The efficacy of preemptive analgesia for acute postoperative pain management: a meta-analysis

Ong C K, Lirk P, Seymour R A, Jenkins B J

CRD summary
This meta-analysis compared the efficacy of analgesic regimens administered to patients pre- or post-surgery. The authors concluded that preemptive epidural analgesia provided the most effective strategy in terms of lowering post-operative pain, reducing supplemental analgesic requirements and prolonging time to the first rescue dose. The reliability of the authors’ conclusions is unclear, given some potential uncertainties in the review process.

Authors’ objectives
To investigate whether preemptive analgesic regimens were of superior efficacy to the same regimens administered after surgical incision in the treatment of post-operative pain.

Searching
MEDLINE, EMBASE, CINAHL and PubMed were searched from January 1987 to October 2003; the search terms were given and a restriction to English language articles was imposed. The reference lists of retrieved articles were also checked. Reference to unpublished material, abstracts and contact with authors did not form part of the search strategy.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion in the review.

Specific interventions included in the review
Studies of the same analgesic interventions before and after surgical incision (employing the same route) were eligible for inclusion. The interventions included in the review comprised epidural analgesia, peripheral local anaesthetic wound infiltrations, systemic N-methly-D-aspartic acid (NMDA) receptor antagonists, systemic non-steroidal anti-inflammatory drugs (NSAIDS) and systemic opioids.

Participants included in the review
The inclusion criteria were not explicit. The participants (including children) in the review were undergoing a wide variety of surgical procedures.

Outcomes assessed in the review
The inclusion criteria were not explicit. However, the outcome measures extracted and analysed were pain intensity during the first 24 to 48 hours post-surgery, supplemental analgesic requirements post-surgery, and, elapsed time to first rescue analgesic. Pain intensity was measured by visual analogue scale scores.

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. However, the authors stated that they used systematic review methods of the Cochrane Collaboration, and the Cochrane Collaboration Handbook was cited.

Assessment of study quality
The authors stated that a modified version of the Jadad scale was used, but did not state who performed the validity assessment.
Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction. The studies were grouped according to intervention type. Mean and median data (along with dispersion values) or dichotomous values for the three outcome measures were extracted in order to provide summary statistics for the final analysis.

Methods of synthesis
How were the studies combined?
The studies were combined in meta-analysis using a fixed-effect model, unless statistical heterogeneity was observed, in which case a random-effects model was employed. Differences between pre- and post-treatment outcomes were converted into an effect size (ES) index using the standard mean difference to account for variations in the measurement of the same outcome. The extracted data were used to provide a summary statistic for individual study treatment effects, followed by a pooled estimate of the treatment effect across the studies. The data were analysed separately for each of the three outcome variables and also pooled to give a combined ES for each intervention. Forest plots were presented for each outcome measure and intervention. Publication bias was not assessed.

How were differences between studies investigated?
Statistical between-study heterogeneity was assessed using the Cochran Q test. A Mann-Whitney U-test was used to assess whether differences between the study results (positive or negative) were associated with quality scores.

Results of the review
Sixty-six RCTs (3,261 participants) were included in the analysis. There were 19 trials of epidural analgesia, 15 trials of peripheral local anaesthetic, 7 trials of systemic NMDA receptor antagonists, 17 trials of systemic NSAIDs and 8 trials of systemic opioids.

The validity assessment showed a median quality score of 4 (range: 2 to 7); this was the same for studies that favoured pre-treatment or post-treatment. The proportion of trials favouring pre-treatment and post-treatment did not differ significantly (Mann-Whitney U-test, P=0.7). There was also no significant difference between higher quality trials (range: 5 to 7) and lower quality trials (range: 2 to 4) (P=0.44).

Not all trials measured all three outcome measures. Fifty trials measured pain intensity, 44 measured supplemental analgesic requirement and 28 trials measured time to first analgesic as one of the outcome measures. The authors reported that, whilst epidural analgesia showed improvements in all three outcome measures, local anaesthetic wound infiltration and the use of NSAIDs were effective only in improving supplemental analgesic use and time to first rescue dose. The results were equivocal for the use of systemic NMDA antagonist and opioids. Further details were supplied in the paper.

The following represents the combined results from each analgesic intervention type for all three outcome measures. Where the point estimate and confidence interval (CI) exceeded 0, the effect was deemed to be statistically significant.

Data from 19 epidural analgesia trials (reflecting 37 combined outcome variables) showed a combined ES of 0.38 (95% CI: 0.28, 0.47, P< 1E-8), which suggested a highly significant difference in favour of pre-treatment. Fifteen trials of local anaesthetic wound infiltration (26 combined outcome variables) revealed a combined ES of 0.29 (95% CI: 0.17, 0.40, P=0.000001). Seven trials of NMDA antagonist use (16 combined outcome variables) showed a combined ES of 0.09 (95% CI: -0.03, 0.22, P=0.12). Seventeen trials involving the use of NSAIDs (30 combined outcome variables) revealed a combined ES of 0.39 (95% CI: 0.27, 0.48, P< 1E-8), again reflecting a highly significant difference in favour of pre-treatment. Finally, in 8 trials of opioid use (13 combined outcome variables), the combined ES was -0.10 (95% CI: -0.26, 0.07, P=0.25).

Cost information
None. However, the potential economic impact of conclusions regarding the reduction of supplemental analgesic use was discussed.
Authors' conclusions
On the basis of the outcome measures used, preemptive analgesia provided a beneficial effect in selected regimens. The most convincing effect was found for epidural analgesia, local wound infiltrations and systemic NSAID administration.

CRD commentary
The review question was clearly stated for this review. However, the lack of reported inclusion criteria for participants meant that a wide range of surgical patients were included. Whilst this might be a useful approach in terms of generalisability, more information might have been helpful on the relationship between the type of surgery and the results. Several appropriate sources were searched for relevant studies. The fact that only articles published in English were included may mean that important studies were missed; publication bias could not be ruled out. The review process was reported to be based on Cochrane Collaboration methods, but no further details were given on the actual procedures employed for the selection and data extraction of the papers. Studies of reasonable quality were presented in detail and some sources of heterogeneity were explored. However, the process of applying the specified validity measurement tool was not reported.

The synthesis of the data (approached in two stages) seemed appropriate and the results supported the authors’ main conclusions. The reliability of these conclusions is unclear, given the potential uncertainties in the review process.

Implications of the review for practice and research
Practice: The authors stated that preemptive epidural analgesia provided potential clinical and economic benefits in managing post-operative pain, decreasing the requirement for supplemental analgesia and prolonging the time to the first rescue dose. The use of preemptive local analgesia and NSAIDs can also provide benefits in clinical practice.

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

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