √ **co-morbidities (immunosuppressed, cystic fibrosis, prematurity)**
- √ **over 65 years with *acute cough* plus two or more of: diabetes, recent hospital admission (<12 months), congestive heart failure, glucocorticoids**
- √ **over 80 years with acute cough with one of more of: diabetes, recent hospital admission (<12 months), congestive heart failure, glucocorticoids.**

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New contraindications and warning for aliskiren

Aliskiren (Rasilez®) is a direct renin inhibitor licensed for the treatment of essential hypertension. It is not recommended for use in NHS Scotland by the Scottish Medicines Consortium. ***(26 items prescribed in NHS Lothian in the last year.)***

The MHRA issued advice in December 2011 recommending routine (non-urgent) review for all patients taking aliskiren. The EMA have now finalised a review of aliskiren and have concluded that it should be contraindicated in patients with diabetes or moderate to severe renal impairment who take ACE inhibitors or ARBs. They also warn that the combination of aliskiren with ACEi or ARB is not recommended in other patient groups.

The data suggest a higher incidence of adverse outcomes (stroke, renal complications, hyperkalaemia and hypotension). Prescribers should note the following recommendations:

- Diabetic patients, or those with moderate to severe renal impairment, should not be prescribed aliskiren in combination with ACE inhibitors or ARBs
- All patients taking aliskiren should have a routine review of treatment at a non-urgent appointment and alternative treatments considered
- For all other patients the balance of risks and benefits, of taking aliskiren and a ACEi or ARB, should be considered.

Further details can be found on the EMA website.

New way of ordering wound dressings for care homes

As part of continuing work to improve compliance with the Wound Management Section of the Lothian Joint Formulary, a request form '*Care Home Dressing Prescription Request Form*' which contains LJF wound management products has been devised.

The form, which was approved by the General Practice Prescribing Committee, will be sent to all Care Homes in NHS Lothian. Care Homes will be expected to request dressings from GP practices using the form.

The form contains information on the sizes available for each dressing which should make it easier to ensure the correct product is prescribed. It will also highlight when a non-formulary product is being requested. It is hoped that the form will improve compliance to the Lothian Joint Formulary and in turn improve care to patients.

LJF latest updates www.ljf.scot.nhs.uk

Please see the LJF website for full advice; this is a summary of some of the changes.

Chapter 1 Gastro-intestinal system

1.2 Antispasmodics and other drugs altering gut motility

- Hyoscine butylbromide has been added as second choice antispasmodic.
- Domperidone is now first choice and metoclopramide second choice, motility stimulant. This is a switched positioning.
- The prescribing note on domperidone has been amended to include that treatment should be reviewed after 4 weeks.

1.3 Antisecretory drugs and mucosal protectants

- Prescribing notes have been added regarding when the use of esomeprazole may be appropriate.
- It is important to ensure that esomeprazole capsules rather than tablets are prescribed, to ensure the generic product is supplied.

1.4 Acute diarrhoea

- Prescribing note has been added as a reminder to prescribe loperamide capsules rather than tablets. Costs are £0.98/30 capsules or £2.15/30 tablets.

1.5 Chronic Bowel Disorders

- Pentasa® once daily is now the first choice product for maintenance treatment. Mezavant® XL is second choice, where patients have failed or not tolerated Pentasa®.

1.6 Laxatives

- Macrogol powder has replaced senna as second choice product for chromic constipation. Senna remains the first choice for new onset constipation.

Chapter 4 Central nervous system

4.10 (j) cigarette smoking

- Nicorette patches have been discontinued, so the formulary choice for a 16-hour patch is now Nicorette® Invisi
- Niquitin® minis lozenges are now the formulary lozenge choice
- An initial 2-week supply (rather than the previous 4 weeks) should be supplied.
- A repeat course within 6 months for unsuccessful quit attempts should not be prescribed, other than through the specialist stop smoking service.

Supplement: Recent SMC and Lothian Formulary Committee Recommendations

The supplement can be accessed via the LJF website www.ljf.scot.nhs.uk in 'Prescribing Bulletins'. See also New Drug Decisions on the Formulary Committee section of the LJF website.

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View the Lothian Joint Formulary at www.ljf.scot.nhs.uk