Effect of epidural vs parenteral opioid analgesia on the progress of labor: a meta-analysis
Halpern S H, Leighton B L, Ohlsson A, Barrett J R, Rice A

Authors' objectives
To review the effects of epidural versus parenteral opioid analgesia on Caesarean delivery rates.

Searching
MEDLINE (January 1966 to January 1998) was searched using the following search terms as MeSH terms and textwords: 'analgesia, obstetrical', 'analgesia, epidural', 'Caesarean delivery', 'analgesics, opioid'. Additional references were sought in the Cochrane Library (September 1997), the personal files of the authors, and the reference lists of previously published reviews. The tables of contents of the International Journal of Obstetrical Anesthesia (inception to December 1997), which is not abstracted by MEDLINE, were searched by hand. Published abstracts (1993-1997) from the following meetings were reviewed: Canadian Anaesthetists Society, American Society of Anesthesiologists, Society of Obstetric Anesthesia and Perinatology, and Society of Perinatal Obstetricians.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) comparing epidural anaesthesia with parenteral opioids for labour pain relief.

Specific interventions included in the review
Epidural anaesthesia and parenteral opioids for labour pain relief.

Participants included in the review
Nulliparous and multiparous pregnant women in labour. Both labour induced and non-induced women were included.

Outcomes assessed in the review
The primary outcome was the incidence of Caesarean delivery for any indication. Secondary maternal outcomes included Caesarean delivery rate for dystocia, total instrumented delivery rate for dystocia, instrumented delivery rate for dystocia, use of oxytocin after initiation of analgesia, the length of the first and second stages of labour, fever (temperature >38.0 degrees Celsius), hypotension, nausea, pain during the first and second stages of labour and satisfaction. Perinatal outcomes included the incidence of 1- and 5-minute Apgar scores less than 7, umbilical artery pH of less than 7.15 or 7.20, presence of meconium at delivery, foetal heart rate abnormalities during labour, and early (2 to 4 hours) and late (24 hours) infant neuroadaptive capacity scores.

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

Assessment of study quality
Trials were scored using a quality index developed by Jadad et al. (see Other Publications of Related Interest no.1). This scale has a maximum score of 5 points, with 0 to 2 points assigned for the quality of the methods of randomisation and blinding (0, inappropriate; 1, not described; 2 appropriate method) and 1 point given if the study described the outcome of all enrolled participants. Each trial was scored independently by two authors. When initial scores differed, a final score was arrived at by consensus.

Data extraction
Two authors independently extracted data, with any discrepancies resolved by reinspection of the original articles. Data were entered into the statistical programme by one author, and checked by the other.
Methods of synthesis

How were the studies combined?
The studies were combined using a random-effects model. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated for dichotomous variables using the method of DerSimonian and Laird (see Other Publications of Related Interest no.2).

The weighted mean difference (WMD) (random-effects model) and 95% CIs were calculated for continuous variables. A statistical difference between groups was considered to occur if the pooled 95% CI did not include 1 for the OR or 0 for the WMD. An OR of less than 1 or a negative WMD favoured epidural over control.

How were differences between studies investigated?
Tests for heterogeneity were performed using the Breslow-Day method (see Other Publications of Related Interest no.3).

Nulliparous and multiparous patients were analysed as subgroups of the total sample.

Three sensitivity analyses were performed on the primary outcome (total Caesarean delivery rate): high-quality trials only (Jadad score greater than or equal to 3), peer-reviewed articles only, and trials grouping patients by intent-to-treat only.

Results of the review

Ten RCTs enrolling 2,369 patients were included.

There was evidence of heterogeneity among the trials (p<0.05) for the primary outcome of total Caesarean delivery rate. Much of this heterogeneity was attributable to one of the smaller trials, which showed a marked Caesarean delivery rate increase in the epidural group.

Caesarean delivery rate: the total rate of Caesarean delivery did not differ between patients receiving epidural analgesia (8.2%) versus parenteral opioids (5.6%) for labour (OR 1.50, 95% CI: 0.81, 2.76). There was no difference between treatment groups in the rate of Caesarean delivery for dystocia (OR 1.63, 95% CI: 0.79, 3.36).

There was no statistically significant difference in the overall Caesarean delivery rate for nulliparous women (n=1,025): 44 (8.5%) of 516 in the epidural group versus 39 (7.7%) of 509 in the parenteral opioid group (OR 1.28, 95% CI: 0.55, 2.93). For multiparous women (n=364), the Caesarean delivery rate was 4 (2.2%) of 178 in the epidural group versus 5 (2.7%) of 186 in the parenteral opioid group (OR 0.83, 95% CI: 0.22, 3.15).

Sensitivity analyses: of 2,001 patients in published studies, the Caesarean delivery rate was 79 (7.9%) of 999 in the epidural group and 43 (4.3%) of 1,002 in the parenteral opioid group (OR 1.90, 95% CI: 0.93, 3.86). In studies with a Jadad quality score of 3 or better (a total of 1,317 patients), the Caesarean delivery rate was 55 (8.2%) of 668 in the epidural group and 48 (7.2%) of 669 in the parenteral opioid group (OR 1.33, 95% CI: 0.63, 2.81). Of studies grouping patients by intent-to-treat (a total of 1,500 patients), the Caesarean delivery rate was 58 (7.7%) of 751 in the epidural group and 50 (6.7%) of 749 in the parenteral opioid group (OR 1.27, 95% CI: 0.66, 2.46).

Other maternal outcomes: the first and second stages of labour were longer in patients who had epidural analgesia compared with those who did not. The weighted mean differences were 42 minutes (95% CI: 17, 68, p=0.02) and 14 minutes (95% CI: 5, 23, p=0.003) respectively. Hypotension (OR 74.2; 95% CI: 4, 1375, p<0.001), fever (OR 5.35, 95% CI: 3.67, 7.80, p<0.001) and oxytoxin use (OR 1.80, 95% CI: 1.01, 3.21, p=0.04) after analgesia were more frequent in patients receiving epidural analgesia. The total incidence of instrumented delivery was significantly higher in the epidural group (OR 2.19, 95% CI: 1.32, 7.78, p=0.02), but there was no difference in the incidence of instrumented delivery for dystocia (only 2 studies).

Opioid analgesia provided poor pain relief in both the first and second stages of labour. Patients receiving epidural analgesia had significantly lower visual analogue pain scores in both the first (WMD -40 mm, 95% CI: -38, -42, p<0.001) and second (WMD -29 mm; 95% CI: -21, -38, p<0.001) stages of labour. Similarly, fewer patients were dissatisfied with the analgesic method when they received epidural anaesthesia (OR 0.25, 95% CI: 0.20, 0.32, p<0.001).
Neonatal outcomes: There were no differences in the incidence of foetal distress or the intrapartum passage of meconium between the two groups. Significantly fewer infants were born with 1- and 5-minute Apgar scores of less than 7 in the epidural group compared with the parenteral opioid group. The ORs were 0.54 (95% CI: 0.35, 0.82, p=0.001) and 0.38 (95% CI: 0.18, 0.81, p=0.003) respectively. Naloxone was used less often in the newborns of patients receiving epidural analgesia (OR 0.24, 95% CI: 0.07, 0.77, p<0.001). There was no difference between groups in either the early or 24-hour measurement of the neuroadaptive capacity score (only 87 infants were tested). A low umbilical artery pH (<7.15 or 7.20) was recorded less commonly among neonates born after epidural analgesia than after parenteral opioids (OR 0.76, 95% CI: 0.60, 0.97, p=0.04). Only four infants (two from each group) had severe asphyxia, indicated by an umbilical artery pH of less than 6.99. There were no reports of serious neonatal complications related to either analgesic method.

Authors' conclusions
Epidural analgesia is not associated with increased rates of instrumental vaginal delivery for dystocia or Caesarean delivery. Patients receiving epidural analgesia have longer labours. Patient satisfaction and neonatal outcome are better after epidural than parenteral opioid analgesia.

CRD commentary
The review focuses on a well defined question. The validity of included studies was adequately assessed, and subsequent sensitivity analyses were performed.

The literature search was fairly extensive and there is little risk of publication bias, given that published and unpublished data was included. However, the search could also have included other databases, such as EMBASE, and experts in the field could have been contacted to identify recently produced research. Intervention and outcome inclusion criteria were appropriate, but specific participant inclusion criteria and the number of authors who assessed studies for inclusion were not stated. Details of individual studies were presented, although it may also have been useful to provide the age of participants. Studies were combined despite the presence of heterogeneity.

The results and conclusions should be interpreted with caution due to the fact that heterogeneous studies have been pooled.

Implications of the review for practice and research
Practice: The authors state that a policy of withholding epidural analgesia will not reduce Caesarean delivery rates.

They also note that parenteral opioid labour analgesia is not innocuous. Parenteral opioids are associated with poor maternal pain relief and less vigorous neonates. This information should be available to women so that they can make informed choices about labour pain relief.

Research: The authors state that further well-controlled prospective trials are needed to define the mechanisms, magnitude, and clinical relevance of epidural-associated maternal temperature disturbances.

Bibliographic details

PubMedID
9875879

Original Paper URL
http://jama.ama-assn.org/

Other publications of related interest

**Indexing Status**

Subject indexing assigned by NLM

**MeSH**

Analgesics, Opioid /administration & dosage; Anesthesia, Epidural; Anesthetics, Local /administration & dosage; Cesarean Section /statistics & numerical data; Delivery, Obstetric; Dystocia; Female; Humans; Injections, Epidural; Injections, Intramuscular; Injections, Intravenous; Labor, Obstetric; Pregnancy; Pregnancy Outcome; Randomized Controlled Trials as Topic; Risk

**AccessionNumber**

11999008372

**Date bibliographic record published**

31/03/2001

**Date abstract record published**

31/03/2001

**Record Status**

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