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ORIGINAL ARTICLE

Effects of epidural analgesia on labor length, instrumental delivery, and neonatal short-term outcome

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Abstract
Purpose We aimed to clarify whether the short-term adverse neonatal outcomes associated with epidural analgesia are due to the epidural analgesia itself or to the instrumental delivery.
Methods A retrospective case–control study was conducted to evaluate the relationship between epidural analgesia, labor length, and perinatal outcomes. A total of 350 pregnant women at term who delivered under epidural analgesia (cases) were compared with 1400 patients without epidural analgesia (controls).
Results Vacuum extraction (6.5 vs. 2.9 %) and cesarean section (19.9 vs. 11.1 %) were more frequently performed in the cases than controls ($p < 0.001$). Using a Kaplan–Meier algorithm, it was determined that the mean lengths of the 1st and 2nd stages of labor and the overall durations of labor and delivery were significantly longer in cases compared with controls. A Cox regression analysis showed that the longer labor remained even after adjustment for parity. The neonatal variables stratified by mode of delivery were not different in cases and controls, except for a slightly lower umbilical arterial pH in spontaneous delivery for the cases group. However, the Apgar scores and umbilical arterial pH were significantly lower in the neonates delivered by vacuum extraction compared with those in the neonates delivered by spontaneous delivery or cesarean section, regardless of whether epidural analgesia was performed. A multivariable analysis showed that vacuum extraction much more consistently affected the arterial pH than the analgesia itself (the β coefficients were -0.036 for epidural analgesia vs. -0.050 for vacuum extraction).
Conclusion Epidural analgesia was associated with slowly progressing labor, thus resulting in an increased rate of instrumental delivery. This instrumental delivery appears to adversely affect the neonatal outcomes more strongly than the analgesia itself.

Keywords Cesarean section · Duration of the delivery · Dystocia · Epidural analgesia · Instrumental delivery

Introduction

Maternal changes induced by epidural analgesia during labor may affect the baby. Not only adverse effects due to the epidural analgesia, such as hypotension, fever, prolonged labor and delivery, an increased need for oxytocin, and instrumental delivery [1, 2], but also beneficial effects, such as reduced maternal stress hormones and hyperventilation, and uterine vasodilatation [3–5], and fewer episodes of hemoglobin desaturation [6–8] have been reported. The neonatal outcome depends on the balance between the two opposing effects [3]. Several short-term adverse neonatal outcomes have been reported, although it is thought that perinatal mortality is rare [9].

The use of epidural analgesia has also been associated with dystocia [10]. Patients receiving epidurals are more likely to require oxytocin augmentation, have longer second stages of labor, and have persistent occipitoposterior fetal malposition [2, 11–14]. Autonomic imbalance has

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been proposed as an explanation for the association between epidural analgesia and prolonged labor [15, 16].

On the other hand, in a case–control study that Benedetto et al. [17] undertook to evaluate the short-term maternal and neonatal complications in a healthy population at term based on the mode of delivery, they demonstrated that neonatal short-term complications were most closely correlated with instrumental delivery. However, it was not clear whether the instrumental deliveries involved more short-term neonatal adverse effects in comparison with the use of epidural analgesia itself. To our knowledge, there have been no previous reports to compare the adverse effects of epidural analgesia with the effects of the mode of delivery.

We hypothesized that the short-term neonatal outcomes were more strongly associated with instrumental delivery as a result of epidural analgesia, rather than being a side-effect of the analgesia itself. The aim of the present study was to clarify whether the short-term adverse neonatal outcomes associated with epidural analgesia were due to the epidural analgesia itself or to the instrumental delivery.

Subjects, materials, and methods

The subjects were female patients who delivered at our hospital between 2008 and 2009. Because this study was based on a retrospective review of the medical records, the ethics board at our institution did not require any permission to be obtained. A nested case–control study with matched cases/controls was conducted to investigate the relationship between epidural analgesia during labor and the perinatal outcome in the neonates. We selected only subjects with a complete follow up from early gestation to delivery in our hospital. Patients for whom elective cesarean section was performed before the onset of labor, those with a non-vertex presentation, and those with multiple gestations were excluded. When a patient (case) was eligible for the study, four controls with similar demographic characteristics (maternal body mass index [BMI], maternal age, estimated fetal weight by ultrasound at 30–32 weeks' gestation) were also enrolled. Thus, three hundred and fifty patients who received epidural analgesia for labor pain were enrolled (cases) and compared with 1400 controls (1:4 matched pair case–control study).

Epidural analgesia was performed on patients when they had between 3.0 cm and 4.0 cm of cervical dilatation. The epidural space was identified by loss of resistance to air at the L3–L4 (L2–L3; L4–L5) interspace, and a multihole epidural catheter was advanced 3.0–5.0 cm into the epidural space. An analgesic mixture of 20 ml 0.1 % ropivacaine or levobupivacaine with 10 μg sufentanil was administered as a loading dose, and 10 ml 0.1 % ropivacaine or levobupivacaine without sufentanil was repeated during labor on demand (top-ups).

The diagnosis of dystocia was defined as follows: no appreciable change in dilatation for more than 2 h in the active phase, and no appreciable descent by the fetus' presenting part for more than 1 h in the second stage of labor even when oxytocin augmentation and amniotomy were performed. The vacuum-assisted fetal delivery devices used were the Kiwi® (Clinical Innovations, UT, USA) or Mityvac M style Mushroom cups® (CooperSurgical, CT, USA), and they were employed upon maternal or fetal indication, but no forceps delivery was employed.

The baseline demographic and clinical characteristics of the patients were retrieved from the patient charts and were tabulated for the analysis. The data were entered into a computerized data analysis program [Statistical Package for Social Science (SPSS), Windows version 17.0; Chicago, IL, USA]. Categorical variables were reported as percentages and compared using the χ^2test. Continuous variables were compared by Student's *t*-test. Finally, a general linear model (GLM) was used to evaluate the effects of both analgesia and the mode of delivery on the variables of interest. The GLM is a flexible statistical model that can be used to evaluate the multivariable effects of a set of categorical or continuous independent variables on a normally distributed dependent variable. In this study, the dependent variable was the umbilical arterial pH, and the independent predictors were analgesia, the mode of delivery, and the interaction between them. By analyzing the coefficients generated for each predictor and its associated *p* value, the strength of the correlation with the dependent variable can be estimated.

The cumulative probability of the duration of labor and delivery, measured from the onset of labor until the baby was born, was estimated by the Kaplan–Meier method. Delivery by spontaneous vaginal birth was taken to be the "event". An emergency cesarean section and vacuum extraction were taken as "censors". Survival curves were compared using the log-rank test. The influence on survival of the potential prognostic factors was assessed by a multivariate analysis with the Cox proportional hazards model, using a stepwise selection of variables to calculate the hazard ratio. Statistical significance was defined as a *p* value of <0.05.

Results

The demographics of the subjects are shown in Table 1. There were no significant differences between the cases and the controls in terms of the maternal BMI, age, gestational age (weeks) at the delivery, or neonatal birth weight, but there were differences in parity. The study

Table 1 Demographics of the patients

	Epidural ($n = 350$)	Control ($n = 1{,}400$)	p value
Nulliparous	74.1 %	53.1 %	<0.001
Maternal body mass index (BMI)	22.4 ± 3.50	22.6 ± 2.61	0.317
Maternal age (years)	32.2 ± 6.3	32.0 ± 5.2	0.583
Gestational weeks	38.4 ± 1.8	38.3 ± 2.4	0.194
Neonate's body weight (g)	3,220 ± 458	3,180 ± 614	0.175

The values are means ± standard deviations, and p values were determined using the χ^2 test or Student's t-test

group of patients who received epidural analgesia had a higher rate of nulliparae (74.1 vs. 53.1 %, $p < 0.001$). A cumulative survival plot of the total duration of labor and delivery stratified according to groups is shown in Fig. 1. By a Kaplan–Meier algorithm, the mean lengths of the 1st stage and 2nd stage of labor were 176 and 31 min in controls versus 269 and 39 min in cases. The overall duration of deliveries was 204 and 300 min in controls and cases, respectively, as reported in Table 2. The Cox regression analysis (Table 3) showed that the longer labor length due to epidural analgesia remained even after adjustment for parity, as expressed by means of the hazard ratio (0.69, 95 % CI 0.59–0.79).

The differences in neonatal outcomes between cases and controls, stratified by the mode of delivery, are shown in Table 4. Vacuum extraction and cesarean section were more frequently performed in cases than controls ($p < 0.001$). However, the neonatal variables did not differ significantly between cases and controls even when subjects were stratified by the mode of delivery, except for the umbilical arterial pH in cases who delivered spontaneously.

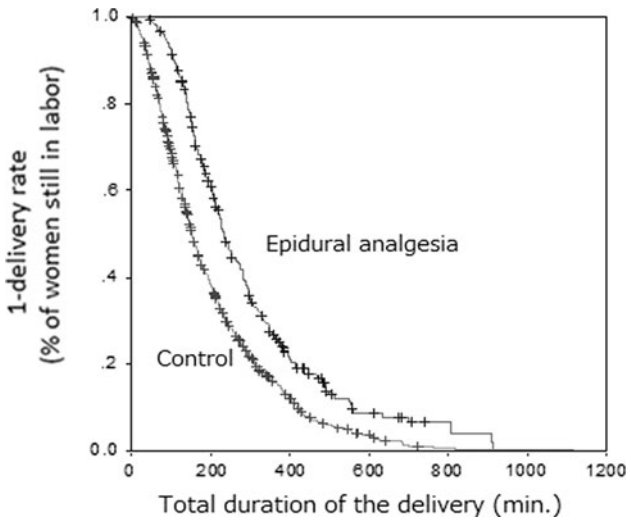

Fig. 1 A 1-delivery rate (% of patients still in labor) plot of the total duration (min) of labor and delivery stratified according to the patient group

Table 2 Analysis of the duration of labor length between cases and controls

	Mean	95 % Confidence interval (CI)
Total duration of labor (min)		
Control	204.45 (5.61)	193.46–215.45
Epidural	300.55 (13.71)	273.67–327.43
Duration of first stage (min)		
Control	176.29 (5.33)	165.83–186.74
Epidural	269.27 (12.97)	243.85–294.70
Duration of second stage (min)		
Control	30.98 (1.00)	29.02–32.94
Epidural	38.81 (2.08)	34.72–42.90

Data are expressed as means (SE) and 95 % confidence intervals

Table 3 The Cox regression analysis output

Predictor	Hazard ratio	95 % CI	p value
Epidural analgesia	0.69	0.59–0.79	<0.001
Multiparous patients	1.46	1.29–1.65	<0.001

The spontaneous or surgical delivery rate was the variable event. A higher hazard ratio (>1.00) was associated with a shorter duration of labor and delivery. A lower hazard ratio (<1.00) was associated with a longer duration of labor and delivery

The Apgar scores and umbilical arterial pH were significantly lower in the neonates delivered by vacuum extraction compared with those in infants with spontaneous delivery or infants delivered by cesarean section, regardless of whether epidural analgesia was performed.

The GLM output (Table 5) statistically validated this result, showing an independent effect of both analgesia and the mode of delivery on the umbilical arterial pH, because both the associated β coefficients were significant ($p < 0.001$). The mode of delivery much more consistently affected the arterial pH compared with the analgesia itself, as shown in Table 5 (the β coefficients were -0.036 vs. -0.050, respectively). Again, the interaction between the two terms yielded a significant effect on the umbilical arterial pH estimation.

Discussion

We demonstrated that the total duration of labor and delivery was prolonged in women (cases) using epidural analgesia, and that the vacuum delivery and cesarean section rates due to dystocia or fetal distress were higher in the epidural group, similar to the findings of a previous report [18]. Furthermore, the results of the present study suggested that the Apgar score and umbilical arterial pH were

Table 4 Neonatal outcomes (Apgar score and umbilical arterial pH) in cases and controls stratified by the mode of delivery

	Epidural ($n = 350$)	Control ($n = 1400$)	p value
Vacuum extraction	23 (6.5 %)	43 (2.9 %)	<0.001[a]
Cesarean section	70 (19.9 %)	166 (11.1 %)	<0.001[a]
Apgar score at 1 min			
Spontaneous delivery	8.8 ± 0.6*,¶	8.9 ± 0.7*,¶	0.151[b]
Cesarean section	8.6 ± 0.8§,¶	8.3 ± 1.6§,¶	0.131[b]
Vacuum extraction	7.7 ± 1.8*,§	7.7 ± 1.9*,§	0.962[b]
Apgar score at 5 min			
Spontaneous delivery	9.9 ± 0.4*	9.9 ± 0.5*,¶	0.151[b]
Cesarean section	9.7 ± 0.6§	9.5 ± 0.9§,¶	0.135[b]
Vacuum extraction	9.3 ± 0.8*,§	9.2 ± 1.1*,§	0.611[b]
Umbilical arterial pH			
Spontaneous delivery	7.27 ± 0.10*	7.31 ± 0.09*,¶	<0.001[b]
Cesarean section	7.28 ± 0.10§	7.27 ± 0.10§,¶	0.504[b]
Vacuum extraction	7.21 ± 0.11*,§	7.20 ± 0.11*,§	0.685[b]

[a] The data are frequencies, and p values were determined using the χ^2 test for maternal variables

[b] The values are means ± standard deviations, and the p values were determined using Student's t-test

*, §, ¶ Significantly different values compared among mode of deliveries using multivariate analysis of covariance ($p < 0.01$)

Table 5 General linear model (GLM) output showing the effect of both analgesia (NO = 0 vs. YES = 1) and the mode of delivery (spontaneous = 0, cesarean = 1, vacuum = 2) on the umbilical arterial pH

Parameter	β coefficient	Standard error	p value	Power[a]
Intercept	7.310	0.003	<0.001	1.000
Analgesia	−0.036	0.006	<0.001	1.000
Mode of delivery	−0.050	0.006	<0.001	1.000
Analgesia × mode of delivery	0.033	0.010	0.001	0.892

[a] Type I error = 0.5

lower in subjects with vacuum extraction than in those without, regardless of whether epidural analgesia was administered. A previous report that compared instrumental delivery with cesarean section showed that instrumental delivery significantly increased the risk of neonatal complications (odds ratio [OR] 4.2, 95 % CI 2.4–7.4) [17], a finding which supports our present results.

Caliskan et al. [19] compared the fetal oxygen saturation values in term pregnant patients who received epidural analgesia with those in patients who did not. Their results suggested that the fetal oxygen saturation values in the first and second stages of labor, cesarean delivery rates, results of the neonatal cord blood gas analysis, Apgar scores, and neonatal outcomes were similar in the two groups, although the first stage of labor lasted significantly longer in the epidural group. A meta-analysis by Reynolds et al. [20] also demonstrated no adverse effect of epidural analgesia on fetal oxygenation.

Although opioids are well recognized as producing direct fetal and neonatal depression and impairing breast-feeding when used systemically, their potential for doing so is less pronounced when they are used for epidural analgesia [21]. Fentanyl is freely transported across the placenta, with a slightly higher concentration in the fetal compartment because of its comparatively acidic pH [22]. Since the year 2000, we have used sufentanil instead of fentanyl for labor analgesia in our department because it has been demonstrated that the maternal-to-fetal clearance of fentanyl is considerably greater than that of sufentanil, while the fetal-to-maternal clearance is greater with sufentanil, and sufentanil is sequestered in larger amounts within the placenta [23]. Although clinically significant opioid concentrations are unlikely to be present in the neonate at birth, we observed that the umbilical arterial pH in spontaneous deliveries was slightly lower in the patients who had epidural analgesia than in those who did not. It is difficult to explain the potential adverse effects on the umbilical arterial pH of using epidural analgesia with sufentanil.

Finally, the multivariable analysis in the present study demonstrated that the mode of delivery much more consistently affected the arterial pH than analgesia itself, based on a comparison of the β coefficients (−0.036 vs. −0.050). An analysis of the neonatal outcomes stratified by the mode of delivery showed that neonatal adverse outcomes were dependent on vacuum delivery due to dystocia rather than the epidural analgesia itself.

In conclusion, epidural analgesia induced slowly progressing labor, resulting in an increased rate of instrumental delivery. Instrumental delivery due to dystocia and/or fetal distress may adversely affect neonatal outcomes, and it appears that instrumental delivery more strongly affects the outcomes than the epidural analgesia itself. Additional information regarding such short-term neonatal adverse outcomes due to epidural analgesia should be explained to the patient before using analgesia in the clinical situation.

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Conflict of interest There are no conflicts of interest to disclose.

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