Personalising OTC analgesia

In the second part of an article on over-the-counter analgesics, Andrew Dickman discusses the precautions and special considerations needed in order to recommend a product and ensure appropriate use.

Despite analgesics being readily available, there are a number of risks associated with their inappropriate use.

Despite the fact that, in most situations, over-the-counter analgesic products are safe to use, some patients, such as elderly people, need special consideration. Moreover, alarmingly, a recent survey has indicated that one in six people are unaware that some analgesics may not be suitable for those with cardiovascular disease, asthma or gastrointestinal (GI) conditions (YouGov survey of 2,112 UK adults, data on file). Pharmacists and their staff need to be able to ensure the safe use of OTC analgesics. Not only do they need to determine a person’s risks for adverse effects but if, as often happens with OTC analgesics, the product is to be kept for occasional use, they must make the purchaser aware of conditions that could pose a risk so that the product is not offered to another person inappropriately.

The elderly

Chronic pain is associated with age. Pain is often under-treated and under-recognised in the elderly population (arbitrarily defined as people over 65 years of age).

Managing pain in the elderly is challenging because of age-related changes in pain perception and cognition, and particularly in the pharmacokinetics and pharmacodynamics of drugs. In addition, elderly patients may be reluctant to report pain, either because of the belief that pain is a normal part of the ageing process or of the fear that pain may be caused by a serious underlying disease, such as cancer. Poorly treated pain in the elderly has several consequences, including reduced independence, anxiety and sleep disturbance.

Probably the most important change that occurs during ageing that affects the pharmacokinetics of many drugs is the reduction in renal elimination. The effect of age on hepatic drug metabolism remains a controversial issue.

Paracetamol should be considered as the first-line OTC analgesic for the elderly. Non-steroidal anti-inflammatory drugs (NSAIDs) should be used cautiously in this group because age is an accepted risk factor for NSAID-induced gastrointestinal toxicity with the risk increasing significantly over the age of 75 years. Elderly people are also more likely to suffer from co-morbidities relevant to the use of NSAIDs and to be taking medicines such as low-dose aspirin (see below).

In February 2008, the National Institute for Health and Clinical Excellence issued guidance on the management of osteoarthritis. In it, paracetamol or topical NSAIDs or...
both, were recommended ahead of oral NSAIDs, recognising the potential toxicity of NSAIDs in the elderly.2

Combination products containing paracetamol and caffeine may be used provided that there are no cardiovascular concerns (see below). OTC preparations containing codeine or dihydrocodeine should be avoided; there is little, if any, analgesic benefit and elderly people are more susceptible to the adverse effects, such as constipation.

Rubefacients may offer short-term relief of musculoskeletal problems.

Cardiovascular and renal concerns
When selecting an OTC analgesic, caution is needed in people with congestive heart failure, hypertension, or ischaemic heart disease. In people with conditions such as congestive heart failure, renal prostacyclin production may be increased in order to maintain adequate renal blood flow. NSAIDs can impair renal function in patients reliant on these prostaglandins for normal kidney function because they inhibit prostaglandin synthesis. Potential consequences are reduced renal blood flow, reduced glomerular filtration rate and increased sodium and water retention, resulting in oedema and hypertension.

NSAIDs can increase the risk of cardiovascular events, such as a myocardial infarction, especially in those at high risk (eg, established cardiovascular disease, diabetes, renal impairment). A review of the cardiovascular safety of NSAIDs identified that diclofenac and high dose ibuprofen (2,400mg/day) were associated with a small increased thrombotic risk. Low-dose ibuprofen (ie, usual OTC doses, <1,200mg/day) and naproxen (<1,000mg/day) did not have this association.2 OTC use of ibuprofen (ie, maximum daily dose of 1,200mg) is believed to relatively safe.3

In combination with low-dose aspirin — commonly prescribed in patients with cardiovascular disease — there is a potential for the cardioprotective effect to be reduced. It has been suggested that doses of ibuprofen 400mg tds may reduce the inhibition of platelet aggregation produced by aspirin.4 The combination of an NSAID with low-dose aspirin also significantly increases the risk of GI toxicity. Finally, NSAIDs increase the risk of heart failure in patients with hypertension, renal impairment or diabetes.5 Attention must also be paid to the greater likelihood of drug interactions in these people (eg, with antihypertensives).

While paracetamol is clearly the analgesic of choice in patients with renal impairment or cardiac disease, due consideration should be given to the sodium content of effervescent or soluble preparations. For example, a person can exceed the 6g recommended daily intake of salt if they take eight soluble paracetamol tablets (see later).

Combination products containing caffeine should also be used cautiously. Caffeine has a mild stimulant effect and may increase the heart rate and aggravate conditions, such as ischaemic heart disease and hypertension.

Panel 1: Cautions and contraindications with NSAIDs
People in whom NSAIDs, including aspirin, should be avoided include those who:
- Have a history of, or existing GI ulceration, perforation or bleeding including that associated with NSAIDs
- Have a history of bronchospasm, asthma, rhinitis, or urticaria associated with aspirin or other NSAIDs
- Have severe heart, severe hepatic or severe renal failure
- Are pregnant (There is a risk of premature closure of the fetal ductus arteriosus and risk of delayed labour if NSAIDs are taken in the third trimester. Aspirin should be avoided throughout pregnancy.)
- Are using other NSAIDs
- Are on concurrent anticoagulant or corticosteroid medicines
- Have a glucose 6 phosphate dehydrogenase (G6PD) deficiency*
- Have haemophilia*
- Are breast-feeding*
- Have gout*
- Are under 16 years old*
- Have a history of, or existing GI ulceration, perforation or bleeding, including that associated with NSAIDs
- Are using other NSAIDs
- Are under 16 years old*
- Are on concurrent anticoagulant or corticosteroid medicines
- Have a glucose 6 phosphate dehydrogenase (G6PD) deficiency*
- Have haemophilia*
- Are breast-feeding*
- Have gout*
- Are under 16 years old*

* Aspirin only

In all cases, adverse effects can be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms. Topical preparations, including topical NSAIDs, may be considered for musculoskeletal pain.

Patients with renal impairment should use opioids with caution because there may be failure to excrete active metabolites. It would be worth considering paracetamol alone for these patients.

Hepatic and alcoholic concerns
It is a common misconception that patients with hepatic impairment are more susceptible to paracetamol-induced hepatic toxicity. In fact, paracetamol is the drug of choice. Most of these patients can safely take paracetamol at usual doses, providing they are not malnourished.

Use of NSAIDs in patients with hepatic impairment, however, is not a sensible option. While the risk of direct liver toxicity is low with usual OTC doses, the risk of GI bleeding is increased due to thrombocytopenia and the increased risk of bleeding often associated with advanced liver disease. Patients with liver disease may also have impaired renal function (the consequences of NSAID administration in renal impairment were discussed above).

The use of paracetamol by patients with alcoholic liver disease is a matter of debate. The misconception that paracetamol is unsafe in alcoholic patients, even at usual doses, stems from a series of case reports with confounding issues. A potential for a drug interaction between alcohol and paracetamol does exist but the interaction is complex because acute and chronic alcohol consumption can have different effects.

In patients who chronically consume alcohol, the metabolism of paracetamol to toxic metabolites is increased. (Chronic alcohol consumption has been defined as more than 50g ethanol per day for at least three months [one UK unit is equal to 8g alcohol], but the...
Some studies have shown that an alternating regimen of paracetamol and ibuprofen lowers fever faster than either drug alone in children aged six to 36 months (PJ, 25 February 2006, p224). However, recent guidance from the National Institute for Health and Clinical Excellence on treating fever in children under five years of age has advised against using paracetamol and ibuprofen at the same time and routinely giving them alternately. (PJ, 26 May, p599).

More recently, researchers concluded that ibuprofen should be given first then the relative benefits of giving both over 24 hours considered. It is hoped that NICE will consider this new evidence when it conducts its review. The two analgesics may be given one after the other, but not mixed in one solution. It is important to ensure the parent of carer does not accidentally administer an overdose.

Panel 2: OTC analgesics and fever in children

People should be advised not to drink more than three units of alcohol daily while taking an NSAID

US Food and Drug Administration uses an arbitrary “three drinks a day” figure, without reference to alcohol content.) Conversely, acute consumption in a non-alcoholic patient can prevent liver toxicity.

Chronic alcohol consumption leads to the induction of CYP2E1, the isoenzyme responsible for the formation of N-acetyl-p-benzoquinoneimine (NAPQI); the highly reactive intermediate metabolite, so there is a theoretical increased risk of liver damage. Acute alcohol consumption (ie, at the same time as paracetamol) may reduce the risk of liver damage through competitive inhibition and reduction of NAPQI formation.

Despite the theoretical risk, paracetamol at usual doses has been shown to be safe in people with alcohol problems and remains the analgesic of choice. However, while using paracetamol, it would be sensible to limit alcohol intake to no more than three alcoholic drinks per day. It should also be noted chronic alcohol consumption is often associated with poor nutrition (see PJ, 29 November 2008, p631).

It is clear that alcohol increases the risk of GI bleeding with NSAIDs and, for this reason, people should be advised not to drink more than three units of alcohol daily while taking an NSAID. Should chronic alcohol consumption be evident, there may well be a degree of liver damage present and NSAIDs should not be recommended.

Products containing codeine or dihydrocodeine should be avoided in patients with hepatic impairment due to the risk of hepatic encephalopathy.

Gastrointestinal conditions

Non-selective NSAIDs (ie, those available OTC) are contraindicated in people with a history of, or existing G1 ulceration, perforation or bleeding, including that associated with NSAIDs. Panel 1 gives a summary of the main cautions and contraindications for recommending NSAIDs.

NSAIDs have, rarely, been associated with exacerbation of inflammatory bowel disease so patients with Crohn’s disease or ulcerative colitis should use these drugs with a degree of caution.

Children

Paracetamol suspension can be given to babies over the age of two months. It is especially important to distinguish between strengths for infants and those for children.

The summary of product characteristics for Calpol suspension states that for babies between two and three months old, two doses (60mg four to six hours apart) can be given for fever (and not only for post vaccination pyrexia) or mild to moderate pain providing they were born at more than 37 weeks gestation and weigh more than 4kg; other product SPCs do not make such specifications.

A recent study linked the use of paracetamol in infancy and childhood to an increased risk of developing asthma and eczema (PJ, 27 September, 2008, p352) however, the researchers pointed out that causality could not be established and there was insufficient evidence to advise against taking paracetamol.

Ibuprofen suspension is available for use in children aged three months and over and is a suitable treatment for fever, post-immunisation pyrexia and mild to moderate pain. However, for infants between three and six months old, it should only be used for 24 hours, after which a doctor should be consulted if further treatment is necessary.

The use of OTC analgesics to treat fever in children is discussed in Panel 2.

Pregnancy or breastfeeding

Paracetamol remains the OTC analgesic of choice both in pregnant women and in infants despite the link to the development of asthma and eczema in children. In order to reduce the risk, it is recommended that paracetamol should not be used unnecessarily after 20 weeks’ gestation. Paracetamol is safe for use in breastfeeding women.

Formulations and preferences

Tablets, soluble tablets, capsules, liquid capsules, “meltlets”, suspensions, gels, creams and sprays — the choice of formulations of OTC analgesics can be confusing for patients and, although there is little evidence to rely on,
pharmacists can help by explaining the pros and cons of different formulations, taking into account a person’s preferences.

Some formulations, particularly effervescent and soluble tablets, tend to act faster than standard formulations. Other options might include ibuprofen lysine (which is more water-soluble than ibuprofen so may have a more rapid onset of action), and, as previously explained (PJ, 29 November 2008, p631–4), products containing caffeine. A product launched last month provides a fast acting option for people who should avoid products with high sodium, caffeine and NSAIDs. Paracetamol has recently been formulated with a disintegration system called Optizorb (Panadol Advance) which, the manufacturers claim, allows the tablets to disperse in the stomach up to five times faster than ordinary tablets.

As with other types of medicine, enquiring about ease of swallowing and circumstances of use (eg, if the person intends to carry the product around or keep it at home) will help pharmacists to recommend an appropriate product.

Advice
Given the potential for misuse of analgesics, especially those containing codeine or dihydrocodeine, pharmacists and their staff should always counsel patients on the proper use, including recommended duration of use and possible adverse effects (eg, patients should also be informed of the potential for rebound headaches that may occur with analgesic overdose). Panel 3 (p703) lists advice that can be given.

Non-pharmacological options
Non-pharmacological options can also be used to manage pain, either alone or in combination with OTC analgesics. As mentioned in the first part of this article (PJ, 29 November, p631–4), pain is both a physical and emotional experience. Drugs can be taken to address the physical aspects of pain, but this approach does not always work with emotional aspects. Non-pharmacological approaches can help in the overall management of pain by addressing both the physical and emotional aspects of the pain experience.

There are a range of non-pharmacological options that can be considered initially, such as heat (eg, hot water bottle for muscular aches), cold (eg, compresses for sprains) and exercise (eg, for osteoarthritis). There are many different measures that can be used, from simple non-invasive approaches to complex and invasive procedures. For example, approaches such as cold compresses, hot water bottles, massage, or warm wheat packs are simple measures that may help with the physical aspects of pain.

More complex non-pharmacological methods for relieving physical aspects of pain include acupuncture, radiotherapy, spinal cord stimulation and transcutaneous electrical nerve stimulation.

There are also many non-pharmacological approaches that can help with the emotional aspect of pain by attempting to alter a patient’s sentence. Aromatherapy, laughter, music, and pet therapy can improve a patient’s tolerance to pain not only through distraction but possibly through the involvement of endorphins.

Conclusion
The pharmacy is often the first point of call for many people affected by an episode of acute pain. The choice of suitable OTC product for pain can be confusing because a variety of generics or brands, formulations and combination products are available and more are becoming so, partly in line with the Government’s self care strategy.

Despite analgesics being readily available, there are a number of risks associated with their inappropriate use. Paracetamol is one of the leading causes of drug-related poisoning (it is important to reinforce its ubiquity) and NSAIDs can cause serious adverse effects, such as GI bleeding and ulceration.

With due consideration of patient characteristics such as age, allergies, co-morbidity and concurrent medication and preferences, pharmacists and their staff can help people make an informed choice and ensure that OTC analgesics are used appropriately.

Optimising the use of OTC analgesics can potentially reduce the burden to the NHS, while contributing to an improvement in the patient’s management of pain.

Action: practice points
Reading is only one way to undertake CPD and the Society will expect to see various approaches in a pharmacist’s CPD portfolio.

1. Ask another pharmacist what is his or her top three OTC analgesic products and discuss his or her choices.
2. Think about how you would deal with a query from a worried parent about the apparent link between paracetamol and asthma and eczema.
3. Talk to your staff about strategies against the abuse and misuse of OTC analgesics.

Evaluate
For your work to be presented as CPD, you need to evaluate your reading and any other activities. Answer the following questions: What have you learnt? How has it added value to your practice? (Have you applied this learning or had any feedback?) What will you do now and how will this be achieved?

References