PAIN MANAGEMENT: PART 1

Four experts on pain medicine answer readers' questions on this ubiquitous area of general practice

Dr Marcia Schofield
Senior Lecturer in Pain Management, Cardiff

Dr Ashish Shetty
Consultant in Pain Medicine, University College London Hospitals

Dr Michael Spencer
Consultant Psychiatrist, Cambridge and London

Dr Rajesh Munglani
Consultant in Pain Medicine, Cambridge and London

Q What is the latest evidence on NSAIDS and risk of gastrointestinal adverse events?

A All non-selective NSAIDs increase the risk of gastrointestinal bleeding and ulcers. Celecoxib is gastroprotective in the short term. To prevent serious gastrointestinal complications, adding an anti-ulcer drug like misoprostol to non-selective NSAIDs or taking celecoxib are known to have short-term advantages.

There appears to be no difference between different NSAIDs when taken in combination with an anti-ulcer drugs, e.g. a proton pump inhibitor (PPI) or misoprostol, in reducing less severe complications, such as ulcers only discovered on endoscopy. In patients with a history of GI bleed the combination of celecoxib with a PPI is recommended. In elderly patients the available evidence suggests that there may be lower risk of serious gastrointestinal, cardiovascular and renal complications with celecoxib compared with diclofenac of ibuprofen.

In general, minimising the impact of other risk factors, such as *Helicobacter pylori* infection and concomitant peptic ulcer disease, as well as use of drugs like corticosteroids and anticoagulants, should be considered in all patients. For instance, studies (Leontiadis *et al*) have found that eradication of *H. pylori* in patients over the age of 50 years has been found to be most cost-effective strategy for primary prevention of NSAID-associated ulcers.

Q Is there still any role for COX-2 inhibitors?

A There is certainly a use for COX-2 inhibitors.

COX-2 inhibitors are a form of NSAIDs which inhibit COX-2 enzymes responsible for inflammation and pain. The advantage of using this class of drug is a reduced risk of peptic ulceration. The COX-2 inhibitor rofecoxib was taken off the market in 2004. This was a result of a particularly large increase in risk of myocardial infarction (MI) and cerebrovascular accidents (CVAs) associated with use of this agent. This adverse effect has now been shown to occur with other non-selective NSAIDS, though to a lesser degree. The prescription of any NSAID is therefore associated with an increased risk of cardiovascular events, both fatal and non-fatal, particularly in those with a previous history of MI.

COX-2 inhibitors are routinely used in the postoperative period for treating acute pain following surgery. In managing chronic pain, it is used in patients with inflammatory conditions with caution, and many would suggest using alternative therapy such as moderate strength opioids.

However, we have used COX-2s in patients in whom even low dose codeine causes excessive nausea or constipation and of course those in whom opioid medication is ineffective. Counselling the patient is very important. Although topical NSAIDs are much maligned, they can and do help some patients without the risks of systemic NSAIDs, although evidence for a significant effect of topical NSAIDs over placebo is lacking in larger studies.

we have used COX-2s in patients in whom low dose codeine causes excessive nausea or constipation

Q Can you recommend a good pain rating scale?

A In our experience, rating scales are pretty useless. Most of our patients will always say their pain is 11/10. Rating out of ten is useful for considering the effectiveness of any treatment (so what was your pain out of 10 before? And what is it now?). We use either the Brief Pain Inventory (BPI) or the EuroQual 5D as a screening tool. For cancer pain assessment, we find that LANSS (Leeds Assessment of Neuropathic Symptoms and Signs) is useful.

A further issue, of course, is that pain, physical impairment and disability are very different things, and the correlation between these three dimensions is very poor indeed. Typically, this means that patients who often have very few signs of significant physical impairment may complain of high levels of pain and disability. When asked about pain most people express their feelings about "suffering".

In such situations a behavioural approach looking at outcomes – for example how far one can walk, what one gets done during the day, etc – is far more useful. The only situation in which we suggest pain scales may prove to be helpful is – if one is particularly looking at neuropathic pain for example – to decide whether a first-line trial of a gabapentinoid would be appropriate. In practice, simply asking whether the pain is shooting or whether there is superficial sensitivity of the skin seems to be just as good, according to many clinicians. As mentioned above, however, there is very little evidence in fact that the character of pain will help to determine the most successful treatment.

When asked about pain most people express their feelings about 'suffering'

Q Why does carbamazepine work for trigeminal neuralgia, and does it work for other neuropathic pain?

A Trigeminal neuralgia has an annual incidence of three to five per 100,000 people. Carbamazepine (CBZ) is the drug of choice in treating trigeminal neuralgia (TGN), mainly for historical reasons. It is the preferred drug to treat pain in trigeminal neuralgia based on four small-randomised controlled trials of poor quality. In two double-blind placebo controlled studies carbamazepine has been found to be effective in treating pain of diabetic neuropathy. It has also been shown to be effective in post-herpetic neuralgia.

CBZ has a similar action to benzodiazepine. It stabilizes the voltage gated Na^+ channels, making the cells less excitable by decreasing the conductance in Na^+ channels. It also potentiates GABA receptors. Both these mechanisms have a role in pain pathways.

All of the anticonvulsant drugs used for neuropathic pain have slightly different mechanisms of action, so some patients will do better with a tricyclic antidepressant (TCA), some with a gabapentinoid and some with a sodium channel blocker such as mexilitine lamotrigine or even phenytoin. As mentioned above, there is a very simple explanation: the evidence for CBZ in TGN was published before the gabapentinoids were widely available. However, there are patients who respond to or tolerate a gabapentinoid better than CBZ or vice versa. Phenytoin has also been shown to be helpful in addition to CBZ, so combination therapy might be helpful. Although most drugs used in chronic pain are not licensed for these indications, the British Pain Society accepts and endorses such practice (www.britishpainsociety.org/book_usingdrugs_main.pdf), which in turn is underlined by the principal of Bolam applies in that a doctor acted in accordance with a practice accepted as proper by a responsible body of medical men skilled in that particular art.

Q What sort of questions should we ask a patient about pain, and what are the key criteria for referral?

A The old assessment of "SOCRATES" (see below) is still helpful. These questions will often resolve the "neuropathic vs. nociceptive pain" issue.

SOCRATES – MNEMONIC FOR PAIN ASSESSMENT
Site
Onset (time of onset. sudden/gradual, etc)
Character of pain
Radiation of the pain
Associations - symptoms associated with the pain
Time course (Does the pain follow any pattern?)
Exacerbating/Relieving factors
Severity

We find the question: "if you did nothing but stay in bed, would you still have pain?" helpful to distinguish rest from incident pain. Asking about sleep is also helpful. We would like to see difficult pains – e.g. resistant trigeminal neuralgia (TGN), pain in children, CRPS, complex cancer and renal pain – early, as those patients need non-pharmacological strategies taught straightaway. If you are struggling with the patient's management, or there are prominent "yellow flags" (psychosocial indicators suggesting increased risk of progression to long-term distress, disability and pain), refer to the pain clinic.

It is also important to identify patients in whom pain is being perpetuated by psychological factors, or where there is significant risk of this occurring. The largest group of such patients are those who have developed depression (often secondary to the experience of chronic pain) – indeed the prevalence of depression in chronic pain clinic populations is around 60%.

Questions to screen for depression (i.e. asking whether the patient has been bothered by feeling down, depressed or hopeless, and with little interest or pleasure in doing things) may be asked. Within primary care, the Patient Health Questionnaire (PHQ-9) is frequently used to screen for depression. Where clinically significant depression is present, this requires treatment in its own right – particularly as depression may heighten pain perception and contribute to the process of entrenchment in chronic pain.

Q How effective is capsaicin cream – and in what types of pain can it be used?

A Capsaicin cream is used to treat aches and pain of the muscle or joints. It can be used in arthritis, backache and sprains. It has also been used in neuropathic pain. Capsaicin is the active component of chilli and is thought to work by decreasing substance P, a naturally occurring neuropeptide in the body involved in transmitting pain to the brain

Low concentration (0.025% and 0.075%) capsaicin cream is available over the counter and does not need a prescription. However, 8% capsaicin is only available for use by a trained physician in the hospital setting to treat patients with specific neuropathic pain conditions. Capsaicin should not be used over areas of the body with broken skin.

There is a lot of good quality evidence showing the effectiveness of topical capsaicin. In 1991, a study in osteoarthritis (OA) and rheumatoid arthritis (RA) patients showed that application of 0.025% cream to the knees applied four times daily reduced pain in 80% of patients after two weeks of treatment. RA patients showed 57% pain reduction and OA showed 33% pain reduction. A further four-week trial evaluating capsaicin 0.075% demonstrated a reduction in RA but not OA generally.

In back pain, studies with capsaicin plaster have demonstrated that 60% of patients experienced at least 30% reduction in pain, compared to 42.1% in the placebo group. In cancer patients with post-operative neuropathic pain, use of capsaicin cream resulted in an average reduction of 53% pain compared to 17% for the placebo group. In a study involving 143 patients with post herpetic neuralgia, use of 0.075% capsaicin cream demonstrated significant reduction in pain after six weeks' treatment.

The clinical impression is that the effects of capsaicin cream take time to develop, so we would not expect capsaicin to work effectively in acute sprain. However, the placebo effects are not insignificant for any topical application (topical NSAIDS are little better than placebo according to Cochrane), so the suggestion to buy some OTC capsaicin may not be unreasonable.

NEXT ISSUE

Answers to more of your questions on pain management

Please send questions on the following future topics to BJFM@pavpub.com

- Infant nutrition
- Type 2 diabetes