Association Between Epidural Analgesia During Labor and Fever

Daniel C. Vinson, MD; Ronnie Thomas; and Tom Kiser, MD
Columbia, Missouri, and Little Rock, Arkansas

Background. Epidural analgesia has been associated in previous research with an increase in maternal temperature.

Methods. Three studies were done: a retrospective chart review of women in labor, a prospective cohort study of women in labor, and a case-control study of newborns with fever. The prospective study enrolled 28 women, 14 of whom received epidural analgesia. Maternal temperature was measured hourly with a tympanic membrane thermometer. Other variables examined included duration of labor, duration of ruptured membranes, and room temperature. To further explore the possible association between maternal epidural exposure and newborn fever, a case-control study of newborns with fever at birth was carried out.

Results. In both the retrospective and prospective studies of women in labor, the duration of epidural analgesia was correlated with maximum maternal temperature during labor, with an increase, in the prospective study, of 0.07°C per hour of exposure to epidural analgesia ($P = .002$). Controlling for other variables did not change the magnitude of this effect or its statistical significance. Similar trends were seen in the newborn's first temperature in both the prospective study of women in labor and the case-control study of newborns, but the associations were not significant ($P = .07$ and .08, respectively).

Conclusions. Epidural analgesia is associated with an increase in maternal temperature during labor and possibly with an elevation of newborns' first temperatures.

Key words. Analgesia, epidural; fever; anesthesia, obstetrical; infant, newborn; body temperature.
(*J Fam Pract 1993; 36:617-622*)

In a monograph written in 1954, Bromage[1] pointed out that epidural analgesia affects a variety of human thermoregulatory mechanisms by its blockade of the sympathetic nervous system. Since, in his view, the majority of these changes result in heat retention, he believed that "there is a tendency for heat retention to occur in warm surroundings. This is seldom sufficiently marked to cause a noticeable rise of temperature, but in a hot theatre, or in the presence of fever, an additional rise of 1°–2°F may result."

In 1989, Fusi and associates[2] in Britain reported an association between epidural analgesia and maternal fever during labor. They prospectively followed 33 women in labor, 15 of whom received meperidine and 18 of whom received epidural analgesia. Beginning within 1 hour of the start of epidural analgesia, those women who received epidural infusions showed a linear increase in temperature of 0.14°C per hour. Fusi et al found no change in temperatures in women whose pain was managed with narcotics.

There is, however, evidence against an association between epidural analgesia and maternal temperature. Goodlin and Chapin[3] and Kapusta and colleagues[4] have presented data that failed to show such an association, although the women in the latter study were observed for only 1 hour. Furthermore, Hocquelet and associates,[5] in a large case series, stated that clinically significant infec-

Submitted, revised, December 29, 1992.

From the Department of Family and Community Medicine, School of Medicine, University of Missouri-Columbia (D.C.V., R.T.), and the Department of Family Medicine, School of Medicine, University of Arkansas, Little Rock (T.K.). Requests for reprints should be addressed to Daniel C. Vinson, MD, M231 Medical Sciences, University of Missouri, Columbia, MO 65212.

ISSN 0094-3509

tions were present in over one half of their patients who developed intrapartum fever. Even though 90% of the febrile patients had received epidural analgesia, compared with 51% of the afebrile patients, these investigators concluded that maternal fever usually indicates a serious infection and is not caused by epidural analgesia.

Other more recent studies, however, support Fusi's findings. Camann et al[6] found an average rise of 0.1°C per hour in women who received epidural analgesia, but the average maximum temperature among women who received epidural analgesia was only 37.2°C. And Macaulay and his colleagues[7] found a rise in temperature during labor of 0.37°C among women who received epidural analgesia, compared with a drop of 0.12° among women who did not.

Kennell and his colleagues[8] found evidence not only of an association between epidural analgesia and maternal fever, but also between epidural analgesia use and neonatal fever and medical interventions for it. Their study, however, focused on other issues and only peripherally addressed these findings.

To further explore the relationship between epidural analgesia and maternal fever, we conducted three studies: (1) a retrospective chart review of women in labor, (2) a prospective observational cohort study of women in labor, and (3) a case-control study of infants born with elevated temperatures. The primary questions addressed were whether epidural analgesia causes an increase in maternal temperature during labor or in the newborn infant's first temperature, and if such an increase occurs, whether it is associated with clinically meaningful complications other than fever.

Methods

Retrospective Cohort Study of Women in Labor

We began our study of this issue with a retrospective cohort study of women in labor. A woman was eligible for inclusion if she had a singleton pregnancy delivered at term during 1990 at the University of Missouri–Columbia Hospital (UMCH). Using a table of random numbers, charts were selected for the study from two office billing lists, one of women who received epidural analgesia and the other of women who did not. Women were excluded if they had fever or signs of active infection at admission. Data collected included maximum maternal temperature during labor, first temperature taken postpartum, the duration of epidural analgesia, duration of labor, and the time elapsed between rupture of membranes and delivery.

Prospective Study of Women in Labor

To examine variables that were not available in the retrospective study, we carried out a prospective observational study at UMCH from June 1991 through April 1992. Women with singleton pregnancies who presented at term in spontaneous labor were recruited for the study by the nursing staff. Women with recognized infections or with fever at the onset of labor were excluded.

Independent variables included hourly measurement of maternal temperature with a tympanic membrane thermometer. Oral temperatures, we believed, would be influenced by the patients' eating ice, and rectal measurements were unacceptable to patients. While some have found tympanic membrane temperatures to be poorly correlated with measurement of oral, axillary, or rectal temperatures with glass thermometers,[9] others have found satisfactory correlation with an electronic rectal thermometer ($r = .93$)[10] and with a pulmonary artery thermistor ($r = .98$).[11] Other independent variables examined included maternal age, parity, and weight; history of prenatal urinary infection or sexually transmitted disease; duration of ruptured membranes and of labor; use of narcotic analgesics during labor; duration of epidural analgesia; hourly measurement of room temperature and humidity; and hourly assessment of maternal sweating and shivering. Women were not randomly assigned to types of analgesia, and no efforts were made to influence the process of their obstetrical care.

Dependent variables analyzed were the mother's maximum temperature during labor, her last prepartum and first postpartum temperatures, and the infant's first temperature. The primary question addressed was whether the duration of intrapartum epidural analgesia was associated with maximum maternal temperature.

Case-Control Study of Febrile Newborns

If a woman develops a fever during labor, the infant may be born with an elevated temperature, which would prompt an evaluation for neonatal sepsis. In our studies of women in labor, however, no infant was born with a fever or was suspected of having bacterial sepsis. Since this outcome was not observed in any patient in either the retrospective or the prospective study of women in labor, a case-control study of febrile newborns was done to further investigate a possible relationship between maternal epidural analgesia and fever in the newborn.

Charts of infants who were born at UMCH and admitted to the normal newborn nursery were reviewed. To achieve the desired sample size of 35 cases and 70 controls, the charts of 600 babies born between April 8 and July 31, 1991, were reviewed. Infants whose first

Rate of Temperature Rise per Hour of Epidural Exposure in Women in Labor and Newborns

Study Group	Temperature Variable	Rate of Rise per Hour (°C)	*P* Value*
Retrospective, of women in labor	Maximum maternal temperature	0.05	.008
Prospective, of women in labor	Maximum maternal temperature	0.07	.002
	Last prepartum temperature	0.10	.006
	First postpartum maternal temperature	0.09	.005
	Infant's first temperature	0.07	NS
Case-control of newborns	Infant's first temperature	0.035	NS

**P values by linear regression, controlling for duration of labor.*
NS denotes not significant.

temperatures were ≥37.5°C were selected as cases. To control for time of day and season of delivery, the infants listed just before and just after the case infant in the nursery's chronological admission log were selected as controls. Infants were not excluded because of prematurity or postmaturity or because of abnormal weight for gestational age as long as they were transferred from labor and delivery to the normal newborn nursery.

In the case-control study, maternal variables examined included duration of labor and duration of epidural analgesia if it was used. Newborn variables included blood counts, blood cultures, lumbar puncture, and chest radiograph, if any were done, and whether the infant was transferred from the well-baby nursery to the neonatal intensive care unit (NICU). During the time of this study, no term infant born at UMCH was admitted directly from labor and delivery to the NICU solely because of fever or possible sepsis, or because of a maternal fever. We therefore believe that this study captured all newborns with an elevated temperature at or shortly after birth who did not have major congenital problems.

Statistical Analysis

Bivariate analyses included Wilcoxon rank-sum test for variables that were not normally distributed, χ^2 tests or Fisher's exact test for dichotomous variables, and *t* tests for normally distributed parametric data. Multivariate analyses used linear regression for the cohort studies and logistic regression for the case-control study. Sample size calculations were based on data from the retrospective study, and used an α and a β of .05.

Results

Retrospective Cohort Study of Women in Labor

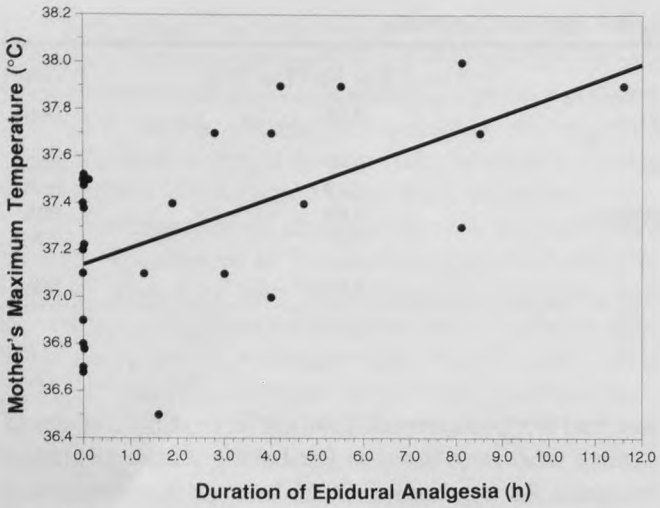
Of 53 charts of women who were listed as having received epidural analgesia, 11 were excluded because of preterm (<37 weeks) labor and 1 because her temperature had not been recorded during labor. Of 72 charts of women who were listed as not having received epidural analgesia, 36 were excluded: 25 because the women had received epidural analgesia, 7 because of preterm labor, 1 whose temperature had not been recorded, and 3 whose charts were consistently unavailable for review.

Of the 41 women in the epidural analgesia group, 11 had a maximum temperature of ≥37.5°C, in contrast to 3 of the 36 in the no-epidural analgesia group (P = .05 by two-tailed Fisher's exact test). When a higher threshold was used to define a clinically significant fever (38.0°C), the findings were more striking. Of 6 women who developed a temperature of greater than 38.0°C, all had received epidural analgesia (P = .03 by two-tailed Fisher's exact test).

Using duration of epidural analgesia as the independent variable in a linear regression equation, maximum maternal temperature rose 0.08°C per hour of epidural analgesia (P < .001). Duration of labor and of time elapsed between rupture of membranes and delivery were also significantly correlated with maternal temperature (P = .009 and < .001, respectively), but their effects were smaller (0.03°C and 0.04°C per hour, respectively). The effect of epidural analgesia on maternal temperature was essentially unchanged when we statistically controlled for duration of labor (0.05°C per hour of epidural analgesia, P = .008) or for duration of ruptured membranes (0.07°C per hour of epidural analgesia, P = .001).

Maternal age, parity, history of prenatal urinary infection, history of sexually transmitted disease, and maternal weight were not associated with maternal temperature and had no effect on the relationship between duration of epidural analgesia and maximum maternal temperature. A summary of per-hour effects of epidural analgesia on various temperature-measurement variables is given in the Table.

Of the 77 women, 51 received narcotics during labor (2 received meperidine and 49 nalbuphine). They were significantly less likely to receive epidural analgesia (relative risk 0.6, 95% confidence interval 0.4 to 0.95).



Scatter plot of maximum maternal temperature during labor (in °C) vs the duration of epidural analgesia (in hours). The regression line, after adjustment for duration of labor and duration of ruptured membranes, is also shown.

No association between maternal temperature and use of narcotics or total narcotic dose in milligrams was found.

Prospective Study of Women in Labor

Recruitment into the prospective study was slower than anticipated. After 28 patients had been enrolled, the study was closed and the data were analyzed.

Women who received epidural analgesia tended to have lower parity and longer labors than those who did not. The differences were not statistically significant, presumably because of the small sample size.

All 14 women who received epidural analgesia were given initial test doses of lidocaine followed by a bupivacaine bolus and infusion, typically at 10 to 14 mg per hour. All but one also received sufentanil in the epidural infusion, usually at a rate of 10 to 20 μg per hour.

Maximum maternal temperatures were higher among those mothers who received epidural analgesia than among those who did not, 37.5°C vs 37.2°C (P = .04 by t test). By linear regression, maximum maternal temperature rose 0.07°C per hour of epidural analgesia use (P = .001). Duration of labor, time elapsed between rupture of membranes and delivery, room temperature, and use of narcotic analgesics had no significant association with maximum maternal temperature and did not alter the association with epidural analgesia (Figure).

Similar effects were seen in the last prepartum temperature taken, first postpartum temperature taken, and the first temperature taken of the infant. Controlling for other variables had no effect on the relationship between duration of epidural analgesia use and maternal temperature variables. The relationship with the infant's first temperature was not changed in magnitude, but was no longer statistically significant when we controlled for duration of labor or duration of ruptured membranes (Table). Maternal sweating and shivering had no effect on the association between epidural analgesia and maternal temperature.

Women who received epidural analgesia tended to have lower temperatures at admission (36.9°C) than those who did not (37.1°C), but this difference was not statistically significant (P = .07 by t test) and had no effect on the association between epidural analgesia and maximum maternal temperature. Unlike Acker and his colleagues,[12] we found no association between admission time and admission temperature, probably because of the smaller size of our study. Although the time of admission differed between those women who received epidural analgesia (average 10 AM) and those who did not (average 2:30 PM, P = .07 by Wilcoxon rank-sum test), controlling for this difference had no effect on the association between epidural analgesia and outcome temperature variables.

No intrapartum or postpartum cultures were obtained on any patient, and no woman was noted to have a postpartum complication. No cultures were obtained on newborns in this study, and no infection was diagnosed in any of them.

Case-Control Study of Febrile Newborns

The newborns' first temperatures were taken at the time of admission to the well-baby nursery, an average of 30 minutes after birth. Although temperatures of febrile infants tended to be taken sooner (25 minutes ± 15 standard deviation [SD]) than those of afebrile infants (32 minutes ± 23 SD), the difference was not statistically significant (P = .07 by t test). Average admission temperatures were 37.7°C (±0.2°, range 37.5° to 38.4°) for the 35 febrile newborns compared with 36.7°C (±0.4°) for the 70 afebrile infants.

Of febrile infants' mothers, 18 (51%) had received epidural analgesia, compared with 32 (46%) of afebrile infants' mothers (odds ratio [OR] = 1.26, P = 0.6 by χ^2). Febrile infants' mothers had received epidural analgesia for an average of 3.1 hours, compared with 1.2 hours for mothers of afebrile infants (P = .008 by t test). Each hour of epidural analgesia significantly increased the probability that an infant would be febrile (OR = 1.23, P = .004 by logistic regression), but when we controlled for the duration of labor, the duration of epidural analgesia was no longer a significant factor.

To facilitate comparison with the findings in the other studies, we used linear regression to determine a

per-hour estimate of the effect of epidural analgesia on temperature. Each hour of epidural analgesia was associated with an increase of 0.07°C in the newborn's temperature. However, as with the logistic regression analysis, when the duration of labor was controlled for, the magnitude of the effect of epidural analgesia was reduced by 50% (0.035°C per hour of epidural) and was no longer statistically significant ($P = .08$).

Twelve newborns had been given antibiotics or had one or more diagnostic procedures performed for evaluation of fever. These events were evenly distributed between those infants whose mothers received epidural analgesia and those whose mothers did not. One infant was found to have bacteremia (α-hemolytic streptococci); three others were treated for presumed sepsis. All four were febrile at birth, but only two of the infants' mothers had received epidural analgesia.

Discussion

These three studies provide evidence that intrapartum epidural analgesia is associated with an increase in maternal temperature that may be clinically significant. The association persisted after controlling for duration of labor, duration of ruptured membranes, room temperature, and other possible confounding variables.

In our series of studies, however, a clinically meaningful effect of epidural analgesia on maternal temperature was not common. Maximum maternal temperature rose to ≥38.0°C in only 6 of 41 women (15%) who received epidural analgesia in the retrospective study and 1 of 14 (7%) in the prospective study. Furthermore, these fevers prompted no change in clinical management; cultures were not done with any of these febrile women and none was treated with antibiotics.

In both the prospective study of women in labor and the case-control study of newborns, each hour of epidural analgesia was associated with an increase of 0.07°C in the newborn's first recorded temperature. In each study, however, when duration of labor was controlled for, the association between maternal epidural analgesia exposure and newborn temperature was no longer statistically significant ($P = .07$ and $.08$).

Some of the febrile newborns in the case-control study, unlike the febrile women in our other two studies, were aggressively evaluated and treated. Therefore, we believe it is important to further pursue the question of whether epidural analgesia is associated with newborn fever. If epidural analgesia causes fever in the newborn, prompting aggressive but unnecessary evaluation, the ability to accurately distinguish between neonatal fever due to epidural analgesia and fever due to sepsis could avoid emotional stress in the mother as well as be of economic benefit.

Our studies, however, did not answer the first question, whether there is an association between epidural analgesia and newborn fever, and cannot address the second issue, the differentiation of newborns with fever caused by maternal epidural analgesia exposure from those with sepsis. Addressing the second issue would require a much larger study. Considering that only four of 600 newborns were suspected of having bacterial sepsis (two had been exposed to maternal epidural analgesia and two had not), a definitive study would require a total sample size of over 8000 newborns to be able to detect even a 50% difference in rates of presumed sepsis with a power of 0.8.[13] Moreover, even a study of 8000 newborns would be unlikely to answer the second question with enough certainty to make clinicians willing to forgo treating febrile newborns, as sepsis is an often subtle but devastating disease.

The sample sizes in our three studies were all small, but in the analyses of the association between epidural analgesia use and maternal temperature, the P values are small enough to remove concern about random error. A P value of $<.01$, especially when replicated with several dependent variables in two studies, essentially rules out random error as a cause of the association found, regardless of the sample size. Statistical significance, however, does not address systematic error. It is possible that patients who consented to participate in the prospective study were different from those who did not, limiting the generalizability of the prospective study's findings. Finding the same association in the retrospective study, in which subjects were chosen randomly from an entire year's lists, provides assurance that such a bias is unlikely to be a major factor.

In addition, these studies have another source of bias that may account for some or all of the associations found: each of the women chose her own form of analgesia. We know that women who choose to have epidural analgesia tend to be of lower parity and to have longer labors than those who do not. Those factors have been accounted for in the analyses that we have reported. Nevertheless, there may be other unmeasured factors associated with the choice of regional analgesia that are in some way associated with maternal temperature. These other factors could be dealt with only through a clinical trial in which women in labor were randomly designated to receive epidural analgesia or to be in a control group, but such a trial is unlikely to be carried out.

These studies leave other questions unanswered, including the mechanism by which epidural analgesia might cause an increase in maternal temperature. In the prospective study, room temperature was not a signifi-

cant factor, and sweating and shivering, which were transient, had no effect on the relationship between epidural analgesia and maternal temperatures.

The study by Kennell and his colleagues[8] suggests that the use of epidural analgesia may lead to an elevated temperature in the mother and thus an evaluation for possible sepsis in the newborn when the baby is not clinically sick. On the other hand, the study by Hocquelet and associates[5] suggests that most babies born to febrile mothers are clinically sick. Further work is needed to define the extent, clinical significance, and physiology of the association between epidural analgesia and maternal temperature in labor.

References

1. Bromage PR. Spinal epidural analgesia. Baltimore: Williams & Wilkins, 1954:27.
2. Fusi L, Steer PJ, Maresh MJA, Beard RW. Maternal pyrexia associated with the use of epidural analgesia in labour. Lancet 1989; 1:1250–2.
3. Goodlin RC, Chapin JW. Determinants of maternal temperature during labor. Am J Obstet Gynecol 1982; 143:97–103.
4. Kapusta L, Confino E, Ismajovich B, Rosenblum Y, David MP. The effect of epidural analgesia on maternal thermoregulation in labor. Int J Gynaecol Obstet 1985; 23:185–9.
5. Hocquelet C, Cormier P, Leng JJ, Janky E, Duthil V. Hyperthermies du travail: rôle de l'analgésie péridurale. Rev fr Gynécol Obstét 1989; 84:737–41.
6. Camann WR, Hortvet LA, Hughes N, Bader AM, Datta S. Maternal temperature regulation during extradural analgesia for labour. Br J Anaesth 1991; 67:565–8.
7. Macaulay JH, Randall NR, Steer PJ. Continuous monitoring of fetal temperature by noninvasive probe and its relationship to maternal temperature, fetal heart rate, and cord arterial oxygen and pH. Obstet Gynecol 1992; 79:469–74.
8. Kennell J, Klaus M, McGrath S, Robertson S, Hinkley C. Continuous emotional support during labor in a US hospital: a randomized controlled trial. JAMA 1991; 265:2197–201.
9. Freed GL, Fraley JK. Lack of agreement of tympanic membrane temperature assessments with conventional methods in a private practice setting. Pediatrics 1992; 89:384–6.
10. Stewart JV, Webster D. Re-evaluation of the tympanic thermometer in the emergency department. Ann Emerg Med 1992; 21: 158–61.
11. Shinozaki T, Deane R, Perkins FM. Infrared tympanic thermometer: evaluation of a new clinical thermometer. Crit Care Med 1988; 16:148–50.
12. Acker DB, Schulman EB, Ransil BJ, Sachs BP, Friedman EA. The normal parturient's admission temperature. Am J Obstet Gynecol 1987; 157:308–11.
13. Kraemer HC, Thiemann S. How many subjects? Newbury Park, Calif: Sage Publications, 1987.