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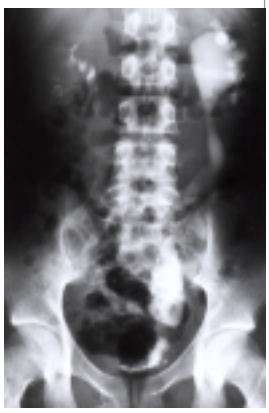

Cover Picture:
IVU post-micturition radiograph.
(Refer to page 233-237)

Editorial

NSAIDS, COX-2 Inhibitors and Tramadol: Acute Postoperative Pain Management in Day-Case Surgery Patients

Y W Chan

Adequate postoperative pain relief in day-surgery patients determines the numbers of patients undergoing such surgery, and the range of day surgical operations undertaken. The widespread use of local analgesia and potent intraoperative opioids has been well established in day surgery. There is a need, however, for powerful non-opioid analgesics, to provide complete analgesia for minor operations and to reduce the opioid requirements for more intermediate surgical procedures. Non-steroidal anti-inflammatory drugs (NSAIDs), COX-2 inhibitors and Tramadol can fill this need.

BALANCED ANALGESIA STRATEGY

Anaesthetists and surgeons must learn to use the combination of opioids, NSAIDs and local anaesthetics to improve the efficacy of pain relief in the acute postoperative surgical patient. Balanced analgesia[2] (combination therapy with two or more different types of analgesic agents) has the advantage of decreasing the doses of each drug administered, thus diminishing the risk of adverse reactions. In addition to an opioid-sparing effect, balanced analgesia do provide equivalent or enhanced pain relief as compared with opioids or local anaesthetics alone[3,4].

PARACETAMOL AND ASPIRIN

In most minor day surgery procedures, simple oral analgesics such as paracetamol and aspirin, used alone or in combination with the 'milder' opioids such as dextropropoxyphene and codeine, are effective pain relief agents to discharge patients home comfortably and with no drug-induced side effects.

NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS)

NSAIDs are used increasingly to provide postoperative analgesia. They do not have the troublesome side effects of opioids[5], like postoperative nausea and emesis; dose-dependent drowsiness and respiratory depression; pruritus and urinary retention. NSAIDs have been shown to reduce the postoperative opioid requirements in a variety of surgical procedures[6-9] and hence facilitate early home discharge. They can also act as effective adjuvants to simple oral analgesics after minor surgery[10].

NSAIDs act primarily by their inhibitory effect on cyclo-oxygenase, which converts arachidonic acid to prostaglandins. Together with other mediators, prostaglandins have a role in promoting pain associated with tissue trauma and inflammation. They act primarily on the peripheral nervous system.

It has been shown that NSAIDs are more effective when administered preoperatively[11-13] as they require an onset of action to effective analgesia

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of up to 40 minutes. The presence of drug levels in the tissues before surgery reduces the inflammatory response mediated by arachidonic acid and thus dampens the effect of a nociceptive stimulus[14]. Moreover, NSAIDs have duration of action that exceeds those of short-acting opioids (fentanyl, alfentanil and remifentanil) used in day surgery, lasting well into the discharge period.

Commonly used NSAIDs in day surgery include aspirin, diclofenac, ibuprofen, indomethacin and ketorolac (Toradol). They usually come in oral or suppository preparations. The injectable form of ketorolac has analgesic efficacy comparable to opioids[15]. It has provided more treatment options for relief of postoperative pain after major surgical procedures.

NSAIDs have a number of side effects that are well known, e.g. bronchoconstriction in asthmatics[16]; stomach ulceration and haemorrhage[17]; renal failure in those with compromised renal function[18]; and an anticoagulant effect by influencing platelet function[19]. However, the increased risk of wound bleeding from the perioperative use of NSAIDs has been found to be clinically insignificant[20]. Careful patient selection with proper history taking; physical examination and gastric acid prophylaxis before the use of NSAIDs remains critical.

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SELECTIVE COX-2 INHIBITORS

In our body there are two isoforms of COX (cyclooxygenase), namely COX-1 and COX-2. COX-1 is found in a variety of tissues. The prostaglandin it produces protects gastric mucosa, limits acid secretion, enhances renal perfusion, and preserves platelet function.

Pain and inflammation induce COX-2. Selective COX-2 inhibitors can alleviate pain and inflammation without the unwanted side effects of the regular NSAIDs, which block both enzymes[21].

Celecoxib (Celebrex) and Rofecoxib (Vioxx) belong to this new class of selective COX-2 inhibitors, also known as "safer NSAIDs". These COX-2 inhibitors are available for oral use in the treatment of rheumatological pain.

A parenteral preparation of COX-2 inhibitor is under clinical trial for postoperative pain control and has been shown to be comparable to ketorolac in analgesia potency but without its deleterious side effects[22]. Selective Cox-2 inhibitors are safer than conventional NSAIDs and will eventually play a more extensive role in the management of acute postoperative pain.

TRAMADOL[23,24]

Tramadol hydrochloride (Ultram) is a new centrally-acting synthetic analgesic with low affinity for mu-opioid receptors. The rate of production of its major active metabolite, O-desmethyl-tramadol, is influenced by debrisoquine-type polymorphism. This metabolite shows a higher affinity for the opioid receptors than the parent drug and contributes to its analgesic effect. However, in most animal tests and human clinical trials, the analgesic effect of tramadol is only partially blocked by the opioid antagonist naloxone, suggesting an important nonopioid mechanism.

The nonopioid mechanism exerts its effect through direct modulation of the central monoaminergic pathways, resulting in an increase in central neuronal synaptic levels of two neurotransmitters, serotonin and noradrenaline.

It has been known that the combination of an antidepressant monoamine reuptake inhibitor and an opioid analgesic has been efficacious in the treatment of certain types of chronic pain conditions. Tramadol acts along similar complementary dual mechanism of action.

Tramadol is effective in different types of moderate-to-severe pain, including neuropathic pain. The mode of action of tramadol does not overlap with that of the NSAIDs and is a useful analgesic to be combined with these drugs. Tramadol induces fewer opioid adverse reactions like nausea, dizziness and vomiting for a given level of analgesia compared with the traditional opioids.

A few cases of idiopathic seizures have been reported in users of tramadol. It is recommended that the drug be avoided or used with caution in epileptics, or in individuals who are taking tricyclic antidepressants (TCAs) or selective serotonin reuptake inhibitors (SSRIs) concomitantly. Both TCAs and SSRIs are known to reduce the convulsive threshold. Postulated mechanism of this rare adverse effect is the inhibition of monoamine reuptake by the drug.

This novel drug is a definite addition in acute postoperative pain management of surgical patients with moderate to major procedures.

CONCLUSION

The pain experienced by patients after surgery can be considerable. The limit on which operations may safely be performed on a day-case basis will depend very much on the adequacy of postoperative pain management.

The balanced analgesia strategy helps to provide efficacious pain management with minimal side effects, to allow patients to discharge home comfortably and safely. NSAIDs and local anaesthetics are important components of this strategy.

Selective COX-2 inhibitors and Tramadol enable the anaesthetists and surgeons to further fine-tune this balance. SMJ

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