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## Effects of preemptive epidural analgesia on post-thoracotomy pain

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### CRD summary

The authors concluded that preemptive thoracic epidural analgesia (TEA) appeared to reduce the severity of acute post-operative pain compared with TEA initiated after completion of surgery for patients undergoing unilateral thoracotomy, but did not affect the incidence of chronic post-thoracotomy pain. Overall, the review was well-conducted and the authors' cautious conclusions appear appropriate.

### Authors' objectives

To determine whether preemptive thoracic epidural analgesia (TEA) initiated before surgical incision reduces the severity of acute post-thoracotomy pain and incidence of chronic post-thoracotomy pain compared with TEA initiated after completion of surgery.

### Searching

MEDLINE, EMBASE and the Cochrane CENTRAL Register (Issue 3, 2004) were searched from inception to December 2004; the search terms were reported. No language restrictions were employed. In addition, the references of all relevant articles were checked.

### 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 that compared preemptive TEA with TEA initiated after completion of surgery were eligible for inclusion. Studies comparing TEA only to non-epidural methods of analgesia were excluded from the review, as were studies that examined the effects of lumbar epidural analgesia for upper abdominal surgery. The included studies evaluated epidural analgesics inserted at the upper thoracic level. The intervention groups used bupivacaine, adrenaline and alfentanil; mepivacaine; bupivacaine and morphine; and bupivacaine and fentanyl. The control groups used bupivacaine and fentanyl; mepivacaine; and bupivacaine and morphine. Some of the included studies maintained post-operative analgesia with patient-controlled epidural analgesia.

#### Participants included in the review

Studies of adult patients undergoing unilateral thoracotomy were eligible for inclusion. Studies with mixed patient populations in which data for those undergoing thoracotomy were not reported separately were excluded from the review. The included studies were all of patients undergoing elective open thoracotomy.

#### Outcomes assessed in the review

Studies that reported acute pain scores in the immediate post-operative period up to 48 hours after surgery and the incidence of chronic pain 6 months after surgery were eligible for inclusion. The included studies also reported acute post-operative pain on coughing at 24 and 48 hours post-surgery and adverse events. The included studies assessed pain using visual analogue scales or numeric rating scales.

#### How were decisions on the relevance of primary studies made?

Two reviewers independently assessed studies for relevance. Any disagreements were discussed with a third reviewer and resolved through consensus.

### Assessment of study quality

Two reviewers independently assessed the validity of the studies. Any disagreements were discussed with a third

reviewer and resolved through consensus. The criteria employed were allocation concealment, randomisation, blinding, use of intention-to-treat analysis, and loss to follow-up.

### Data extraction

Three reviewers independently extracted the data. Authors were contacted for additional data where necessary. Data on mean pain scores at 24 and 48 hours, together with standard deviations (SD), were extracted where reported. The number of patients pain-free at 6 months post-operatively was also extracted. Weighted mean differences (WMDs) and 95% confidence intervals (CIs) were calculated for acute pain, whilst relative risks (RRs) and 95% CIs were calculated for chronic pain.

### Methods of synthesis

#### How were the studies combined?

The studies reporting adequate data were combined in fixed-effect meta-analyses where no statistical heterogeneity was detected, and in random-effects analyses where such heterogeneity was detected. A narrative discussion of the included studies was also provided.

#### How were differences between studies investigated?

Differences between the studies were discussed in the narrative synthesis and statistical heterogeneity between the studies was examined using I-squared tests. A sensitivity analysis was performed: this excluded a study in which no opioid was used.

### Results of the review

Six RCTs with a total of 458 patients were included in the review. Five RCTs were included in the meta-analyses (n=355 with adequate data)

In terms of study quality, 4 studies reported prior power analysis, two reported adequate allocation concealment, five were at least double-blinded and three used intention-to-treat analysis. One study reported no exclusions from analysis; rates of exclusion from analysis in the other 5 studies ranged from 17 to 23.6%.

Acute pain at rest at 24 hours post-surgery (5 studies).

There was no significant difference between interventions in acute pain at rest at 24 hours (WMD -0.27, 95% CI: -0.91, 0.37; favours preemptive TEA). A sixth study, which could not be pooled, also showed no significant difference between the groups. Statistically significant heterogeneity between the studies was detected (I-squared 98.6%). The results of the analysis were not changed by the exclusion of a study in which no opioid was used.

Acute pain at rest at 48 hours post-surgery (5 studies).

There was a significant reduction in acute pain in the preemptive TEA group (WMD -0.59, 95% CI: -1.14, -0.04). Statistically significant heterogeneity between the studies was detected (I-squared 98.2%). The sensitivity analysis, which excluded a study in which no opioid was used, showed no significant difference between the groups (WMD -0.08, 95% CI: -0.30, 0.14).

Acute post-operative pain on coughing (2 studies).

There was a significant reduction in pain on coughing in the preemptive TEA group at 24 hours (WMD -1.17, 95% CI: -1.50, -0.83) and at 48 hours (WMD -1.08, 95% CI: -1.17, -0.99). No statistically significant heterogeneity was detected.

Chronic pain at 6 months post-surgery (3 studies).

The pooled RR showed no statistically significant difference between the groups (RR 1.32, 95% CI: 0.76, 2.30). Statistically significant heterogeneity between the studies was detected (I-squared 73.6%). The results of the analysis were not changed by the exclusion of a study in which no opioid was used.

Adverse events (4 studies).

There were few adverse events and no epidural catheter-related complications.

### **Authors' conclusions**

Preemptive TEA appeared to reduce the severity of acute pain but did not affect the incidence of chronic pain.

### **CRD commentary**

The review question and the inclusion criteria were clear and the search was adequate. Attempts were made to minimise language bias, but no specific attempts to reduce publication bias were reported. The authors used appropriate methods to minimise reviewer bias and error in the study selection, validity assessment and data extraction processes of the review. Appropriate criteria were employed to assess the validity of the included studies but, although the results of this assessment were reported, study validity was not considered in the statistical analysis. The decision to employ meta-analysis seemed appropriate and reasonable steps were taken to explore study heterogeneity. This was a well-conducted review and the authors' cautious conclusions appear appropriate.

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

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

Research: The authors stated that a large RCT designed to evaluate the effects of preemptive TEA would be required to determine whether preventing acute pain would reduce the risk of chronic pain. Any such study should be adequately powered to detect a significant difference in acute pain, and should have a follow-up period of sufficient length to detect a difference in the incidence of chronic pain.

### **Bibliographic details**

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