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Parecoxib

A Viewpoint by Daniel Carr

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The importance of postoperative pain control to optimise health-related quality-of-life and functional outcomes is now widely accepted. Despite consensus that a nonsteroidal anti-inflammatory drug should, unless otherwise indicated, be part of the postoperative analgesic regimen for all patients, this strategy is not as widely implemented as it should be. A major reason for this shortfall is that oral agents are precluded when nausea and vomiting are present, as is often the case perioperatively even in patients who have not had gastrointestinal operations. Ketorolac has been a valuable adjunct to the analgesic formulary because it is effective in moderate to severe pain and may be administered intravenously. On the other hand, post-release experience suggests that the risks of significant gastrointestinal bleeding, as well as renal dysfunction, are substantial during ketorolac therapy. Risks of ketorolac-induced gastrointestinal blood loss are greater when the dose is increased, when patients are older than 65, or when there is a history of prior peptic ulcer or bleeding. When patients have such a history, are over 65, and are treated with ketorolac 60mg every 6 hours, the incidence of substantial adverse effects increases to an unacceptable level (approximately one-third of patients).

New data suggest great promise for the clinical application of parecoxib. In particular, a randomised double-blind study in volunteers aged 65 to 75 years demonstrated expected high rates of gastrointestinal, gastric, and duodenal ulcers after administration of a relatively modest dose of ketorolac (15mg 4 times daily) for 5 days. In contrast, gastrointestinal effects with parecoxib were indistinguishable from those with placebo in this trial. Moreover, the median time to the first request for rescue medication in 304 patients with postoperative dental pain was approximately 23 hours for those receiving intravenous parecoxib 40mg versus 13 hours for those treated with intramuscular ketorolac 60mg. Adverse effects after single intravenous doses of parecoxib 20 or 40mg, intravenous ketorolac 30mg, or intravenous morphine 4mg were indistinguishable from those with placebo in 202 female patients with moderate to severe pain following abdominal hysterectomy or myomectomy in a multicentre, double-blind, randomised trial. Such effects included nausea, abdominal pain, headache, abdominal fullness or dizziness.

In summary, these early data from clinical trials are most encouraging. The therapeutic promise of COX-2 selective nonsteroidals appears to be a reality in practice as demonstrated by the rapid market acceptance of rofecoxib and celecoxib. Now that parecoxib offers clinicians the option of intravenous or intramuscular therapy with similar efficacy to ketorolac but with fewer adverse effects, an important barrier to the widespread routine use of nonsteroidals in the perioperative population appears to have been removed. ▲