Hot Topics October 2017

Prescribing....

- A good quality randomised controlled study conducted in the USA has reported that the self-monitoring of blood glucose (SMBG) added nothing to HbA_{1c} levels or to key adverse events in non-insulin treated Type 2 diabetes.
- Nefopam is a centrally-acting analgesic, but the evidence to support its use has been described by Cochrane as "poor".
- There has been a very significant reduction in the prescribing of Lidocaine Plasters since restrictions were introduced on August 1st 2017.

1. Value of SMBG in non-insulin treated type 2 diabetes.

The value of self-monitoring of blood glucose (SMBG) levels in patients with non-insulin-treated type 2 diabetes in primary care has been assessed in an open-label randomised trial of 450 American patients. This was a publically-funded study which is less likely to be biased than if it was industry-sponsored. The study's authors suggest that more than 75% of patients in this group regularly perform SMBG, despite conflicting results from studies on whether it improves outcomes. The trial's two primary outcomes were improvement in glycated haemoglobin (HbA1c) level and health-related quality of life (HRQOL). Patients with type 2 non-insulin-treated diabetes eligible for the study were aged older than 30 years and had HbA1c levels higher than 6.5% (48mmol/mol) but lower than 9.5% (80mmol/mol) within the 6 months before screening. A total of 450 patients in North Carolina, USA, were randomised to one of three interventions:

- No SMBG
- Standard once-daily SMBG consisting of glucose values immediately reported to the patient through the blood glucose meter
- Enhanced once-daily SMBG consisting of glucose values immediately reported to the patient plus automated, tailored messages. The messaging algorithm accounted for blood glucose value, time of day and relationship to food intake. Messages were intended to educate and motivate.

Patients were followed up for a mean of 52 weeks. Compliance dropped consistently in both SMBG groups, with a larger initial decrease after 1 month in the SMBG with messaging arm. A total of 418 (93%) patients completed the final practice visit. The authors found no significant differences in HbA1c levels or HRQOL across all three groups. There were no notable differences in key adverse events, including hypoglycaemia frequency, health care use or insulin initiation.

The place of SMBG in people with non-insulin-treated type 2 diabetes has long been questioned and this study should provide reassurance that it is not routinely warranted. The cost of monitoring products had become a major issue for healthcare providers, leading to restrictions being placed on self-monitoring. Although there are benefits for some people with type 2 diabetes, for others routine SMBG offers little advantage. Current advice from the National Institute for Health and Care Excellence is not to routinely offer SMBG for adults with type 2 diabetes **unless the person is on insulin**, or there is evidence of **hypoglycaemic episodes**, or the person is on **oral medication that may increase their risk of hypoglycaemia while driving or operating machinery** or the person is **pregnant** or is **planning to become pregnant**.

2. Nefopam

Nefopam hydrochloride is a non-opioid analgesic considered to act centrally, although its mechanism of action is unclear. It also has some antimuscarinic and sympathomimetic actions. Nefopam Hydrochloride is indicated for the relief of acute and chronic pain, including post-operative pain, dental pain, musculoskeletal pain, acute traumatic pain and cancer pain. It may have a place in the relief of persistent pain unresponsive to other non-opioid analgesics. Unlike opiates, nefopam causes little or no respiratory depression. Common side effects include: nausea, nervousness, urinary retention, dry mouth and

light-headedness. As with other drugs with anticholinergic properties, confusion and urinary retention can be a problem in the elderly. Nefopam may interfere with some screening tests for benzodiazepines and opioids. These tests for benzodiazepines and opioids may give false positive results for patients taking nefopam.
Nefopam can be fatal in overdose. Clinical features may include convulsions, hallucinations, agitation and tachycardia. All patients who have taken a deliberate overdose should be referred for assessment.

There is very limited evidence is available for the effectiveness of nefopam in the treatment of persistent or chronic pain. Most published guidelines and reviews refer to the use of nefopam in the treatment of postoperative or acute pain.

In December 2013, a SIGN guideline titled "Management of Chronic Pain" identified insufficient evidence on the use of nefopam for chronic pain relief to support a recommendation. The authors recommended NSAIDs, COX inhibitors, and paracetamol before nefopam for patients with chronic non-malignant pain.

Similarly a Cochrane Review titled "Single dose oral nefopam for acute postoperative pain in adults" found that there was an absence of evidence of efficacy and its use in this indication is not justified. Because trials clearly demonstrating analgesic efficacy in the most basic of acute pain studies are lacking, use in other indications should be evaluated carefully.

A Cochrane Review, titled "Neuromodulators for pain management in rheumatoid arthritis", concluded that based on 3 small trials, which were all at high risk of bias, there is weak evidence that nefopam and capsaicin are superior to placebo in reducing pain in patients with RA, but both are associated with a significant side effect profile. The implications for practice were that with many other safer analgesics available on the market today and no head-to-head trials suggesting superior efficacy, the review does not support the use of nefopam in patients with RA.

A further Cochrane Review titled "Single dose oral analgesics for acute postoperative pain in adults" found no trial data for reviews of nefopam but good evidence for a number of analgesics including NSAIDs, COX inhibitors, and combination analgesics.

The Regional Drug & Therapeutics Centre in Newcastle have produced a bulletin on nefopam highlighting safety issues and place in therapy. They recommend that prescribers be aware of the risks associated with nefopam and assess whether potential benefits outweigh risks in individual patients.

3. Lidocaine 5% Plasters

Since August 1st 2017 Lidocaine Plasters have been locally restricted to either their licensed indications i.e. post herpetic neuralgia or for Pain Clinic initiation for peripheral neuropathic pain. These plasters are one of a number of products considered to be high cost and low or no value by the UK government which may be removed from NHS prescribing. There are also significant restrictions on their use in Southern Ireland where one three month course per patient for post herpetic neuralgia only is publically funded.

In mid-2016 there were on average 169 prescriptions dispensed per month at an eye-watering cost of £14,182 per month plus fees. In August 2017 there were 59 prescriptions dispensed at a cost of £5,419. Many thanks to medical and pharmacy colleagues who have reviewed and supported their patients . It is obviously important that this work continues and that patients with on these plasters PHN are reviewed regularly and stopped. The summary of product characteristics states that
" *Treatment outcome should be re-evaluated after 2-4 weeks. If there has been no response to Versatis after this period (during the wearing time and/or during the plaster-free interval), treatment must be discontinued as potential risks may outweigh benefits in this context. Long-term use of Versatis in clinical studies showed that the number of plasters used decreased over time. Therefore treatment should be reassessed at regular intervals to decide whether the amount of plasters needed to cover the painful area can be reduced, or if the plaster-free period can be extended".*

At the time of writing it is not known what will happen with these products in the UK. However the influential Community Pharmacists' body the PSNC is advising the DoH to consider blacklisting as opposed to restricting the products on the list.

References : JAMA Intern Med 2017; 177, UKMI QA Nefopam July 2017, EPACT.net, Medicines.org , BNF no 74
Written by : Geraldine O'Riordan, Prescribing Advisor, Edward T Wheadon House , Le Truchot St Peter Port , GY1 3WH
Tel: 01481 732460