LOTHIAN PRESCRIBING BULLETIN

Supporting prescribing excellence - informing colleagues in primary and secondary care

Issue No. 69

September 2014

In this issue …

Statins – analysing evidence

A multicentre observational study, published in the BMJ in June 2014, confirms that the use of higher potency statins (≥ 10mg rosuvastatin; ≥ 20mg atorvastatin; ≥ 40mg simvastatin) is associated with a moderately increased rate of new onset diabetes.[1] It is thought that statins may impair pancreatic beta cell function. However, it has been calculated that 225 people have to be treated with a high potency statin over four years for one new case of diabetes mellitus.[2] This is in the context of five fewer cardiovascular events. Despite this new concern regarding the safety of statins a Cochrane review shows that statins are safe and well tolerated and patients are no more likely to stop taking them than a placebo.[3]

The newly published NICE guideline on lipid modification[4] suggests some fundamental changes to the existing recommendations for statin use:

- Consider primary prevention at the lower cardiovascular risk of 10% in 10 years (using QRISK2 score)
- Use atorvastatin 20mg for primary prevention with **no** lipid monitoring
- Use atorvastatin 80mg for secondary prevention with lipid monitoring

These recommendations are not based on new clinical studies, but from analysis of existing data.

With regards to the first recommendation, critics point out that statin trials have never used risk scoring as an enrolment criterion. [5] NICE now recommends atorvastatin as the first line agent due to its improved cost effectiveness with manufacturing patency expiry in 2012. NHS Lothian is continuing to use the ASSIGN risk calculator.

The key challenge for prescribers of statins for primary prevention will be using clinical judgement and giving patients the information to make informed choices. The numbers needed to treat (NNT) to prevent a major cardiovascular disease event for primary prevention may be of some help[6]:

- 30% 10 year CVD risk – NNT 25 over five years
- 20% 10 year CVD risk – NNT 37 over five years
- 10% 10 year CVD risk – NNT 74 over five years

Following patient selection the further challenge will be considering the appropriateness of prescribing a high potency statin (atorvastatin 20mg).

The NICE guideline[4] was informed by current medical evidence and medical economic analysis. It is likely to take some time to review how this should be used in Lothian and even longer for clinical practice to respond to these recommendations.

The MHRA recently provided safety advice regarding the risks and benefits of statin therapy, concluding that the benefits of using any statin in its licensed indication outweigh the risks in most patients.[7]

The LJF advice is currently being reviewed and any changes will need subsequent approval by the Formulary Committee.

References

1. Dormuth CR *et al.* Higher potency statins and the risk of new diabetes: multicentre, observational study of administrative databases. BMJ 2014;348:g3244 www.bmj.com/content/348/bmj.g3244
2. Huupponen R, Viikari J. Editorial. Statins and the risk of developing diabetes. BMJ 2013;346:f3156 www.bmj.com/content/346/bmj.f3156
3. Taylor F *et al.* Statins for the primary prevention of cardiovascular disease. The Cochrane Library. January 2013. DOI: 10.1002/14651858.CD004816.pub5. www.onlinelibrary.wiley.com
4. Lipid modification: cardiovascular risk assessment and the modification of blood lipids for the primary and secondary prevention of cardiovascular disease. NICE clinical guideline 181. National Institute for Health and Care Excellence. July 2014. www.nice.org.uk/Guidance/CG181
5. Editorial. Statins for millions more? The Lancet 2014;383 (9918):669. doi:10.1016/S0140-6736(14)60240-3. www.thelancet.com
6. Ebrahim S *et al.* Statins for the primary prevention of cardiovascular disease. BMJ 2014;348:g280. www.bmj.com/content/348/bmj.g280
7. Drug Safety Update volume 7 issue 10, May 2014: H1. Medicines and Healthcare products Regulatory Agency. www.mhra.gov.uk

Testing, eradicating and treating: changes in the LJF

Blood glucose testing strips

LJF advice for capillary blood glucose monitoring has been reviewed and amended. In contrast to the previous advice, the testing strips are detailed alongside the compatible meter. The testing strips can be prescribed and can also be purchased in a pharmacy. The meters are not available on prescription.

Patients with type I diabetes

	Test strip	Compatible meter
First choices	Freestyle Optium	Freestyle Optium Freestyle Optium Neo
	Glucomen LX Sensor	Glucomen LX Glucomen LX Plus
Second choice	As advised by specialist diabetes team	

Patients with type II diabetes treated with insulin

	Test strip	Compatible meter
First choices	Contour Next	Contour XT
	BGStar	BGStar iBGStar My Star Extra
Second choice	As advised by specialist diabetes team	

Patients with uncomplicated type II diabetes who require blood glucose monitoring

	Test strip	Compatible meter
First choice	CareSens N	CareSens N CareSens NPop CareSens Voice
Second choice	As advised by specialist diabetes team	

H. pylori eradication

First and second choice treatments for *H. pylori*-associated dyspepsia have been amended, based on Health Protection Agency guidance. Note eradication failure requires 14 days treatment.

First choice *(for 7 days treatment):*	
	omeprazole 20mg twice daily *or* **lansoprazole** 30mg twice daily
plus	**amoxicillin** 1g twice daily
plus, one of	**clarithromycin** 500mg twice daily (not if treated with macrolide for any infection within the past year)
	metronidazole 400mg twice daily (not if treated with metronidazole for any infection within the past year)
Second choice *for eradication failure (for 14 days treatment):*	
	omeprazole 20mg twice daily *or* **lansoprazole** 30mg twice daily
plus	**tripotassium dicitratibismuthate (De-Nol®)** 120mg four times daily
plus, two of	**amoxicillin** 1g twice daily
	metronidazole 400mg three times daily
	tetracycline 500mg four times daily

Irritable bowel syndrome

Some GPs will be interested to know that linaclotide is now approved for symptomatic treatment of moderate to severe irritable bowel syndrome with constipation. It should be initiated on specialist advice only and for use in patients who have not adequately responded to or cannot tolerate all other suitable treatment options.

Migraine management - not a headache

The Lothian Joint Formulary section on migraine management has been updated with changes made to the second choice medications for acute management, prophylaxis and cluster headaches. SIGN[1] and NICE[2] recommendations were taken into consideration. Current formulary choices are summarised below with recent *changes highlighted*.

Key Prescribing Points

Migraine treatment in adults

Acute Attack

Step 1: aspirin (900mg dose) or ibuprofen or paracetamol

- Opioid analgesics, including combination products, should not be routinely used for acute migraine, due to the potential for development of medication overuse headache.

Step 2: sumatriptan (1st choice) or *rizatriptan* (2nd choice)

- Use of triptans for more than 10 days/month should be avoided due to the risk of medication overuse headache.

Migraine Prophylaxis

LJF recommendations; propranolol (1st choice) or *topiramate* (2nd choice)

- Prophylaxis should be given for 3-4 months at optimum doses before effectiveness can be reviewed. If effective, continue for 4-6 months, and then consider gradual withdrawal.
- All women of child bearing potential should be advised of potential foetal malformations with migraine prophylactic medications. Ensure that risks during pregnancy are explained and the importance of adequate contraception.

Treatment of cluster headaches

All patients require specialist advice

Acute Attacks

sumatriptan subcutaneous (1st choice) or *zolmitriptan nasal* (2nd choice)

Prophylaxis

verapamil

A further dose of simple analgesia may be repeated after initial dose, however, if this is not adequate then consider moving to next step of treatment. Repeated doses of simple analgesia are not beneficial in treatment of migraine headache.

Medication overuse headache must be excluded in all patients with chronic daily headache (headache ≥15 days / month for >3 months). Clinicians should be aware that patients using any acute or symptomatic headache treatment are at risk of medication overuse headache. Patients with migraine, frequent headache and those using opioid-containing medications or overusing triptans are at most risk.[1]

It is good practice when initiating acute treatment for migraine that the risks of medication overuse headache are discussed with the patient. If overuse headache is suspected patients should be advised to abruptly withdraw the medication. If frequent headaches persist after symptomatic medications have been withdrawn, prophylactic agents may be effective and should be considered.[1]

Prophylactic migraine treatment can be considered in patients with attacks occurring more than twice per month, or when less frequent attacks are particularly severe and prolonged and interfere with daily routine.

References:

1. Diagnosis and management of headache in adults. Clinical Guideline 107. Scottish Intercollegiate Guidelines Network. November 2008. www.sign.ac.uk
2. Diagnosis and management of headaches in young people and adults. Clinical Guideline 150. National Institute for Health and Care Excellence. September 2012. www.nice.org.uk

Thanks to Ms Hazel Garven, Prescribing Support Pharmacist, for contributing this article.

Rivaroxaban now an option for first DVT

***A** new Lothian-wide DVT pathway was approved by the Thrombosis Committee in May and includes rivaroxaban as a treatment option. Rivaroxaban can now be used instead of warfarin and low molecular weight heparin (LMWH) for the treatment of DVT in adult patients (>18 years old) who meet the selection criteria. However, patients who are currently on warfarin or LMWH should not be switched to rivaroxaban.*

Rivaroxaban is restricted for use in patients with clear precipitating risk factors deemed to require three to six months of anticoagulation and is not on the formulary for long-term use.

The first three weeks of treatment (15mg twice daily) will be initiated and supplied in secondary care and day 22 onwards will be prescribed in primary care.

All patients will be counselled on rivaroxaban in secondary care, supplied with a patient alert card, a patient information leaflet and a letter for their GP.

During the first three weeks if a patient misses one 15mg dose, the patient should take a dose of 15mg immediately to ensure intake of 30mg per day. 30mg can be taken as a single dose if required. Continue with the regular 15mg twice daily on the following day.

A protocol for the use of rivaroxaban in pulmonary embolism is awaiting approval by the drug and therapeutics committee.

Selection criteria

- ✓ First DVT with a **clear precipitant,** e.g. plaster immobilisation
- ✓ Not pregnant or breast feeding
- ✓ Normal renal function
- ✓ No bleeding disorder or increased risk of bleeding
- ✓ No liver disease with cirrhosis and/or coagulopathy
- ✓ Not taking the following medications
  - Triazole and imidazole antifungals (except fluconazole)
  - Protease inhibitors (HIV and HCV antivirals)
  - Strong CYP3A4 inducers (e.g. rifampicin, phenytoin, carbamazepine)
- ✓ Patient understands and agrees to treatment having received explanation of risks [bleeding, haematuria, lack of reversal agent, etc.] and that there is an option of starting warfarin instead
- ✓ Anticipated duration of treatment is three to six months.

Key messages

- **Rivaroxaban can be used instead of warfarin and LMWH as a first line treatment of DVT in patients meeting patient selection criteria.**
- **Rivaroxaban is restricted for use in patients with clear precipitating risk factors deemed to require three to six months of anticoagulation and is not for long-term use or recurrent DVT.**
- **There is no specific antidote for reversal. Contact haematology for advice if bleeding develops. Management in the event of bleeding is mainly supportive care until the drug effect wears off.**

Thanks to Dr Ross Murphy, Consultant Acute Medical Unit and Karen Reid, Lead Pharmacist, for contributing this article.

Supplement: Recent SMC and Lothian Formulary Committee Recommendations

The supplements can be accessed via the LJF website www.ljf.scot.nhs.uk in 'Prescribing Bulletins'.

Correspondence address:
Medicines Management Team (MMT)
Pentland House
47 Robb's Loan
Edinburgh
EH14 1TY Tel: 0131 537 8461
Email: prescribing@nhslothian.scot.nhs.uk