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Correspondence

Choice of opioid analgesics in postoperative care

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Although many aspects of the Clinical Update on post-operative analgesia by Paul Myles and Ian Power (March 10, p 810)1 were extremely helpful, we were surprised that it laid such emphasis on the use of tramadol and oxycodone as opioid analgesics of choice for moderate and severe pain.

These newer choices will seem unusual to many readers who will be more familiar with the use of paracetamol plus codeine and of morphine in such circumstances. The advice will impose greater costs on health-care services and increase the range of opioid drugs in use. Although optimum therapeutic strategies are always in evolution, important changes are usually based on reliable evidence from well conducted randomised controlled trials that show superiority of an alternative strategy.

Tramadol, in particular, is subject to pharmacogenetic variability in its conversion to the active opioid metabolite (by CYP2D6) and to the metabolites of serotonin-selective reuptake inhibitors (by CYP3A4). These enzymes are variably expressed and will influence efficacy, and, more importantly, adverse-effect profiles. This variability makes tramadol inherently unlikely to be an effective drug for all, or possibly even most, patients. Its number needed to treat (NNT) for at least 50% pain relief over 4–6 h in patients with moderate to severe pain seems much greater than that for other analgesic choices.2

Myles and Power should be asked to provide more specific evidence for the superiority of tramadol and oxycodone.

We declare that we have no conflict of interest.

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Choice of opioid analgesics in postoperative care – Authors' Reply

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Simon Maxwell and Nicholas Bateman are correct that the pharmacogenetics of tramadol are variable. That is one of the reasons why we recommend its use as a second-line or third-line analgesic drug in the postoperative setting. Tramadol does, however, offer several advantages over opioid-based regimens in that there is less sedation, respiratory depression, and constipation,1 each of which can be problematic postoperatively.

Codeine, a prodrug, has its own pharmacogenetic variability because of its dependence on CYP2D6 to produce the pharmacologically active metabolite, morphine.2,3 Codeine has been shown to be an unreliable analgesic postoperatively.2 Tramadol, unlike codeine, can still provide analgesia in patients lacking CYP2D6 activity because its direct monoaminergic analgesic effect is independent of CYP2D6.3

Codeine 60 mg has weak analgesic efficacy, with a number needed to treat (NNT) of 17 and a poor side-effect profile.4,5 Similarly, dihydrocodeine, a synthetic form of codeine, was found to have weak analgesic properties in a meta-analysis of trials in a moderate-to-severe postoperative pain setting, with an NNT of 8 (95% CI 4–540) when compared with placebo.4

A meta-analysis of 18 surgical or dental pain trials found that tramadol was an effective analgesic when compared with placebo, and had a clear dose response: higher doses of tramadol were associated with higher benefit and lower NNTs. Tramadol 100 mg had an NNT of 4·6 (3·6–6·4).4

Unlike codeine, and to a lesser extent tramadol, oxycodone is not a prodrug and is not dependent on cytochrome P450 enzymes for its analgesic efficacy. For a single dose of oxycodone 15 mg compared with placebo, the NNT was 2·4 (1·5–4·9) for moderate to severe postoperative pain, indicating comparable analgesic efficacy to that of morphine 10 mg and oral non-steroidal anti-inflammatory drugs.4 Widespread experience in Australia with oxycodone has found it to have practical advantages postoperatively:1 reliable oral bioavailability, ease of dose adjustment, and a sustained release preparation. This factor improves the simple and effective administration of oral opioid therapy in the postoperative setting where pain intensity is fluctuating and reducing over time.

We believe that there is sufficient evidence to recommend the preferential use of oxycodone,5 tramadol, or both over codeine. There is, however, a need for head-to-head clinical trials of these drugs in the postoperative setting to determine the optimum first-line and second-line therapy in specific patient groups and types of surgery.

We declare that we have no conflict of interest.

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