Intrapartum Epidural Analgesia and Neonatal Sepsis Evaluations

A Casual or Causal Association?

PAIN relief during childbirth has been maligned since Biblical times, and these attacks continue apace as we approach the next millennium. In particular, a litany of adverse maternal and fetal outcomes, such as increased cesarean section rates, prolonged labor, maternal fevers, adverse neonatal effects, interference with breast-feeding, among others, have been blamed on epidural analgesia. A recent controversy concerns the effect of epidural analgesia on maternal fever and subsequent neonatal sepsis work-ups. This issue of ANESTHESIOLOGY contains an article that shows lack of effect of an independent effect of epidural analgesia during labor on neonatal sepsis work-ups.1 This trial is a randomized, prospective evaluation of epidural analgesia versus patient-controlled intravenous analgesia (PCIA) in labor. The authors confirm previous observations that maternal fever is associated with epidural analgesia, nulliparity, and prolonged labor. Purported mechanisms for this observation include infectious (e.g., chorioamnionitis) and noninfectious (e.g., thermoregulatory effects on heat dissipation). However, they find no association between epidural analgesia and neonatal sepsis work-ups in febrile or afebrile women.

Why is this important and what prompted these authors to do this study? The answer stems from an article that appeared in 1997, apparently without input from any anesthesiologist, alleging that epidural analgesia was responsible for many instances of neonatal sepsis work-ups, thus disturbing maternal-infant bonding, exposing neonates to antibiotics, blood cultures, and other invasive tests.2 This study by Lieberman et al.2 received extensive national media coverage, caused considerable distress among obstetric anesthesiologists, and even prompted an official statement by the president of the American Society of Anesthesiologists emphasizing the safety of epidural analgesia in labor.3

There are similarities between the two studies.1,2 Both are reanalyses of data from previously published reports. Philip’s study is from a trial comparing epidural to patient-controlled intravenous analgesia for evaluation of labor outcome,4 Lieberman’s from a trial evaluating the technique of active management of labor.5 Both studies showed vanishingly small or no evidence of actual neonatal sepsis, only work-ups for sepsis were increased, in the epidural group in the Lieberman et al.4 study. Both articles also confirmed the association of elevated maternal temperature with epidural analgesia, a finding previously reported by others.

However, there are important and noteworthy differences between the two articles. Foremost is the fact that the Lieberman et al.2 database was originally obtained from a trial comparing active management of labor to “usual care.” In this trial, epidural analgesia was not part of the study protocol and was administered at patient request; no attempt was made to randomize analgesic options. Such a design led to an unavoidable selection bias: patients who requested and received epidural analgesia were more likely to have painful, dysfunctional, prolonged or induced labor or both, and all the expected consequences, namely maternal fever and neonatal implications. The Philip et al.1 study was performed as a randomized, prospective trial of epidural analgesia versus patient-controlled intravenous analgesia. Minimal “crossovers” between groups were noted, and all data are analyzed by intent-to-treat methods, thus including all patients enrolled in the trial. Such a study design is appropriate to answer the posed question; the retrospective Lieberman et al.2 study did not address and could not answer this question.

Another important difference between the Philip et
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at.\(^1\) and the Lieberman et al.\(^2\) studies involves the analysis of parturients without fever. Lieberman et al.\(^2\) describe a threefold increase in neonatal sepsis work-ups in infants born to mothers with epidural analgesia, versus no epidural, even in the absence of maternal fever. In fact, two thirds of all neonatal sepsis work-ups in the Lieberman et al.\(^2\) study were performed in infants born to mothers without fever (defined as greater than 100.4°F). The authors do not explain the indications for these work-ups. These women could have met other criteria for neonatal work-up, such as lower-grade fever (< 100.4°F), prolonged rupture of membranes, or positive group B strep colonization; no data were provided. Even in a subsequent reply to this direct query in a “letter to the editor,” Lieberman et al. still provide no answer, stating only that re-review of the medical records is planned.\(^6\) In contrast, Philip et al.\(^1\) found no increase in neonatal work-ups in infants born to mothers who were afebrile, with or without epidural analgesia. What lessons can be learned from these two articles?\(^7\)\(^8\)

Association Does Not Equal Causality

We know that two events can be associated, but not in a cause-and-effect manner. In the studies by Lieberman et al.\(^2\) and Philip et al.,\(^1\) and in every clinical practice that I am aware of, maternal use of epidural analgesia per se is not an indication for neonatal sepsis evaluation. Nonetheless, Lieberman et al.\(^2\) state that 61 and 66% of neonatal sepsis work-ups and neonatal antibiotic treatment, respectively, are “attributable” (her words, not mine) to epidural use.\(^2\) This implication is difficult to understand, especially in an afebrile patient. This leads to my last point, which is . . .

Informed Consent Should Be Evidence-based

Proper informed consent is essential, but must be based on careful consideration of the evidence. Patient choices based on information that is untrue, unfounded, or misleading cannot be labeled informed consent; misinformed consent would be more appropriate. Lieberman et al.\(^2\) state: “The possible consequences of fever resulting from epidural use should be discussed by women and their health care providers when making the decision about the method of pain relief to be used during labor.”\(^7\) In this context, an honest discussion of confounding factors related to epidural use, fevers, and neonatal outcome would be appropriate. Conversely, if a woman is counseled that avoidance of epidural analgesia during labor will prevent (or even markedly decrease) the likelihood of her infant undergoing a sepsis evaluation, then in my opinion, she has been sadly misinformed. Based on this misinformation, a woman may choose to suffer the pain of labor, or, in what arguably could be an even worse scenario, being unable to tolerate the pain, would ask for and receive epidural analgesia, and then bear the guilt if events such as labor augmentation, operative delivery, or neonatal sepsis evaluations occur. As stated in another recent editorial: “Labour can be extremely painful for many women. They are entitled to receive extradural analgesia if they wish without being exposed to unsubstantiated scare stories.”\(^9\) At least with regard to epidural analgesia and neonatal sepsis work-ups, the prospective randomized trial by Philip et al.\(^1\) in 1999 will, I hope, put this issue to rest.

Media Coverage of Medical Issues Can Be Misleading

Virtually every media report that discussed the Lieberman et al.\(^2\) study focused on the issue of fever, despite the observation that two thirds of the neonatal work-ups in patients with epidural analgesia were performed in the absence of maternal fever.

Epidurals lead to more infant tests: Babies get antibiotics more often.

USA Today, March 11, 1997*

Study finds problems with epidurals: When labor pain drugs cause fevers, babies face tests.

New York Times, March 12, 1997†

The clear implication in many of these reports was that the use of epidural analgesia (rather than other confounding issues) was directly responsible for the work-ups, antibiotics, blood draws, among others, that these infants experienced. Thus, media coverage was not accurate. This, of course, should be no surprise. Two recent editorials in major medical journals, in my opinion well worth everyone’s reading, carefully described the frequent inaccuracies portrayed when the general public reads about medical findings in the newspapers.\(^7\)\(^8\)

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Spinal Anesthesia in Severely Preeclamptic Women

When Is It Safe?

THE use of subarachnoid block for cesarean delivery has been increasing in the United States. Indeed, spinal anesthesia may be a better and more cost-effective technique for routine cesarean delivery than epidural block. Nonetheless, epidural anesthesia has been the preferred method of anesthesia for cesarean delivery in women with severe preeclampsia because the severity and incidence of hypotension may be less with epidural as compared to spinal anesthesia due to a slower onset of sympathetic blockade. In the current issue of Anesthesiology, Hood and Curry present the results of a retrospective chart review, comparing the effects of spinal and epidural anesthesia for cesarean delivery in severely preeclamptic women. The criteria for enrollment in the study were the diagnosis of preeclampsia and severe hypertension, with a systolic or diastolic blood pressure, or both, of greater than 160 and 110 mmHg, respectively. This is particularly important because most, but not all, patients meeting the American College of Obstetricians and Gynecologists criteria for severe preeclampsia have significant hypertension. The authors also limited participation to those women who were not in labor, because labor itself has been shown to reduce the frequency and severity of hypotension during regional anesthesia for cesarean section. In the current study, the mean change in mean arterial blood pressure was similar with spinal and epidural anesthesia, being approximately 15 mmHg. The lowest mean arterial blood pressure (calculated from the author's data), not necessarily during the induction to delivery interval, was also similar: namely, 58 mmHg in the spinal group and 55 mmHg in the epidural group. There was also no difference between the two techniques in the requirement for ephedrine. However, it is important to note that women receiving spinal anesthesia were given approximately 400 ml more crystalloid than those in the epidural group. The authors correctly indicate that their findings may be affected by their use of a retrospective study design. For instance, selection of an anesthetic technique for an

References