Why doctors should think more carefully before prescribing

Each year, adverse reactions to medications kill more people than road traffic accidents. In fact, they are one of the biggest killers after cancer and heart disease (Bates et al, 1995). But medical advancement is a wonderful thing, and a massive investment in the development of medical products has given doctors new, improved drugs with greater efficacy and selectivity, the end result of which is fewer adverse reactions and deaths.

At first sight, some of these drugs may appear expensive, and indeed some are, compared to their less effective predecessors, but to prescribe a drug based purely on acquisition cost would be short-sighted. Using the new generation drugs has the potential to save money in the long run: first they can lead to faster treatment times and second they can avoid side-effects which may need a co-prescription. There is also a question of ethics — practitioners should prescribe medications which result in greater patient satisfaction and quality of life.

HARMFUL EFFECTS

Although it is difficult to estimate the amount of resources consumed by adverse drug events, we can get a fairly good idea of what damage they can cause by looking at non-steroidal anti-inflammatory drugs (NSAIDS) used for the treatment of arthritis. A paper published last year (Tramer et al, 2000) revealed that on average, one in 1220 patients taking NSAIDs for at least 2 months will die from serious gastrointestinal bleeds and other complications caused by the commonly-used painkillers. This equates to an estimated 2000 preventable deaths each year in the UK alone. Translated into pounds sterling, adverse effects caused by NSAIDs may cost the NHS an estimated £251 million each year.

Doctors appear to be well-aware that NSAIDs can cause troublesome side-effects, the most common of which involves the gastrointestinal tract — stomach ulcers which can progress to cause gastric bleeding and in some cases death (Hawkey, 1996). Other side-effects include a variety of renal effects, such as fluid retention which occurs in 5% of patients (Whelton and Hamilton, 1991), congestive heart failure, and bleeding complications resulting from NSAID inhibition of prostaglandin biosynthesis interfering with platelet function.

So, why then do practitioners stick to old habits and not opt for a more satisfactory drug? The cyclooxygenase (Cox)-2 inhibitors have been available for a decade (Brooks et al, 1999) and are proven to be equally effective as NSAIDs but without the adverse reactions. Supratherapeutic doses of both rofecoxib and celecoxib have been shown in prospective 8000 patient trials to reduce admission rates for ulcer complications by 57% compared with average doses of NSAIDs (Bombardier et al, 2000; Silverstein et al, 2000).

CLINICAL FEATURES OF OSTEOARTHRITIS

Osteoarthritis is one of the most common forms of arthritis and affects nearly five million people in the UK, most of whom are elderly (Knott, 2000). Its characteristics include chronic and permanent erosion of cartilage in the joints of the hands, knees, hips, cervical and lumbar spine. Left untreated, it eventually leads to severe limitation of movement, joint deformity and instability and, consequently, can have profound effects on patients' quality of life.

Treatment for osteoarthritis primarily focuses on pain relief and the preservation of joint function. Lifestyle measures include weight reduction (if the patient is overweight) and muscle strengthening exercises involving the use of hydrotherapy, local heat and ultrasound (Zeb and Edwards, 1998). Walking aids may also help to reduce some of the disability, but some patients will eventually need hip or knee replacement surgery.

Drug treatments for osteoarthritis include simple analgesics, NSAIDs and Cox inhibitors. NSAIDs work by inhibiting two Cox enzymes (cyclooxygenase-1 or Cox-1 and cyclooxygenase-2 or Cox-2), but an increasing body of evidence has shown that inhibition of Cox-1 results in adverse events such as gastrointestinal irritation and damage (Brooks et al, 1999).

Cox-2 inhibitors work by selectively targeting the Cox-2 isoform of the cyclooxygenase enzyme which is thought to be responsible for mediating the inflammatory process (Vane, 1994). Unlike NSAIDs, Cox-2 inhibitors have little effect on the Cox-1 isoform of the cyclooxygenase enzyme which is believed to be important in protecting the gastric mucosa against injury (Vane, 1994).

BRITISH SLOW ON UPTAKE

A survey of 209 general practitioners published last year (Knott, 2000) revealed that the therapeutic aim of nearly half of those surveyed was to minimize gastrointestinal side-effects by starting on a low dose of NSAID, rather than prescribe the Cox-2 inhibitors. In comparison to other developed countries, the UK is one of the slowest in Cox-2 inhibitor uptake (IMS Health, London, unpublished data, 2000).

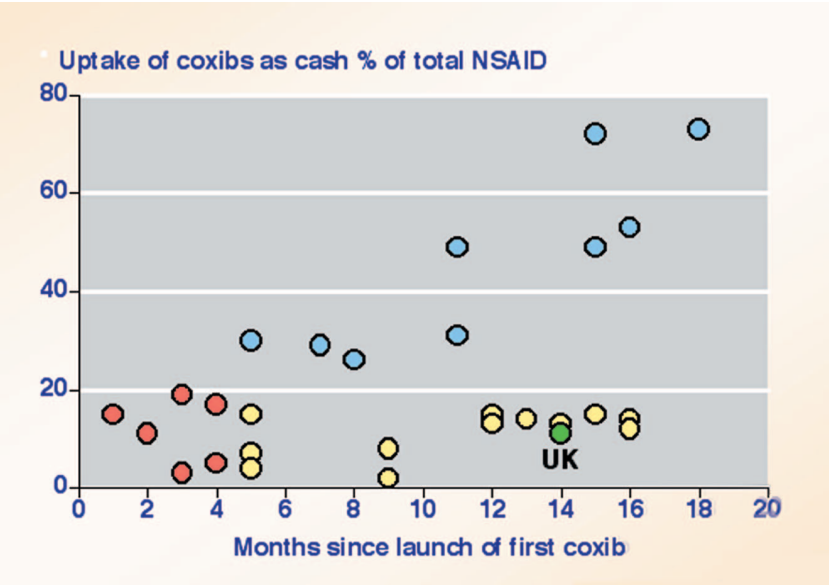

Figure 1. Uptake of cyclooxygenase-2 inhibitor (coxib) sales as a percentage of total non-steroidal anti-inflammatory drug (NSAID) sales against the number of months since coxibs were first launched in each country. From IMS Health, London, unpublished data, 2000.

Figure 1 plots the uptake of Cox-2 inhibitor sales as a percentage of total NSAID sales against the number of months since Cox-2 inhibitors were first launched in each country. After 4 months, there are a group of countries (blue) where uptake is rapid, and another group (yellow) where uptake is slow. The UK (marked in green) sits in the latter group. What this means is that while we spend less on drug acquisition, we soon lose out by expending on patients damaged by NSAIDs.

MORE POOR PRESCRIBING

Another example of poor uptake of effective medication is in the treatment of gastro-oesophageal reflux. The more widely-used treatment for this condition in the UK is the alginates which, although effective, have much less systematic supporting data than for proton-pump inhibitors (PPIs). Once again, it seems that prescribers are influenced more by their budgets than the potentially damaging effect of medications, in this case the sodium content of alginates on heart failure.

Practitioners may lean on the excuse of waiting for the National Institute of Clinical Excellence (NICE) before prescribing newer drugs. In the case of oesophageal reflux, NICE has now published guidelines on their use and recommends use of PPIs with interstep down for moderate to severe symptoms and erosive oesophagitis.

Hopefully, NICE will also get around to recommending wider use of Cox-2 inhibitors, helping to make the gastrointestinal hazards of NSAIDs a thing of the past. Guidelines aside, it is the conservative nature of British prescribing that needs to be placed under the spotlight. Habits need to change, so that we make better use of potentially life-saving 21st and 22nd century innovations. HM

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KEY POINTS

- Adverse reactions to medications kill more people than road traffic accidents and are one of the biggest killers after cancer and heart disease.
- Prescribing new generation drugs which are more expensive but have fewer side-effects than their predecessors can make good economic sense.
- Doctors in the UK are slow to uptake new drugs compared to doctors in many other developed countries.
- Adverse effects caused by non-steroidal anti-inflammatory drugs cost the NHS an estimated £251 million each year.
- Cyclooxygenase-2 inhibitors, while more expensive, have significantly fewer adverse effects than non-steroidal anti-inflammatory drugs.
- Doctors should prescribe new effective drugs with fewer side-effects, rather than conventional drugs with potentially life-threatening adverse reactions.