Efficacy and safety of patient-controlled opioid analgesia for acute postoperative pain: a quantitative systematic review

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Authors' objectives
To analyse the efficacy and safety data on patient-controlled devices for opioid analgesia, compared with conventional opioid analgesia, in post-operative patients.

Searching
The authors searched MEDLINE to January 2000, EMBASE to January 2000, and the CENTRAL Register in the Cochrane Library (2000, Issue 1). The search terms were restricted to 'PCA' and 'Patient-Controlled Analgesia' in the title, combined with the free text term 'random*'. Publications in any language were considered. Additional studies were identified by examining the bibliographies of retrieved reports, a previous meta-analysis and relevant review articles. The authors did not contact either the manufacturers of the PCA devices, or the authors of the primary studies, and they did not search for unpublished data.

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

Specific interventions included in the review
Studies in which an opioid administered intravenously using patient-controlled analgesia (PCA) devices was compared with the same opioid given subcutaneously, intravenously or intramuscularly, were eligible for inclusion. Comparisons between different opioids, with another route of administration, with combined control treatments, or with other techniques of analgesia, were excluded.

The following opioids were compared in the included studies: morphine (bolus 0.5 to 2.5 mg, lock-out 5 to 15 minutes); pethidine (bolus 8 to 20 mg, lock-out 5 to 20 minutes); piritramide (bolus 1.5 to 2 mg, lock-out 10 to 20 minutes); nalbuphine (bolus 2 mg, lock-out 10 minutes); and tramadol (bolus 30 mg, lock-out 5 minutes).

Participants included in the review
Post-operative patients. Trials were performed in a variety of surgical settings.

Outcomes assessed in the review
The authors did not report clear inclusion and exclusion criteria in terms of the outcomes. The outcomes of interest appeared to be: opioid consumption; pain intensity at rest; duration of hospital stay; patient satisfaction, including preference, different qualities of decreased pain intensity, different qualities of increased pain relief, and need for rescue analgesics; and adverse effects.

How were decisions on the relevance of primary studies made?
Abstracts of retrieved reports were screened by two authors.

Assessment of study quality
Methodological validity was assessed using the 5-point, 3-item Oxford scale of Jadad et al. (see Other Publications of Related Interest no.1). The scale took into account proper randomisation, double-blinding, and the reporting of withdrawals. The minimum score of an included RCT was 1, and the maximum score was 5. All four authors independently assessed the methodological validity of each included study. Consensus was reached by discussion.

Data extraction
The data were extracted by one investigator and checked by two others. Information was extracted on patients, PCA programmes and control regimens, efficacy data, and adverse effects. Both continuous and dichotomous efficacy data were extracted. Where possible, the continuous data were converted into dichotomous data. The data on adverse drug reactions were extracted only when reported in dichotomous form. The data on respiratory depression were analysed only when the end point was clearly defined.

Methods of synthesis
How were the studies combined?
For the continuous data, the weighted mean differences (WMD) with 95% confidence intervals (CIs) were calculated when both the mean and standard deviation (or standard error) were reported. For the dichotomous data, the relative risk (RR) was calculated along with the 95% CIs. The number-needed-to-treat (NNT) was calculated for the dichotomous efficacy and harm data using the weighted means of the pooled event rates.

How were differences between studies investigated?
A fixed-effect model was used when data from no more than two trials were combined or when the data were homogeneous (p>0.1). A random-effects model was used in all other situations.

Results of the review
Thirty-two RCTs (n=2,111) were eligible for inclusion.

The quality scores ranged from 1 to 3.

Opioid consumption.
Eight trials (n=430) reported the cumulative morphine consumption during the first 20- to 24-hour post-operative period, and 7 trials (n=81) reported the consumption during the 42- to 55-hour period. For both periods, there was no significant difference between the PCA and control groups. The WMDs were 5.53 mg (95% CI: -0.20, +11.3) and 9.43 mg (95% CI: -15.2, +34.0), respectively. Three trials (n=314) reported the cumulative pethidine consumption during the first 24 hours; there was no significant difference between the PCA and control groups (WMD -23.5 mg, 95% CI: -146.5, +99.6)).

Continuous efficacy data.
Six morphine trials (n=328) reported the average pain intensity at 24 hours, and 4 trials (n=259) reported the outcome at 48 hours. There was no significant difference between the PCA and control groups at either time point. The WMDs (0- to 10-point visual analogue scale) were -0.50 (95% CI: -1.51, +0.51) and -0.13 (95% CI: -0.60, +0.34), respectively. Three morphine trials (n=228) and 2 pethidine trials (n=128) reported on the duration of hospital stay. There was no difference between the PCA and control treatments (WMD -0.10 days (95% CI: -0.39, +0.18).

Dichotomous efficacy data.
Data on patient satisfaction were reported in 3 morphine trials (n=231). The difference between the PCA and control groups was not significant (RR 1.04, 95% CI: 0.92, 1.18; NNT 30, 95% CI: 7.5, -15). Patient preference was reported in 3 morphine trials and 1 pethidine trial (n=352). The data were in favour of PCA when combined in a random-effects model; the RR was 1.41 (95% CI: 1.11, 1.80) and the NNT was 4.2 (95% CI: 3.1, 6.4). When three of the pain outcomes (pain intensity, pain relief and rescue analgesic) were combined using a random-effects model (n=691), the data were also in favour of PCA; the RR was 1.22 (95% CI: 1.00, 1.50) and the NNT was 7.6 (95% CI: 5.1, 15). However, it must be borne in mind that the results were not statistically significant when the data on pain intensity and pain relief were combined. Two morphine trials (n=147) reported on pulmonary complications. When data were pooled, there was a statistically-significant result in favour of PCA; the RR was 1.07 (95% CI: 1.01, 1.14) and the NNT was 15 (95% CI: 8.1, 98).

Adverse effects.
Bradypnoea, hypoxia, nausea and/or vomiting, sedation, pruritus, and urinary retention occurred with both the PCA and control treatments. There was no evidence of any difference between the two analgesic techniques.

**Authors’ conclusions**

These trials provided some evidence that PCA with opioids, compared with conventional opioid treatment, improved analgesia and decreased the risk of pulmonary complications in the post-operative pain setting. The trials also indicated that patients preferred PCA.

**CRD commentary**

Generally, the methodology of this review was mixed. The authors reported a clear review question but it was unclear what the primary outcome of interest was. The search was comprehensive but the authors did not undertake an assessment of publication bias. Study validity was adequately assessed, and the data were well described in tabular format.

A large variety of different analgesia end points were reported in the included studies. However, the manner in which the data were combined did not always appear to be appropriate (i.e. all pain outcomes combined). Sources of heterogeneity were not adequately investigated; it is not sufficient to simply use a random-effects model as this does not explain why the heterogeneity exists (see Other Publications of Related Interest no.2). There appears to be an error in the reporting of the NNT for patient satisfaction, since the reported value (30) lies outside of the confidence range (95% CI: 7.5, 15).

The authors’ conclusions follow on from the results but should be viewed with caution due to the methodological limitations outlined.

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

Practice: The authors did not state any implications for practice.

Research: The authors state that more data are needed on the cost-effectiveness of both acute pain services and PCA pumps. In addition, further trials are needed to identify patients who are most likely to profit from PCA. These should be in the form of randomised trials of a reasonable size, reporting on all important outcomes, including long-term results.

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**Other publications of related interest**

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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.