Oral valdecoxib and injected parecoxib for acute postoperative pain: a quantitative systematic review

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CRD summary
This review assessed the efficacy, duration of analgesia, and safety of oral valdecoxib and injected parecoxib, for acute post-operative pain. The authors concluded that both oral valdecoxib and injected parecoxib were effective analgesics. The authors’ conclusions should be viewed with some caution due to variation in the patient populations examined.

Authors' objectives
To assess the efficacy, duration of analgesia, and safety of oral valdecoxib and injected parecoxib for acute post-operative pain.

Searching
PubMed (December 2002) and the Cochrane Library (Issue 4, 2002) were searched; the search terms were reported. The authors did not state whether any language restrictions were applied in their search strategy. The reference lists from systematic reviews, articles in previous reviews, and an in-house bibliographic database were also checked. The manufacturers of valdecoxib and parecoxib, Pfizer and Pharmacia, were contacted for copies of relevant posters or abstracts.

Study selection
Study designs of evaluations included in the review
Double-blind, randomised controlled trials (RCTs) were eligible for inclusion. All included studies had to have a minimum of 10 participants per group.

Specific interventions included in the review
Comparisons of oral valdecoxib or injected parecoxib with placebo in an acute pain setting were eligible for inclusion. Other analgesic comparators used in the studies included morphine, ketorolac, oxycodone plus paracetamol, and rofecoxib. The drugs were administered as a single post-operative dose.

Participants included in the review
Participants over the age of 15 years, experiencing moderate to severe post-operative pain, were eligible for inclusion. Patients undergoing either dental, orthopaedic, or gynaecologic surgical procedures were included in the primary studies. The mean age of the participants in the included studies ranged from 20 to 65 years. The baseline mean pain intensity ranged from 62 to 81 mm on a visual analogue scale (VAS).

Outcomes assessed in the review
Studies that assessed post-operative pain were eligible. Analgesic efficacy was assessed by a variety of standard pain measures; only studies that evaluated total pain relief (TOTPAR), or summed pain intensity difference (SPID) over a 4- to 6-hour period, or provided sufficient data for their calculation, were included. Time to remedication, the proportion of participants experiencing any adverse effects, and the proportion of patients experiencing specific adverse effects (headache, nausea, vomiting and alveolitis), were also included.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The validity of the primary studies was assessed using the Jadad scale, which considers randomisation, blinding and...
withdrawals. At least two unblinded reviewers independently assessed the validity of the primary studies; any disagreements were resolved by consensus.

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction. For each trial, the mean TOTPAR, SPID, VAS TOTPAR or VAS SPID values for the first dose were converted to %maxTOTPAR, according to Cooper (1991). The number of patients with at least 50% maxTOTPAR was used to calculate the relative benefit and number-needed-to-treat (NNT).

Methods of synthesis
How were the studies combined?
The relative benefits and relative risks for 'pain relief' and 'adverse events' were pooled in a meta-analysis, using a fixed-effect model. The NNT and number-needed-to-harm, along with 95% confidence intervals (CIs), were calculated from the pooled estimates.

How were differences between studies investigated?
The studies were grouped by intervention and dose. L’Abbe plots were used to visually examine homogeneity within the primary studies. In addition, sensitivity analyses appear to have been conducted for post-operative procedure (dental versus orthopaedic and laparotomy) in relation to pain relief within the parecoxib trials.

Results of the review
Eight RCTs were eligible for inclusion: 4 valdecoxib trials (n=574) and 4 parecoxib trials (n=519). Numbers for the parecoxib trials were based on intravenous injection, although one trial reported results for parecoxib intramuscular injection.

Valdecoxib (4 RCTs).

Pain relief: 68% (69 of 101) of patients receiving valdecoxib 20 mg reported at least a 50% maximum TOTPAR over 6 hours, compared with 8% (8 of 103) of patients treated with placebo. Compared with placebo, the NNT for one patient receiving valdecoxib 20 mg to have at least a 50% reduction in pain over this period was 1.7 (95% CI: 1.4, 2.0). Seventy-three per cent (204 of 279) of patients receiving valdecoxib 40 mg reported at least a 50% maximum TOTPAR over 6 hours compared with 10% (19 of 194) of patients treated with placebo. Compared with placebo, the NNT for one patient to have at least a 50% reduction in pain over this period was 1.6 (95% CI: 1.4, 1.8).

Remedication: the weighted median times to remedication were more than 17.5 hours and more than 24 hours in the valdecoxib 20 mg and 40 mg groups, respectively; the median time to remedication for the placebo group was 1.7 hours. Two additional analgesics were also compared: the weighted mean time to remedication was 8.8 hours for oxycodone 10 mg plus 1,000mg paracetamol, and more than 24 hours for rofecoxib 50 mg (based on 1 trial).

Adverse events: it was not possible to calculate pooled estimates for the valdecoxib 20 mg group; no statistical differences in the number of adverse events were reported between valdecoxib 40 mg and placebo.

Parecoxib (4 RCTs).

Pain relief: 50% (85 of 170) of patients receiving parecoxib 20 mg and 63% (109 of 173) of patients receiving parecoxib 40 mg reported at least a 50% maximum TOTPAR over 6 hours, compared with 16% (29 of 176) of patients treated with placebo. Compared with placebo, the NNTs for one patient receiving parecoxib 20 mg or 40 mg to have at least a 50% reduction in pain over this period were 3.0 (95% CI: 2.3, 4.1) and 2.3 (95% CI: 2.0, 2.6), respectively.

Remedication: the weighted median times to remedication were 5.6 hours and 8.7 hours in the parecoxib 20 mg and 40 mg groups, respectively, compared with 1.6 hours in the placebo group. Two additional analgesics were also compared: ketorolac 30 mg intravenous and morphine 4 mg gave mean remedication times of 5.5 hours and 3 hours, respectively.
Adverse events: 65% of participants receiving parecoxib 20 mg and 55% of those receiving parecoxib 40 mg reported an adverse effect, compared with 55% of patients receiving placebo. Sensitivity analysis: a significant difference in pain relief was demonstrated between dental and postsurgical procedures for parecoxib 20 mg and 40 mg. Fewer postsurgical patients experienced 50% pain relief compared with patients with dental pain.

**Authors’ conclusions**

Oral valdecoxib was an effective analgesic with an extended duration of action in dental pain. Injected parecoxib was an effective analgesic with a duration of action that was comparable to that of older non-steroidal anti-inflammatories.

**CRD commentary**

The aims were stated clearly, and the inclusion criteria were defined in terms of the study design, intervention and outcomes. Two relevant databases were searched, although the authors did not state whether any language restrictions were applied in their search strategy. The possibility of publication bias was not evaluated and could not, therefore, be ruled out, although the manufacturers of both drugs were contacted. The authors did not describe the method by which the studies were selected or the data extracted, thus the potential for reviewer error or bias could not be assessed. Relevant details of the primary studies were presented in tabular format on the BioMed Central website (accessed 23/08/2005). See Web Address at end of abstract.

Statistical homogeneity was examined visually, and a sensitivity analysis was used to examine the possible effect of surgical procedure in the parecoxib trials. It might not have been appropriate to pool the parecoxib trials, as these trials involved different patient groups. In addition, any conclusions relating to valdecoxib could not be generalised beyond post-operative dental pain. The authors' conclusions should be viewed with some caution due to the stated problems.

**Implications of the review for practice and research**

Practice: The authors suggested that parecoxib is potentially useful in the peri-operative and immediate post-operative period, as well as in patients who are unable to swallow or are nauseated and vomiting.

Research: The authors did not state any implications for further research.

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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.