The effects of continuous epidural analgesia on Doppler velocimetry of uterine arteries during different periods of labour analgesia

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Background. The transient effects of epidural bupivacaine 0.25–0.5% on the Doppler velocimetry of umbilical and uterine arteries had been reported, but the effects of continuous lower dose epidural bupivacaine (0.05–0.1%) infusion for labour analgesia have never been reported. In this study, we evaluated the effects of continuous epidural bupivacaine 0.075% on the Doppler velocimetry of uterine arteries.

Methods. Twenty pregnant women for labour analgesia received continuous epidural bupivacaine 0.075% infusion. We used a 4-MHz continuous-wave Doppler probe (Multigon 500A) with a 200 Hz thump filter to detect uterine blood flow velocity. We recorded the velocimetry data for uterine relaxation and contraction during five time periods: pre-epidural insertion, 1, 2, and 4 h post-epidural infusion, and after delivery of fetus.

Results. Our data showed that the velocimetric indices of uterine vascular resistance were significantly increased 1, 2, and 4 h after epidural infusion when compared with the pre-epidural level; these returned to the baseline after delivery.

Conclusion. Continuous epidural analgesia with bupivacaine 0.075% increases the resistance of uterine artery and therefore possibly reduces the uterine blood flow.

Keywords: analgesic techniques, epidural; blood, uterine blood flow; measurement techniques, Doppler indices

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Modern obstetric practice encourages use of epidural analgesia for the relief of pain during labour. However, epidural analgesia can prolong the course of labour and increase the rate of instrument delivery.¹–⁴ Benefits to the fetus from epidural analgesia remain controversial, however, to date there are no reports to indicate that epidural analgesia would bring harmful effects to the fetus.⁵–⁷ The effects of epidural anaesthesia for Caesarean section, or labour, on maternal uterine and fetal umbilical artery blood flow velocity waveforms have been reported.⁸–¹⁴ The studies largely focused on transient changes in uterine blood flow after relatively high concentration (0.25%) of epidural bupivacaine. Furthermore, these studies did not compare the Doppler indices during the contraction and relaxation period.

Continuous epidural bupivacaine infusion for labour analgesia usually is utilized for a number of hours. In this study, we evaluated the effects of continuous epidural bupivacaine (0.075%) infusion for labour analgesia on the uterine blood flow, in particular during the contraction and the relaxation phase.

Methods

This study was approved by the Research Ethics Board of the National Taiwan University Hospital and an informed consent was obtained from all participants. From October to December 2002, all the women who underwent normal labour and met the inclusion criteria were approached; those who gave consent to continuous epidural bupivacaine infusion for labour analgesia were enrolled. According to a previous study,⁹ analysis showed that 17 patients would provide 80% power to detect a 50% increase, at significance
of $P<0.05$, in Doppler velocimetry indices after epidural anaesthesia. To accommodate possible patient dropout, 28 patients were recruited. The main inclusion criteria was parturient’s compliance to the study protocol and adequate control of labour pains [visual analogue score (VAS)<3] at all time points of the study period. The other inclusion criteria included gestational age of 36 weeks or above, singleton pregnancy with an engaged vertex presentation, no significant medical or obstetric complications, active phase of labour with cervical dilatation between 2 and 4 cm and uterine contractions occurring at least every 5 min, and no evidence of fetal or maternal compromise during the preceding period of labour. The exclusion criteria were inadequate analgesia (VAS>3), poor parturient compliance, pre-eclampsia, gestational diabetic mellitus and mothers with cardiovascular diseases that have the probability of influencing the uterine blood flow. All patients included in this study had received continuous epidural infusion for at least 4 h. All the patients followed the same protocol. Each patient received i.v. infusion of Ringer’s lactate solution 500 ml which was completed ~20 min before the study. Maternal blood pressure and heart rate were monitored at 5 min intervals using an automated sphygmomanometer.

The epidural administration technique was the same for each patient. The catheter was placed in the L$_{3-4}$ interspace under sterile conditions, with the patient in lateral dorsiflexion position. The patient was then returned to supine position for administration of a test dose (3 ml) of lidocaine 2%. Once it was determined that no adverse effects such as maternal hypotension or fetal bradycardia had occurred, a loading dose (10–12 ml) of bupivacaine 0.075% bupivacaine, depending on the patient’s height, was administrated to ensure a diminished pin-prick sensation caudal to T10 dermatome. The epidural infusion rate was initially set at 10 ml h$^{-1}$ and then adjusted to parturient response; between 8 and 15 ml h$^{-1}$ was required to maintain a stable VAS<3 at all time points of the study period. The labour pain was assessed hourly by nurse anaesthetist on a 10 cm VAS throughout the labour. The infusion rate of bupivacaine 0.075% was carefully titrated to maintain VAS <3 during the uterine contraction phase.

In this study, we recorded and compared the velocimetry data of uterine blood flow (during uterine relaxation and contraction) at five time intervals: before epidural insertion, 1, 2 and 4 h after starting epidural infusion, and 4 h after stopping epidural infusion. The ‘pre-epidural insertion’ period was taken as the baseline period when intense labour pain occurred steadily and cervical dilation warranted placement of epidural catheter; 1, 2, and 4 h after epidural infusion was taken to indicate the time of continuous epidural infusion with low dose bupivacaine, and 4 h after stopping epidural infusion represented the final measurement of Doppler velocimetric parameters in the post-delivery room assuming that the residual effects of bupivacaine would have disappeared. We used a 4-MHz continuous-wave Doppler probe (Multigon 500A) with a 200 Hz thump filter and the velocimetry data obtained during each study period were taken over a total of ~10 min. Sequences of 5–10 cardiac cycles in both the fetus and mother were sampled by the same observer at three different times during 10 min segments to minimize any sampling error or technical bias. Data were recorded to include periods of uterine contraction and relaxation during each study period. For each insonation period, both uterine arteries were identified and insonated according to the technique described by Fleischer and colleagues.15 For each insonation session, the systolic/diastolic (S/D) ratios, pulsatility index (PI) and resistance index (RI) were calculated; mean values were determined for the uterine arteries. The uterine artery velocimetric indices were determined just for placental side for each patient. The variation among any single sets of velocimetric observations was <10%.

During the study standard monitoring during labour continued. The details of the fetal heart rate (FHR) record and uterine activity patterns, along with the outcome of labour and neonatal condition, were analysed retrospectively. The data examined included gestational age, birth weight, placental weight, Apgar scores at 1 and 5 min, and umbilical arterial and venous blood gases. Maternal indicators analysed included mean systolic and diastolic blood pressures and heart rate for each of five different study periods, and 10 min after bolus injection. In addition effectiveness of the epidural anaesthesia (i.e. sensory level obtained), and the presence or absence of any anaesthetic complications were recorded.

The maternal blood pressure and heart rate, FHR during Doppler insonation, and Doppler velocimetric data (uterine S/D ratios, PI and RI) were determined for each study period and compared using analysis of variance for repeated measures. Individual values of these variables were also examined for changes exceeding 20%, or twice the intra-observer variation, for each of the Doppler velocimetric measurements. $P<0.05$ was considered statistically significant.

**Results**

Among the total of 28 pregnant women recruited, 8 were excluded; 2 were excluded because of inadequate analgesia while the other 6 showed poor parturient compliance to study protocol or had an accelerated course of labour ($<4$ h). Of the 20 patients who completed the study, the mean (sd) gestational age was 38.4 (1.8) weeks, fetal birth weight was 3201 (259) g and placental weight was 587 (289) g. There were no adverse outcomes for either the mothers or infants. All 5 min Apgar scores exceeded 8, and all cord blood gas values were within normal limits. There was no FHR tracing suggesting fetal distress.

The maternal systolic and diastolic blood pressure and heart rate are shown in Table 1; these were stable throughout the study period. One patient developed sudden decrease in
blood pressures from 133/75 to 99/58 mm Hg at 10 min after the initial bolus of bupivacaine (12 ml of 0.075%). This episode was promptly corrected by i.v. fluid infusion without any further decrease in blood pressure. The FHR did not change significantly during the study periods. No patient experienced significant hypotension or tachycardia suggestive of hypovolemia.

The uterine velocimetric values were within the normal range and were in accordance with a previous report.16 Table 1 shows the uterine arterial velocimetric indices during uterine relaxation and contraction at different study time periods. At each time period, all measurements (i.e. PI, S/D, and RI) were repeated at least three times to minimize any sampling error or technical bias. The mean uterine artery S/D ratio, PI and RI significantly increased after starting epidural infusion (1, 2, and 4 h) when compared with the baseline, but these returned to the baseline values 4 h after stopping the infusion. The values of Doppler indices were increased during epidural infusion irrespective of whether the measurements were obtained during uterine relaxation (Fig. 1) or contraction (Fig. 2).

Table 1 FHR and maternal blood pressure, heart rate, uterine artery resistance index (RI), systolic/diastolic velocity ratio (S/D), and pulsatility index (PI) during uterine relaxation or contraction in different study periods. Data are mean (sd). *P<0.05, when compared with values at pre-epidural insertion; #P<0.05 when compared with values during uterine relaxation.

<table>
<thead>
<tr>
<th></th>
<th>Pre-epidural insertion</th>
<th>At 1 h during epidural infusion</th>
<th>At 2 h during epidural infusion</th>
<th>At 4 h during epidural infusion</th>
<th>At 4 h after stopping epidural infusion</th>
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<tbody>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>126 (13)</td>
<td>121 (11)</td>
<td>120 (12)</td>
<td>118 (11)</td>
<td>123 (13)</td>
</tr>
<tr>
<td>Diastolic blood pressure (mm Hg)</td>
<td>72 (7)</td>
<td>66 (5)</td>
<td>68 (6)</td>
<td>65 (5)</td>
<td>69 (7)</td>
</tr>
<tr>
<td>Maternal heart rate (beats min⁻¹)</td>
<td>84 (9)</td>
<td>86 (10)</td>
<td>83 (8)</td>
<td>84 (10)</td>
<td>82 (7)</td>
</tr>
<tr>
<td>FHR (beats min⁻¹)</td>
<td>138 (9)</td>
<td>140 (11)</td>
<td>141 (10)</td>
<td>144 (8)</td>
<td>142 (10)</td>
</tr>
<tr>
<td>Uterine artery RI (placental side)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>During uterine relaxation</td>
<td>0.43 (0.04)</td>
<td>0.62 (0.05)*</td>
<td>0.64 (0.06)*</td>
<td>0.71 (0.06)*</td>
<td>0.45 (0.05)</td>
</tr>
<tr>
<td>During uterine contraction</td>
<td>0.75 (0.06)*</td>
<td>0.94 (0.07)**</td>
<td>0.96 (0.07)**</td>
<td>0.99 (0.07)**</td>
<td>0.78 (0.07)*</td>
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<tr>
<td>Uterine artery S/D ratio (placental side)</td>
<td></td>
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<tr>
<td>During uterine relaxation</td>
<td>1.89 (0.06)</td>
<td>2.88 (0.07)*</td>
<td>2.91 (0.08)*</td>
<td>3.01 (0.06)*</td>
<td>2.01 (0.07)</td>
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<tr>
<td>During uterine contraction</td>
<td>2.79 (0.12)*</td>
<td>4.19 (0.08)**</td>
<td>4.23 (0.09)**</td>
<td>4.24 (0.12)**</td>
<td>2.87 (0.14)*</td>
</tr>
<tr>
<td>Uterine artery PI (placental side)</td>
<td></td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>During uterine relaxation</td>
<td>0.65 (0.05)</td>
<td>1.27 (0.07)*</td>
<td>1.28 (0.09)*</td>
<td>1.31 (0.10)*</td>
<td>0.70 (0.08)</td>
</tr>
<tr>
<td>During uterine contraction</td>
<td>1.24 (0.08)**</td>
<td>2.26 (0.09)**</td>
<td>2.29 (0.09)**</td>
<td>2.31 (0.12)**</td>
<td>1.28 (0.11)**</td>
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Discussion
From the results in this study, the resistance indices of uterine arteries were higher during contractions both at baseline and throughout the study. During epidural infusion, there was a consistent trend in all derived indices suggestive of increased uterine artery resistance regardless of the uterine contractile state. This increased resistance disappears 4 h after labour and the cessation of epidural infusion.

This study examined the Doppler velocimetric indices (S/D ratio, PI and RI) of the uterine artery at five different time periods (pre-epidural insertion, 1, 2 and 4 h)
post-epidural infusion and 4 h after delivery). Because the epidural analgesia was performed using similar techniques and the same anaesthetic agent for each patient, the same techniques and lengths of observation were used for obtaining Doppler data, and the phase of labour and patterns of uterine activity were similar for all patients studied.

In this study, we have chosen derived resistance indices. We did not measure the direct velocimetry for several reasons. First, direct measurement of blood flow in volume per unit time depends entirely on an accurate calculation of cross-section area of the vessels, but cross-section area varies extensively because the exact angle of insonation cannot be determined with certainty in the artery of interest. On the other hand, measuring systolic, diastolic, and mean flow velocities have shown substantial variability between the observers. When the ratio of different velocities is obtained, the variable angle values cancel out mathematically. The RI and PI values are mathematical manipulations that correlate well with the S/D ratio. As a result, the consistent reproducibility of our measurement can ensure a reliable result in a small scale clinical study. Secondly, those derived indices (i.e. S/D ratio, PI, and RI) have been used exclusively in previous reports and by using the same parameters we were able to compare our results with theirs.

Previous reports of the effects of epidural anaesthesia on the Doppler velocimetry of umbilical and uterine arteries during normal term labour have been controversial. Lindblad and colleagues\(^1\) found no significant changes in resistance in the umbilical vein or fetal aorta associated with uncomplicated epidural anaesthesia. Hughes and colleagues\(^8\) concluded that effective epidural anaesthesia did not have a significant impact on Doppler flow characteristics of either the maternal or fetal umbilical vasculature, despite lowered maternal blood pressure and heart rate. Morrow and colleagues\(^2\) also concluded that epidural anaesthesia had neither a beneficial nor detrimental effect on uterine or umbilical blood velocity in uncomplicated pregnancy. Giles and colleagues\(^11\) reported a significant decrease in umbilical arterial and maternal S/D ratios after administration of epidural anaesthesia in their small series of eight non-labouring patients with intact amniotic membranes. On the contrary, Halpern and colleagues\(^9\) reported an increase in PI of the uterine arteries after epidural anaesthesia with lidocaine, epinephrine, and fentanyl but there was no change in the umbilical PI.

We measured the Doppler indices both during uterine contraction and relaxation. This has not been reported before. Furthermore, the previous studies reported a higher level (above T6) and more profound spinal block with the regular dose of local anaesthetic agents, that is, lidocaine 2% and bupivacaine 0.25%. This practice clearly represents a more profound blockade to sympathetic innervation and reactive adrenal secretion of circulatory catecholamine. The change of uterine artery and/or umbilical vein resistance, if any, may parallel the systemic vascular resistance in response to standard spinal anaesthesia. In contrast to the previous studies, we used a more diluted concentration of local anaesthetic agent for a much longer period of time. With less extensive sympathetic blockade and sufficient time for maternal compensation, the increased resistance in uterine artery can occur as a result of spared sympathetic reserve both from higher spinal level and from reactive catecholamine response. From our study, we hypothesize that the mechanisms to increased resistance with our epidural regime were through more sympathetic compensation because: (i) the spinal block was not so high, and (ii) there was more time for compensation in our study model.

In our study, another important and possible factor influencing the effects of continuous epidural analgesia with bupivacaine on Doppler velocimetry of uterine arteries was the timing of detecting uterine artery velocimetric indices (during uterine contraction or relaxation). Takeuchi and colleagues\(^18\) have reported that both the RI and PI of the arterial uterine blood flow velocity waveform were significantly increased during uterine contraction than during relaxation. Our results are consistent with those of Takeuchi and colleagues. Unlike our study, however, Takeuchi and colleagues did not compare these indices with those before epidural injection. Our study appears to be the first study to demonstrate that, as compared with the pre-epidural insertion, RI, S/D ratio, and PI of uterine artery significantly increased after continuous epidural infusion with bupivacaine regardless of the state of uterine contraction status. We suggest that the increased resistance of uterine artery is directly related to the continuous epidural infusion with bupivacaine and this increase is further enhanced during uterine contraction.

In conclusion, our data suggested that excluding other confounding factors (such as pre-eclampsia and concomitant medication with either tocolytic or induction agents), long-term continuous epidural analgesia for painless labour with bupivacaine 0.075% increased Doppler indices (S/D ratio, PI, and RI) of uterine blood vessel resistance. These results might indicate that long-term continuous epidural analgesia for labour analgesia with bupivacaine 0.075% would reduce uterine blood flow during labour. The clinical impact of our findings remains to be determined.

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