LOTHIAN PRESCRIBING BULLETIN

Supporting prescribing excellence - informing colleagues in primary and secondary care

NHS Lothian

In this issue …

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Analgesia - increasingly topical

With the increasing number of frail and elderly patients, there is a renewed interest in the place that topical NSAIDs might have in the treatment pathway. The use of topical NSAIDs for pain relief was controversial due to the belief that they are no more effective than placebo, and that they may result in the gastrointestinal and cardiovascular side-effects associated with systemic NSAIDs.

A systematic review[1] demonstrated that topical NSAIDs provide good levels of pain relief for acute conditions such as strains and overuse injuries, similar to that provided by oral NSAIDs. Topical diclofenac, ibuprofen, ketoprofen, piroxicam and indomethacin all demonstrate at least a 50% reduction in pain, when compared to placebo in good quality randomised controlled trials. Reported NNT (number needed to treat) ranged from 1.8 to 3.9, which are considered to be low. Any local skin reactions were generally mild and transient, and did not differ from placebo. There were very few systemic adverse events or withdrawals due to adverse events.

Further studies demonstrate that in the management of osteoarthritis topical NSAIDs can be as effective as oral NSAIDs with far fewer systemic adverse events.[2] This is of particular interest in the context of oral NSAIDs triggering acute kidney injury, especially for patients experiencing a dehydrating illness, or those on other renal-toxic medications such as diuretics and ACE/ARB inhibitors. It is well recognised that frail patients are at far greater risk of these effects. The additional need for PPI cover with oral NSAIDs is not required for topical NSAIDs.

LJF Choice

Ibuprofen 5% gel is currently included in the LJF as it is the least expensive and the NNTs for topical NSAIDs were all low. Clinicians are asked to consider altering their existing practice in order to increase its use for appropriate patients. www.ljf.scot.nhs.uk/LothianJointFormularies/Adult/10.0/10.3/Pages/default.aspx

References

1 Topical NSAIDs for acute musculoskeletal pain in adults. Cochrane Review June 2015

2 Topical NSAID Therapy for Musculoskeletal Pain. Simon Haroutiunian S et al, MSc Daniel A Drennan, MD Arthur G. Lipman, PharmD *Pain Medicine*, Volume 11, Issue 4, 1 April 2010, Pages 535–549, https://doi.org/10.1111/j.1526-4637.2010.00809.x

Single National Formulary

The Scottish Government has committed to establish a Single National Formulary (SNF). The delivery of the SNF is being led by the Effective Prescribing & Therapeutics Branch of the Scottish Government.

The SNF will apply to medicines across primary and secondary care and focus on the areas of greatest medicines use. The development of the formulary will be clinically led, considering effectiveness, safety and cost.

It is anticipated that the initial therapeutic areas developed will be published in Spring 2018.

There is a page on the Effective Prescribing & Therapeutics Branch website providing updates on the project http://www.therapeutics.scot.nhs.uk/snf/

Gabapentin drug safety

We would like to draw attention to the MHRA Drug Safety Update released in October 2017. A previous link has been established with concomitant use of opioid medication and gabapentin causing symptoms of CNS depression. Patients should be carefully monitored when using these medications together. A recent review has now shown a rare association with gabapentin causing severe respiratory depression even without concomitant opioid prescribing.

The MHRA advise health professionals to be aware of this risk and consider whether dose adjustments may be necessary in patients at higher risk of respiratory depression, for example

- elderly people
- compromised respiratory function
- respiratory or neurological disease
- renal impairment
- patients taking other CNS depressants.

The patient information leaflet included with the medication is being updated to include this warning.

NHS Lothian Guidelines: hypertension, hyperlipidaemia and hypertriglyceridaemia

The hypertension, hyperlipidaemia and hypertriglyceridaemia guidelines have all been updated. You can view the full guidelines by following the links in the boxes below. Some of the changes are summarised in this article.

- weekly alcohol limit reduced to 14 units for both men and women
- atorvastatin now recommended as first-line statin of choice (patients who are clinically stable on simvastatin should not be switched to atorvastatin unnecessarily, as per Lothian Joint Formulary)
- continue to use full liver function testing to quantify baseline liver function prior to initiating statin treatment but not again unless clinically indicated; when monitoring statin treatment effect on liver function at 3 and 12 months after initiating therapy, measuring ALT alone is sufficient. Standalone ALT tests are now available.

Lothian Hypertension Guidelines 2017

In step 4 of 'drug choice' section, atenolol and bisoprolol now both recommended as β-blockers for the management of hypertension (4th line agents)

Lothian Lipid Management in Adults Guideline November 2017

ASSIGN is the preferred calculator in Scotland. QRISK2 is an alternative.
The QRISK2 calculator can be used to undertake cardiovascular risk assessment in type 2 diabetes but risk calculators are not needed to assess cardiovascular risk in type 1 diabetes, chronic kidney disease or familial hypercholesterolemia.

Lothian Primary Care Summary Guidance for the Investigation & Management of Hypertriglyceridaemia November 2017

If triglycerides are initially found to be raised, these should be repeated after 1-2 weeks to confirm levels before deciding on management. Repeat samples need to be taken when fasting.

Anticholinergics: an update on choice and side-effects

The LJF choices for urinary frequency due to bladder instability have been revised. This follows a review by the Medicines Management Team looking at formulary compliance in primary care. Tolterodine is now first choice, with solifenacin second line and fesoterodine third line. Previously, treatment options were not ranked despite significant cost differences.

Side effects of anticholinergic drugs

Medicines with anticholinergic properties are prescribed for a wide variety of conditions and are linked to impaired cognition and risk of falls. More recently they have also been linked to increased morbidity and mortality. [1]

They continue to be commonly prescribed to older people, including those with early stage dementia or mild cognitive impairment, who are particularly susceptible to adverse effects even at therapeutic doses. [1]

Five distinct muscarinic receptor subtypes are known to exist and all are present in the brain. The effect of anticholinergics on the central nervous system depends on their ability to penetrate the blood-brain barrier (BBB) and thus their activity in the brain.

Not all individual drugs with anticholinergic properties put patients at risk of severe adverse effects. However, combining medications with anticholinergic activity may have harmful effects when given to a person with more than one clinical condition.

A scale or table that lists the anticholinergic activity of commonly prescribed drugs can guide clinical decision-making to limit anticholinergic load. One such tool is the Anticholinergic Risk Scale (ARS), which was developed using 500 most prescribed medicines[2]. If there is concern about cognitive impairment with anticholinergic medicines, an alternative anticholinergic medicine that is less likely to cross the BBB with a lower rating on the ARS scale may be considered.

The Scottish Government Polypharmacy guidance[1] includes a table with modified ARS. See below.

References

1 Scottish Government Model of Care Polypharmacy Working Group. Polypharmacy Guidance (2nd edition). March 2015. Scottish Government

2 Sumukadas D, et al. Temporal trends in anticholinergic medication prescription in older people: repeated cross-sectional analysis of population prescribing data. *Age and Ageing* 2014 July 1, 2014;43(4):515-21. https://academic.oup.com/ageing/article/43/4/515/15

mARS category: **1** - *Moderate*; **2** - *Strong*; **3** - *Very strong potential* (of anticholinergic side effects)

mARS category 3	mARS category 2	mARS category 1	Guidance
Antidepressants			
amitriptyline, imipramine	desipramine, trimipramine nortriptyline, clomipramine sertaline	trazodone, mirtazapine, paroxetine, lofepramine	venlafaxine, duloxetine, buproprion and trazodone have low-to-nil systemic anticholinergic activity.
Antipsychotics			
thioridazine, fluphenazine perphanazine, chlorphenamine, chlorpromazine, promethazine and trifluorperazine	clozapine, doxepine, olanzapine, levomepromazine, pericyazine	quetiapine, risperidone and halperidol	Avoid phenothiazines Among atypical antipsychotics, aripiprazole and ziprasidone are the least anticholinergic
Nausea and vertigo			
	prochlorperazine	metoclopramide	domperidone (antiemetic) does not penetrate CNS
Urinary antispasmodics			
oxybutynin	fesoterodine, flavoxate, darifenacin, trospium, dosulepin, solifenacin, tolterodine		
Sedatives			
clemastine, hydroxyzine and cyproheptadine			Avoid antihistamine sedatives
Antiallergics			
	cetirizine, loratadine		desloratadine may be an alternative
H2 blockers			
	cimetidine	ranitidine	PPIs may be an alternative
Antiparkinson			
procyclidine and benzatropine	amantadine	levodopa/carbidopa, selegeline, entacapone and pramipexole	
Others			
atropine, dicyclomine, orphenadrine and tizanidine	loperamide, tiotropium, pseudoephedrine, baclofen and propiverine	methocarbamol and reboxetine	

Hepatitis C: curing the incurable?

Hepatitis C is now a recognised curable disease, using all oral Direct Acting Antiviral interferon-free regimens. Clinical trial and real world data sets show a sustained viral response rates of >90%, which equates to cure for this episode of infection. Treatment choices are guided by the National Clinical Guidelines for the treatment of HCV and the majority are 2-3 months in length and are very well tolerated. Local cure rate to date with these regimens has been >90% and all patients with chronic hepatitis C are eligible for consideration of treatment. Any new patient diagnosed with hepatitis C, any patient who failed treatment in the past and any patients not previously treated should be referred in for the new treatments.

Treatment is led by specialist services at either; Regional Infectious Diseases Unit, Western General Hospital or Liver Unit, Royal Infirmary of Edinburgh and all medicines are prescribed by secondary care and supplied via local community pharmacy.

Drug-Drug Interactions (DDI)

Prior to starting HCV treatment, a drug history is taken for all patients and advice is given to both patient and prescriber for any potential DDI. Patients are advised to alert the team if starting any new medicines, including OTC and herbal remedies. Commonly prescribed medicines which have DDI potential are

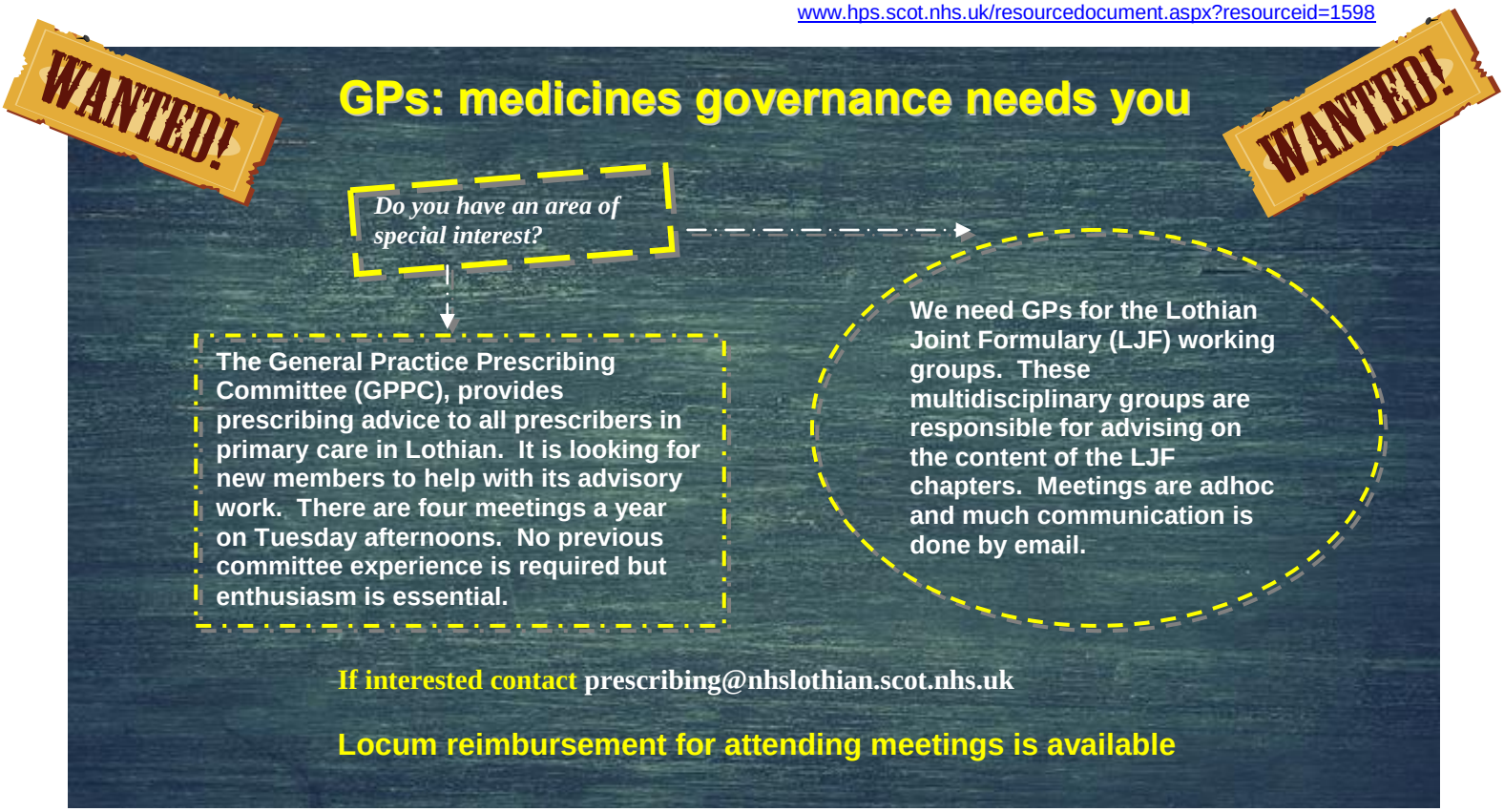
- statins
- drugs that alter gastric pH such as PPI and antacids
- contraceptives
- carbamazepine and phenytoin.

GP and other prescribers should be alert to the potential for DDI. The University of Liverpool DDI website www.hep-druginteractions.org/ is a comprehensive database containing over 700 medicines.

If there are any queries please do not hesitate to contact the specialist team.

References

1. National Clinical Guidelines for the treatment of HCV
www.hps.scot.nhs.uk/resourcedocument.aspx?resourceid=1598



Supplements:
Recent SMC and Lothian Formulary Committee Recommendations
The supplements can be accessed via the LJF website www.ljf.scot.nhs.uk in 'Prescribing Bulletins'.

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