Efficacy of postoperative epidural analgesia

CRD summary
This review evaluated the efficacy of post-operative epidural analgesia. The authors concluded that epidural analgesia (with the exception of thoracic epidural analgesia with opioids for thoracic surgery) was associated with significantly better post-operative analgesia than parental opioids. However, limitations in the review process and an inappropriate analysis mean that the conclusions cannot be considered reliable.

Authors' objectives
To compare the efficacy of post-operative epidural analgesia with parenteral opioids.

Searching
PubMed was searched from 1966 to April 2002 for English language articles. The reference lists of retrieved articles and the authors' personal files were checked for additional studies.

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

Specific interventions included in the review
Studies that compared post-operative epidural with parenteral opioid analgesia were eligible for inclusion. Epidural analgesia was defined as medicine delivered to the epidural space by infusion, patient-controlled analgesic device, or by repeated bolus dosing. Studies of a single epidural dose given at the time of surgery were excluded. Parenteral analgesia was defined as opioid drugs given by infusion, patient-controlled analgesic device, or by bolus dosing via the intravenous, subcutaneous, or intramuscular route. The opioids used included morphine, fentanyl and sufentanil.

Participants included in the review
Studies of adults aged 18 years or older were eligible for inclusion. Participants undergoing abdominal surgery, thoracic or lower extremities surgery, Caesarean delivery, pelvic or spinal surgery, or multiple site surgery were included in the review.

Outcomes assessed in the review
Studies that evaluated pain using a visual analogue scale (VAS), or a similar numerical rating scale, were eligible for inclusion. Major and minor complications were also evaluated in the included studies.

How were decisions on the relevance of primary studies made?
The authors stated that one reviewer assessed the relevance of each retrieved article. However, they also stated that any disagreements were resolved by the agreement of at least two reviewers. It was therefore not clear how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction.
Data on mean VAS pain scores on days 1 to 5 (rest and incident) were extracted from each study and converted to a 0 to 100 scale. If a study measured pain at several time points then all patient observations were included in the analysis.

Data on major and minor complications were extracted as reported in each included study, and used to calculate an incidence rate where sufficient data allowed. Major complications were death, stroke, cardiovascular, pulmonary and renal complications, deep vein thrombosis and pulmonary embolism. Minor complications were nausea or vomiting, confusion or delirium, sedation, pruritus, constipation, urinary retention, headache, backache, and motor block or weakness. If a study reported both nausea and vomiting the highest number was used.

Data on surgical site, location of epidural (thoracic or lumbar), type of epidural infusion (opioid, local anaesthetic, combination of local anaesthetic and opioid) and parenteral route (intravenous, including intravenous patient-controlled analgesia; subcutaneous or intramuscular) were also extracted from each included study.

**Methods of synthesis**

**How were the studies combined?**

To compare the effectiveness of epidural analgesia with parenteral opioids, the results from the individual studies were combined using a fixed-effect meta-analysis. A weighted mean difference (WMD) and 95% confidence interval (CI) were calculated for all studies and observations combined, and for each surgical site (thoracic, abdominal, pelvic and Caesarean delivery, and lower extremity).

To compare the effectiveness of epidural analgesia with parenteral opioids during the recovery period (up to 4 days after surgery), the Mann-Whitney test was used to compare the global mean VAS score between the treatment groups at each post-operative day. A Bonferroni correction was used to account for multiple comparisons.

The incidence rates of complications were compared using an independent t-test weighted by sample size. The results were tabulated and discussed narratively.

The possibility of publication bias was investigated using Rosenthal's fail-safe N technique and funnel plots.

**How were differences between studies investigated?**

Subgroup analyses were performed for each surgical site to determine the effect on post-operative pain control of the following:

- analgesic agent, i.e. local analgesia with or without opioid versus opioid alone;
- location of catheter insertion in relation to surgical incision, i.e. thoracic epidural analgesia (TEA) versus lumbar epidural analgesia (LEA); and
- type of pain assessment, i.e. at rest versus incident pain.

**Results of the review**

One hundred RCTs were included in the review (the number of patients was not provided).

All surgical sites.

Epidural analgesia was associated with significantly better post-operative analgesia than parenteral opioids (WMD 10, 95% CI: 9.5, 10.5, P<0.001), based on all studies and observation points. Analysis by post-operative day also found that epidural analgesia was significantly better than parenteral opioids for each time point after surgery (P<0.01). There was no significant difference between intravenous patient-controlled analgesia and intramuscular or subcutaneous opioid administration (data not provided).

Thoracic surgery (TEA 18 RCTs; LEA 9 RCTs).

TEA was associated with significantly better post-operative pain control compared with parenteral opioids when using
LEA was associated with significantly better post-operative pain control compared with parenteral opioids when using local anaesthetic with or without opioid (WMD 11.2, 95% CI: 9.9, 12.5, P<0.001), or opioids alone (WMD 2.9, 95% CI: 0.4, 5.3, P=0.002).

LEA was associated with significantly better post-operative pain control compared with parenteral opioids when using opioids alone (WMD 4.2, 95% CI: 2.2, 6.2, P<0.001).

When categorised by method of pain assessment, TEA and LEA were generally associated with significantly better post-operative rest and incident pain control than parenteral opioids when using local anaesthetic with or without opioid (P<0.001), or opioids alone (P<0.001). The exception was TEA with opioids alone for rest pain (WMD 0.6, 95% CI: -3, 1.5, P=0.12).

Abdominal surgery (TEA 21 RCTs; LEA 8 RCTs).

TEA was associated with significantly better post-operative pain control compared with parenteral opioids when using local anaesthetic with or without opioid (WMD 10.9, 95% CI: 10.1, 11.6, P<0.001), or opioids alone (WMD 6.7, 95% CI: 3.4, 9.6, P<0.001).

LEA was associated with significantly better post-operative pain control compared with parenteral opioids when using local anaesthetic with or without opioid (WMD 17.8, 95% CI: 15.8, 19.9, P<0.001), or opioids alone (WMD 8.5, 95% CI: 6.2, 10.8, P<0.001).

When categorised by method of pain assessment, TEA and LEA were associated with significantly better post-operative rest and incident pain control compared with parenteral opioids when using local anaesthetic with or without opioid (P<0.001), or opioids alone (P<0.001).

Pelvic and Caesarean delivery (TEA 2 RCTs; LEA 23 RCTs).

TEA was associated with significantly better post-operative pain control compared with parenteral opioids when using local anaesthetic with or without opioid (WMD 10.5, 95% CI: 7.1, 14.0, P<0.001).

LEA was associated with significantly better post-operative pain control compared with parenteral opioids when using local anaesthetic with or without opioid (WMD 7.2, 95% CI: 5.8, 8.6, P<0.001), or opioids alone (WMD 8.6, 95% CI: 7.2, 10.1, P<0.001).

When categorised by method of pain assessment, TEA and LEA were associated with significantly better post-operative rest and incident pain control compared with parenteral opioids when using local anaesthetic with or without opioid (P<0.001), or opioids alone (P<0.001).

Lower extremity surgery (LEA 13 RCTs).

LEA was associated with significantly better post-operative pain control compared with parenteral opioids when using local anaesthetic with or without opioid (WMD 12.6, 95% CI: 10.1, 15.0, P<0.001), or opioids alone (WMD 9.4, 95% CI: 6.8, 11.9, P<0.001).

When categorised by method of pain assessment, LEA was associated with significantly better post-operative rest and incident pain control compared with parenteral opioids when using local anaesthetic with or without opioid (P<0.01), or opioids alone (P<0.01).

Complications. The rates for all complications were relatively low across the included studies. The incidence rate of nausea or vomiting was significantly lower with local anaesthetic LEA than with parenteral opioids. No difference was found for TEA with local anaesthetic with or without opioid, or LEA with opioid alone.

Epidural analgesia was associated with a significantly higher incidence rate of pruritus compared with parenteral analgesia. LEA with opioid alone was associated with a 6-fold increased incidence from parenteral opioid (38% versus 6%, P<0.001).

Epidural analgesia was associated with higher incidence of motor block or numbness compared with epidural. The rate...
of numbness was higher in those given LEA with opioid alone.

TEA with local anaesthetic, with or without opioid, was associated with an increased rate of hypotension compared with parenteral analgesia. However, the overall incidence of hypotension was low.

The authors stated that there were insufficient data to evaluate return of function, major complications, and several other minor complications including confusion-delirium, sedation, constipation, urinary retention, headache and backache.

Publication bias.

It was estimated that additional trials with at least 94,273 participants demonstrating no statistical difference between treatment regimens would be required to invalidate the results of this review. The funnel plot did not suggest the presence of publication bias.

**Authors’ conclusions**

Epidural analgesia (with the exception of TEA with opioids for thoracic surgery) provided a significant and clinically significant improvement in post-operative pain control compared with parenteral opioids, irrespective of analgesic regimen, location of catheter placement in relation to site of surgical incision, or type of pain assessment.

**CRD commentary**

The review addressed a clear question and the inclusion criteria appear appropriate. The search was limited to one electronic database and to English language articles, although the authors did not find evidence of publication bias among the studies included in the review. However, given the subject area, it is highly likely that additional studies have been published in languages other than English, thus suggesting that some relevant studies might have been overlooked. Discrepancies in the reporting of the review process meant that it was unclear whether methods were used to minimise bias in the selection of studies for inclusion. In addition, details of the data extraction processes were not reported, which meant the potential for reviewer error or bias could not be assessed. No formal quality assessment was performed, thus it was not possible to assess the validity of the included studies.

There was limited information on the characteristics of the included studies, although the authors reported that further details are available upon request. This made it difficult to assess whether pooling the studies was appropriate. However, the methods used to pool the results were inappropriate, as individuals from the same study were included more than once in the same analysis. Therefore, the authors’ conclusions could not be considered reliable.

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

Practice: The authors stated that, given the high number of annual surgical procedures performed, physicians should be aware of the analgesic benefits and potential risks of epidural analgesia when discussing options for post-operative pain management with patients.

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

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