LOTHIAN PRESCRIBING BULLETIN

Supporting prescribing excellence - informing colleagues in primary and secondary care

Issue No. 40

August/September 2009

In this issue …

Antimicrobial prescribing quiz

Sore throats and delayed prescriptions… What do you think?

Why don't you take a few seconds to answer this quiz? Test your knowledge on the management of sore throats.

1. In studies of the impact of delayed prescriptions for sore throats, what percentage of patients did not collect or use their prescription?[1]
   A: 29% **B: 49%** **C: 69%**

2. In a randomised clinical trial (RCT) of antibiotics in sore throat, what effect did prescribing an antibiotic have on patients' intention to consult on future episodes?[1]
   A: reduced **B: no effect** **C: increased**

3. If treating a sore throat, by how many hours does an antibiotic reduce the duration of symptoms?[3]
   A: 8-16 hours **B: 24-36 hours** **C: 42-56 hours**

A couple of facts

- Most sore throats are due to viral infection; most patients do not benefit from antibiotics
- Sore throat resolves by one week in 85% of patients, whether due to streptococcal infection or not.[1]

Concerns continue about the inappropriate use of antibiotics in the management of acute upper respiratory tract infections. Consider issuing a delayed prescription, to be used after three days if symptoms are not starting to get better[1], and explain that soreness will take about eight days to resolve.[2] The delayed prescription can be given directly to the patient, or can be collected by the patient at a later date.

Prescribing strategies for sore throat [1]

Outcome Measure	Patients issued with:		
	10 day antibiotic Rx	No antibiotic Rx	Delayed Rx
Number of patients better by day three	No significant difference between the groups		
Duration of illness	4 days	5 days	5 days
Patient satisfaction with treatment	96%	90%	93%
Patients who thought antibiotics were effective	87%	54%	57%
Intend to come to doctor for future infections	79%	54%	57%
Return with sore throat within one year	38%	27%	27%

References

1. Sore throat. MeRec Bulletin 2006;*17*(3):13-4. National Prescribing Centre. www.npc.co.uk/ebt/merec/infect/commoneye/resources/merec_bulletin_vol17_no3_sore_throat.pdf.
2. Management of infection guidance for primary care. Amended 6 July 2009. Health Protection Agency & Association of Medical Microbiologists. www.hpa.org.uk/servlet/ContentServer?c=HPAweb_C&cid=1194947340160&pagename=HPAwebFile.
3. Del Mar, C.B., Glasziou, P.P. and Spinks, A.B. 2006. Antibiotics for sore throat (Cochrane Review). The Cochrane Library. Issue 4. John Wiley & Sons, Ltd. www.thecochranelibrary.com

ANSWERS: 1 C, 2 C, 3 A

Melatonin in children

Treatment of sleep-wake cycle disorders

Having granted a marketing authorisation for Circadin® 2mg tablet, the MHRA have imposed restrictions on the import of unlicensed melatonin products.

The melatonin shared care protocol (SCP) for treatment of sleep-wake cycle disorders in children now recommends:

First line - Bio-Melatonin® (3mg immediate release tablets)
Second line - Circadin® (2mg modified release tablets)

(This is an example of when brand name prescribing is recommended.)

Prolongevity® (3mg modified release capsules manufactured by Life Extension, USA) are no longer recommended.

Dosage and administration
Recommended starting dose:

Bio-Melatonin®: 3mg given 20 to 30 minutes before desired sleep time
Circadin®: 2mg 1 to 2 hours before desired sleep time

Immediate release preparation (Bio-Melatonin®) should be used initially. If the child is unable to swallow tablets, Bio-Melatonin® will dissolve in a small amount of water, if broken and stirred. For children who continue to have a fragmented sleep pattern after an initial two-week trial, consider using a sustained release preparation. The licensed modified release tablet Circadin® is the only preparation recommended for children requiring a modified release product. This should not be crushed as this destroys the matrix, but can be cut in half and swallowed without chewing.

Pharmacy issues
Bio-Melatonin® 3mg tablets, are available as an unlicensed medicine from Pharma Nord (UK) Ltd, telephone 01670 519989, fax 01670 534 903.

As all NHS Lothian prescribers are included in an agreement between Pharma Nord Ltd and the NHS Lothian Board Medical Director, orders from pharmacies do not require a pro-forma from the prescriber. All orders must be faxed, signed and include the pharmacist's registration number.

Circadin® 2mg modified release tablets, licensed product are available via usual wholesaler.

SCPs available at www.ljf.scot.nhs.uk/scp/index.html

Key messages:

- **New patients - Bio-Melatonin® is first choice**
- **Patients currently on immediate release Bio-Melatonin® or modified release Circadin® - continue with present regimen**
- **Patients on Prolongevity® - either switch to Circadin® or to Bio-Melatonin® if unable to swallow tablets whole.**

Thanks to Kirsten Thomson, Clinical Pharmacist, Royal Hospital for Sick Children and Claire Stein Primary Care Pharmacist, North East Edinburgh CHP for contributing to this article.

L-tryptophan for treatment-resistant depression – shared care protocol withdrawn

It has been agreed that a shared care protocol (SCP) for l-tryptophan (Optimax®) is no longer needed. An SCP had originally been required due to the potential risk of the fatal eosinophilia-myalgia syndrome (EMS) and the monitoring this entailed. The problem originated in 1986 when 26 people died of EMS having consumed a faulty batch containing the dimer di-tryptophan, the toxic substance.

Since monitoring was instigated no cases of EMS have been identified; the company dropped the need for registration and blood tests in 2005. However, the requirement remains in the Optimax® summary of product characteristics that treatment should only be initiated by hospital specialists before subsequent prescribing in primary care.

Thanks to Claire Stein, Primary Care Pharmacist, North East Edinburgh CHP.

Taking the heat out of depression

Almost 10% of adults of working age in Scotland take antidepressants on a daily basis. The Scottish Government has set a HEAT target to reduce the increase of antidepressant prescribing to zero by 2009/2010 (and then to reduce by 10% in subsequent years). It is recognised that there is no clear evidence that antidepressants are helpful in *mild* depression (NICE 2004[1]). Screening for depression is now being done routinely in most practices using a validated tool (typically the PHQ-9). This may help to assess the level of depression and the suitability of using non-pharmaceutical treatments. The Lothian Integrated Care Pathway for depression gives a framework of appropriate responses according to the assessment.

Information on alternatives (or additions) to prescribing for low mood, mild to moderate depression or anxiety are available.

Some useful sources can be found at:

- www.refhelp.scot.nhs.uk
- www.edspace.org.uk
- www.livinglifetothefull.com
- Stress control evening classes - delivered by NHS Lothian, in various locations across Edinburgh, telephone 0131 243 0106.

There are also pilot projects in several areas in Lothian using guided self help and exercise referral, developed in partnership with Health in Mind and Edinburgh Leisure. It is hoped that these will become available more widely over the next 12 months.

Reference
1. Depression. NICE Clinical Guideline CG23. December 2004. National Institute for Health and Clinical Excellence. www.nice.org.uk.

Thanks to Dr John Gordon, GP, Pentlands Medical Centre and Clinical Lead Mental Health Collaborative for Lothian.

Potential interaction between clopidogrel and PPIs

Clinical pharmacology

Clopidogrel is an inactive prodrug, and its active metabolite is formed by the hepatic cytochrome P450 2C19 isoenzyme. As a class, PPIs share many pharmacokinetic features, and in vitro studies have found that all 5 products licensed in the UK exhibit competitive inhibition for the same isoenzyme thereby reducing the rate of conversion of clopidogrel to it active metabolite. The affinity of different PPIs for the CYP2C19 isoenzyme varies so the magnitude of the interaction may differ, but there is insufficient evidence to show that any PPI is free from this potential hazard when co-prescribed with clopidogrel.

There may be more than one explanation for the effect of this class of medicines on clopidogrel.

Clinical trial evidence

There have been a number of reports of a clinically significant interaction between clopidogrel and PPIs. The studies are observational and have limitations, however the recent publications seem to have been designed appropriately and they attempt to account for the known biases and confounding factors.[1]

The largest study, the Clopidogrel Medco Outcomes Study[2] (16,690 patients) looked at clinical outcomes following coronary stenting - all patients were taking clopidogrel. The event rate for a composite risk of MI, stroke, unstable angina, or repeat revascularisation was:

- for clopidogrel users without concomitant PPIs (18%),
- for concomitant use of lansoprazole (24%), esomeprazole (25%), omeprazole (25%), and pantoprazole (29%).

All event rates were statistically significant compared with no PPI.

The EU Committee for Medicinal Products for Human Use (CHMP) have concluded that this data supports a clinically significant interaction that makes clopidogrel less effective when given with PPIs. The MHRA have recommended that product information for clopidogrel is amended to discourage concomitant use of a PPI and clopidogrel unless considered absolutely necessary.[1]

Recommendations

On the basis of pharmacokinetic data, other medicines for the treatment of gastrointestinal disorders (such as H_2 blockers or antacids) would not be expected to interact with clopidogrel. However, there are currently no substantial data from clinical-outcome studies.[1]

Key messages:

- **The need for PPI therapy in patients who are also taking clopidogrel should be reviewed at their next appointment: avoid concomitant use of these medicines unless considered essential**
- **The risks and benefits of gastroprotection should be fully considered. (See LJF section 1.3).**

References
1. MHRA Drug Safety Update. July 2009.
2. SCAI statement. 'The Clopidogrel MedcoOutcomes Study'. www.scai.org/drlt1.aspx?PAGE_ID=5870 (accessed July 9, 2009).

Thanks to Dr David Northridge, Consultant Cardiologist, Royal Infirmary of Edinburgh.

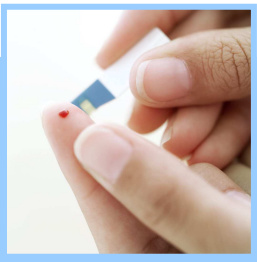
‘The Bottom Line’ No. 6 – Self-monitoring of blood glucose and type 2 diabetes

Earlier this year, NHS Quality Improvement Scotland produced an ‘Evidence Note’ in response to an enquiry from the Scottish Health Technologies Group.[1] The key points from this document , which focused on type 2 diabetes patients not treated with insulin, are as follows:

- Recent systematic reviews, pooling results from randomised controlled trials suggest a modest reduction of approximately 0.2% in HbA1c level in patients undertaking self-monitoring of blood glucose (SMBG) compared to no SMBG
- Interpretation of pooled effect estimates from these reviews is complicated by mixed methodological quality, differences in patient populations, implementation and frequency of SMBG and standard of care in control groups between trials
- Recently published high quality trials have demonstrated the lack of significant benefit of SMBG compared to standard care in certain patient groups
- Studies evaluating cost-effectiveness of SMBG compared to standard care have reported conflicting findings, which reflect different effectiveness data used in the calculations.

Key messages:

Recently published high quality trials have demonstrated the lack of significant benefit of SMBG compared to standard care in certain patient groups.



Lothian advice – So what do we recommend?

LJF section 6.1.6 Blood Glucose Monitoring – Key points

– Home blood glucose monitoring need not be performed by:
  * those treated by diet alone where HbA1c is <7%
  * those whose control is stable and appropriate for that patient as indicated by HbA1c
  * those treated by oral antidiabetes drugs, where hypoglycaemia is unlikely and control is appropriate.

  In these cases, a six-monthly estimate of HbA1c is adequate to monitor glycaemic control

– Home blood glucose monitoring in non-insulin treated Type 2 diabetes and steroid-induced diabetes should routinely be undertaken:
  * where control is poor
  * where treatment change is indicated, especially where there is a risk of hypoglycaemia
  * to monitor a treatment change
  * in patients on sulphonylureas with symptoms which may be due to unrecognised hypoglycaemia

  In such cases, blood glucose monitoring should not require to be performed routinely on more than two days in the week or more than twice in the day although in some cases more frequent testing may be required. The timing of the samples will depend on the particular case but a fasting value is useful.

Reference
1. Clinical and cost-effectiveness of self-monitoring of blood glucose (SMBG) for non-insulin treated type 2 diabetes. NHS Quality Improvement Scotland. Evidence Note No.26, January 2009. www.nhshealthquality.org/nhsqis/files/ClinicalGovernance_EN26ClinicalAndCostEffectivenessOfSMBG_JAN09.pdf

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