Unintended effects of epidural analgesia during labor: a systematic review
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Authors' objectives
To review the literature relating to unintended effects of epidural and combined-spinal epidural techniques used to produce pain relief during labour in low-risk women.

Searching
A literature search was carried out in August 2000 and updated in May 2001. MEDLINE, Pre-MEDLINE, and Current Contents (Clinical Medicine) were searched using an extensive list of search terms, which were reported in the review paper. In addition, the Cochrane Pregnancy and Childbirth Group's Specialised Register was searched for randomised trials, and the bibliographies of included and review articles were examined for additional studies. Articles were limited to English language studies and to original reports published in peer-reviewed journals since 1980, except when neonatal outcomes were measured, in which case articles dating back to 1970 were included. Abstracts were excluded.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) and observational studies were eligible for inclusion. Studies with no control group, case-series studies and case reports were excluded. Studies with analytic choices that made results impossible to interpret, such as studies examining the association of epidural with length of labour or Caesarean delivery separately for women who received and did not receive oxytocin, were excluded if the data from the two groups could not be recombined.

Specific interventions included in the review
Studies investigating the effects of epidural analgesia were eligible for inclusion. Studies investigating specific drug regimens and epidurals administered to produce anaesthesia for Caesarean delivery were excluded.

Participants included in the review
Studies conducted exclusively in high-risk populations were excluded, as were studies where population selection renders results uninformative, e.g. where the criteria for inclusion were based on labour outcome (such as studies limited to women with spontaneous vaginal deliveries or to women who had an uncomplicated labour course).

Outcomes assessed in the review
The inclusion criteria relating to the outcomes were not specified. Studies investigating outcomes only for the overall population of delivering women were excluded.

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 of the reviewers performed the selection.

Assessment of study quality
All of the studies were reviewed with regard to methods, including the strengths of designs and analyses. No formal scoring system was used. The authors do not state how the validity assessment was performed.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the reviewers performed the data extraction. Relative risks (RRs) and confidence intervals (CIs) were calculated for studies when they were not presented.
Methods of synthesis

How were the studies combined?
A narrative synthesis was undertaken. Separate data, rather than combined data, were presented for nulliparous and multiparous women whenever possible.

How were differences between studies investigated?
Each study was weighted according to its overall methodological quality. In addition, some of the data from the studies were reanalysed to eliminate methodological differences.

Results of the review
The total number of studies meeting the inclusion criteria was not reported, and it is not clear from the tables presented.

Caesarean delivery outcomes (10 RCTs and 33 observational studies): the RCTs were either too small or did not allow a clear interpretation of the data. All 5 of the larger RCTs had major problems relating to protocol compliance: either a high proportion of women in the no-epidural group received an epidural or a high proportion of women in the epidural group did not receive an epidural. Few of the observational studies took confounding factors into consideration, but the 3 studies that did found a robust association between epidural and Caesarean delivery. The existing evidence provided insufficient evidence to determine whether an epidural does or does not tend to increase Caesarean delivery status.

Instrumental vaginal delivery outcomes (10 RCTs and 27 observational studies): 7 RCTs presented data for nulliparas. All the RRs were greater than 1 (range: 1.1 to 2.3), but not all reached statistical significance. Only one of the observational studies failed to find a statistically-significant association between epidural and instrumental vaginal delivery. For the 16 studies including only nulliparous women, the RRs ranged from 1.3 to 4.8. For the 4 studies including only multiparous women, the RRs ranged from 3.7 to 5.3. All 8 studies that limited the study population to women with vaginal deliveries also found statistically-significant associations between the use of epidural analgesia and instrumental vaginal delivery. The existing data support an association between epidural and instrumental vaginal delivery.

Spontaneous vaginal delivery outcomes (8 RCTs and 27 observational studies): in 4 of the 6 RCTs conducted in nulliparous women, the proportion of women with a spontaneous vaginal delivery was substantially higher in the control group than in the epidural group, with an additional 9 to 40% of women experiencing a spontaneous vaginal delivery. One of the 3 RCTs investigating spontaneous vaginal delivery in the RCTs with mixed parity populations found a statistically-significant lower rate of delivery in the epidural group.

Length of labour (8 RCTs and 16 observational studies): the 2 RCTs reporting only the overall length of labour found longer labours in women who receive epidural. Three of the 5 RCTs reporting on the length of the first stage of labour found somewhat longer lengths of labour with epidural. However, the data available were insufficient to provide definitive evidence. All 7 RCTs examining the length of second-stage labour found a longer length (range: 7 to 61 minutes) in the epidural group. However, methodological issues hampered the ability of the studies to estimate the magnitude of the difference in length. All observational studies consistently reported that both the first and second stage of labour were longer for women who receive epidural: the ranges for increases in the length of first- and second-stage labour were 2.5 to 4.4 hours and 30 to 45 minutes, respectively, for the 5 studies conducted in low-risk nulliparous women with spontaneous labour. The data concerning first-stage labour were insufficient to provide definitive evidence. However, the data strongly support the occurrence of longer second stages of labour among women who receive epidurals.

Intrapartum fever (2 RCTs and 6 observational studies): both the RCTs and all observational studies reported an increased incidence of intrapartum fever among women who received epidurals.

Foetal malposition (3 RCTs and 2 observational studies): one RCT found a 4-fold increase in the rate of malposition in the epidural group; the other 2 RCTs found smaller differences. Observational studies tended to find higher rates of malposition among women receiving epidurals.

Perineal laceration (5 cohort studies, 1 case-control study and 1 study limited to instrumental vaginal delivery): 5 of the 6 studies not limited to instrumental vaginal delivery found an association of epidural with perineal laceration, with the
RRs suggesting approximately a 2-fold increase. The evidence suggests that epidural use is associated with an increase in 3rd and 4th degree perineal lacerations.

Foetal outcomes: measures of foetal outcome taken immediately after birth did not indicate a difference in well-being associated with epidural use. No differences were found between infants of women receiving and not receiving epidural for either cord pH values or Apgar scores. The few studies examining the presence of meconium-stained amniotic fluid also did not note any difference. There was some evidence of an increase in foetal heart rate abnormalities among women who receive epidural.

Further results relating to epidural techniques and labour outcomes and maternal postpartum effects are reported in the review paper.

Authors’ conclusions
The authors state that much of the evidence is equivocal. Existing RCTs are either small, or do not allow clear interpretation of the data because of problems with protocol compliance. In addition, few observational studies control for the confounding factors that result because women who request epidural are different from women who do not.

There is considerable variation in the association of epidural with some outcomes, particularly those that are heavily practice-based. Despite this variation, there is sufficient evidence to conclude that epidural is associated with a lower rate of spontaneous vaginal delivery, a higher rate of instrumental vaginal delivery and longer labour, particularly in nulliparous women. Women receiving epidural are also more likely to have intrapartum fever and their infants are more likely to be evaluated and treated for suspected sepsis. There is insufficient evidence to determine whether epidural does or does not tend to increase the risk of Caesarean delivery or foetal malposition. Adverse effects on the foetus may occur in the subset of women who are febrile.

CRD commentary
The review objective was clearly set out. However, this was not supported by inclusion or exclusion criteria relating to the outcomes. The literature search was limited to English language studies and studies published in peer-reviewed journals, which means that relevant studies may have been omitted from the review. The total number of included studies was not reported and it was not clear from the tabulated information. The methodological quality of the studies was discussed, but there was no formal validity assessment. The results of the studies were synthesised in a narrative fashion according to the outcome assessed. No details relating to the review process (e.g. how decisions on the relevance of primary studies were made and how the data were extracted) were reported; this makes it impossible to determine how rigorous the process was and whether it may have led to potential bias in the results of the review. The authors' conclusions and the implications that they draw for practice need to be interpreted with some caution in light of the limitations discussed here.

Implications of the review for practice and research
Practice: The authors state that nulliparous women should be told that they are less likely to have a spontaneous vaginal delivery, that they are more likely to have an instrumental vaginal delivery, and that their labour is likely to be longer. They should also be informed of the implications of the higher rate of instrumental vaginal delivery, specifically the increased rate of serious perineal lacerations that accompany its use. Women should also be informed of the higher rate of intrapartum fever. They should be informed that if they develop a fever their infant may be more likely to be evaluated for sepsis, but that there is no evidence that epidural increases infection in mothers or infants. Epidural analgesia should be available as an option for pain relief during labour.

Research: The authors state that additional research is required into the effects of epidural on mother and foetus, particularly with regard to the effects of maternal temperature elevation on the foetus. There is especially a need for additional well-conducted randomised trials. It is preferable that studies comparing epidural with other forms of pain relief randomise women during pregnancy, so that the participants are more representative in terms of the difficulty of their labours. Such a design would enhance the generalisation of the study findings. In addition to continuing research related to epidural, research into other pharmacologic and non-pharmacologic methods of pain relief should also continue.
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