Analgesia in labour and fetal acid-base balance: a meta-analysis comparing epidural with systemic opioid analgesia

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Authors' objectives
To assess the effect of epidural analgesia during labour, compared with systemic opioid analgesia, on the funic acid-base status of babies at birth.

Searching
MEDLINE and EMBASE were searched, although it was not stated between what dates the searches were carried out. [A: MEDLINE was searched between 1966 and 2001, and EMBASE was searched from 1980 to 2001]. Published meta-analyses and reviews, and the authors' card index were also used to identify studies. Some keywords were reported.

Study selection
Study designs of evaluations included in the review
The inclusion criteria specified controlled clinical studies. Included in the review were randomised clinical trials (RCTs) and controlled clinical trials (CCTs). Studies were excluded where there was retrospective selection of the participants, where regional blocking was used, where there was incomplete reporting of statistical data, or where only the numbers of babies with a cord pH below a particular level were reported and further data could not be obtained.

Specific interventions included in the review
The inclusion criteria specified comparisons of epidurals with systemic analgesia during labour. Included in the review were both epidurals with local anaesthetic and without opioid, and low-dose local anaesthetic combined with opioid. All but one of the included studies used bupivacaine with either epinephrine, fentanyl or nothing as the epidural. The remaining study used lidocaine and epinephrine. The control groups received one or more of the following: intramuscular or intravenous pethidine, chlorpromazine, promethazine, butorphanol, fentanyl, promazine, diazepam or inhaled nitrous oxide.

Participants included in the review
The inclusion criteria specified babies born to mothers receiving either an epidural or systemic analgesia during labour. It appears that the babies actually included in the review were those whose mothers were compliant with treatment allocation in the randomised trials. [A: The authors were also able to obtain data from one study for babies of non-compliant mothers].

Outcomes assessed in the review
The inclusion criteria specified funic acid-base balance of umbilical cord blood, assessing pH and base excess, from babies at birth.

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.

Assessment of study quality
The authors did not state that they assessed validity. [A: The authors did not assess validity.]

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction. The data extracted were maternal parity, mode of delivery, umbilical pH, base excess, type of trial, and details of the interventions and controls. The authors were contacted when incomplete data were published. Where raw
data were available, the effect of epidural use was re-estimated using a linear regression with robust standard errors. Where separate subgroup data were given, the mean and standard deviation were calculated for combined data and adjusted.

**Methods of synthesis**

How were the studies combined?
A random-effects model was used to combine the randomised trials and all trials. A funnel plot and Egger's test were used to assess whether publication bias was present.

How were differences between studies investigated?
A chi-squared test for heterogeneity was carried out on both the randomised and the non-randomised studies for both pH and base excess.

**Results of the review**

Thirteen studies (twelve published and one unpublished) with 3,041 mothers (2,257 compliant with treatment allocation) were included. Of these, 8 were RCTs (2,632 mothers; 1,848 compliant with treatment allocation) and 5 were CCTs (409 mothers). The authors stated that the babies of 2,102 mothers were included in the analysis. In one large study it was possible to obtain data on babies of non-compliant mothers whose inclusion did not affect the outcome of the analysis. As in published studies babies of non-compliant mothers were excluded, only babies of compliant mothers were included in the meta-analysis.

In randomised trials (8 studies), the pH difference of 0.009 (95% CI: 0.002, 0.015, P=0.007) favoured epidurals. There was no significant heterogeneity between the studies (values not reported).

In all trials (12 studies), the difference between the treatment groups was non significant. The pH difference was 0.004 (95% CI: -0.005, +0.014). There was significant heterogeneity among the studies (P=0.015).

In randomised trials (4 studies), the difference in base excess between treatment groups was 0.779 mEq/L (95% CI: 0.056, 1.502) in favour of epidurals. The authors did not report whether there was any heterogeneity between the studies.

In all trials (8 studies), the difference in base excess was 0.837 mEq/L (95% CI: 0.33, 1.343). There was significant heterogeneity between the studies (P=0.028).

**Authors’ conclusions**

Epidurals did not increase the level of foetal acidosis. They may provide some protection from foetal hypoxia.

**CRD commentary**

The search was adequate although the dates were not given in the paper. They were subsequently supplied by the authors. The attempts to contact authors for further data are likely to have reduced the possibility of reporting bias. The authors stated that they assessed publication bias, but did not report the results of this assessment. They also did not state that any language restrictions had been applied to the search, making language bias unlikely. The inclusion criteria were clear. However, because the authors did not state how the studies were judged for relevance or how the data were extracted from the studies, it is not possible to determine whether selection bias may have occurred. The authors did not state that they assessed the validity of the studies, but the randomised studies were grouped separately and also contributed to a meta-analysis of all studies. The fact that validity was not assessed may have implications for the reliability of the results of the meta-analyses. The meta-analysis conducted was appropriate and tests for heterogeneity were carried out, although reasons for heterogeneity were not explored. All published data were included as well as some unpublished results in the case of three studies. However, it is unclear why some babies in the original studies appear to have been omitted from the meta-analysis. The authors' conclusions are appropriate, although caution may be required for the reasons highlighted.
Implications of the review for practice and research
Practice: The authors stated that expectant mothers can be reassured that epidural analgesia is not harmful to babies.

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

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