Labour analgesia and fetal bradycardia

Edward T. Riley MD

IN recent years there has been some controversy with regard to the safety of the combined spinal/epidural (CSE) technique for labour analgesia. The technique has been associated with fetal heart rate changes (especially fetal bradycardia) after induction of analgesia for labour.¹ The association with fetal bradycardia has prompted some practitioners to abandon the technique. However, abandoning a specific labour analgesic technique to avoid fetal bradycardia is an ill-conceived strategy. All effective analgesic techniques can lead to fetal heart rate changes and the incidence is probably not substantially different between them.^{2,3} What is important to understand is why there are fetal heart rate changes and to know how to resuscitate the fetus. In this review, I will discuss the mechanism of why labour analgesia will lead to fetal bradycardia, the incidence of fetal bradycardia with different analgesic techniques, and what to do when a fetal bradycardia occurs.

How does labour analgesia cause fetal bradycardia?

The induction of labour analgesia sets up a chain of events that leads to fetal bradycardia. Clarke *et al.*¹ proposed the following mechanism:

1. The pain relief leads to a decrease in the output of the sympathetic nervous system. There is a significant decrease in the level of circulating epinephrine after the induction of labour analgesia. This is true with both the CSE technique and the traditional epidural technique.
2. Epinephrine is a tocolytic. A decrease in epinephrine will cause an increase in uterine tone.
3. Increased uterine tone will decrease placental blood flow.
4. If placental blood flow is decreased significantly enough, there will be a subsequent fetal bradycardia.

Is this cascade of events a plausible explanation for why fetal bradycardias occur? It would seem so. Cascio *et al.*⁴ found that circulating epinephrine decreased about 50% after the induction of labour analgesia with either a lidocaine epidural or a CSE technique (Figure 1).

FIGURE 1 Change in epinephrine levels over time after induction of labour analgesia with either a combined spinal/epidural (CSE) technique or a traditional epidural technique. Note that epinephrine levels drop quickly with both techniques. Adapted from Cascio *et al.*⁴

The next step, the tocolytic effect of epinephrine seems plausible given that beta adrenergic drugs are given for preterm labour and uterine hypertonus. In addition, Segal *et al.*⁵ demonstrated that clinically relevant increases in epinephrine concentrations relaxed uterine muscle strips in the laboratory (Figure 2). Alternatively, one assumes decreases in epinephrine should increase uterine muscle contraction.

Is there clinical evidence that there is an increase in uterine contractions after the induction of labour analgesia? In Clarke *et al.*'s¹ case report on fetal bradycardia and the CSE technique, many of the cases had associated uterine hypertonus. We have a manuscript in preparation that shows a strong correlation between fetal bradycardia after labour analgesia induction and uterine hypertonus. However, it should be noted that not all cases of fetal bradycardia after labour analgesia induction are associated with a clinically evident increase in uterine tone. In addition, labour analgesia has not been shown to affect uterine contraction strength.

From the Department of Anesthesia, Stanford University School of Medicine, Stanford, California, USA.

Address correspondence to: Dr. Edward T. Riley, Department of Anesthesia, Stanford University School of Medicine, Stanford, California, USA. Phone: 650-498-7787; Fax: 650-725-8544; E-mail: edriley@stanford.edu

FIGURE 2 Log concentration of epinephrine *vs* the change in tension in a uterine muscle strip. Note: that epinephrine concentration is increasing from left to right (concentrations are expressed as the negative log of the molar concentration).

However, if the uterus does, on occasion, contract more due to the drop in epinephrine, then it is logical that there would be decreased uterine blood flow. Decreased uterine blood flow will eventually lead to fetal asphyxia. This will then lead to the resultant fetal bradycardia.

An alternative hypothesis was proposed by Scott Segal at the 1998 SOAP meeting (there is no formal citation at this time):

1. Pain relief and/or a sympathectomy from spinal or epidural analgesia leads to a decrease in blood pressure.
2. In response to the decrease in blood pressure, norepinephrine levels increase a little.
3. Increased norepinephrine levels will lead to uterine artery constriction.
4. Uterine artery vasoconstriction will decrease placental blood flow.
5. If placental blood flow is decreased significantly enough, there will be a subsequent fetal bradycardia.

Is this hypothesis valid? Cascio *et al.*⁴ demonstrated that not only does epinephrine decrease after the induction of labour analgesia, but also that norepinephrine stays the same or slightly increases. The contrasting changes between epinephrine and norepinephrine could lead an imbalance that favours vasoconstriction of the uterine vessels. Whether this mechanism is solely responsible, contributes to, or is not involved with fetal bradycardia after labour analgesia, is unclear at this point.

Incidence of fetal bradycardia after labour analgesia

In 1994 Clarke *et al.*¹ reported a case series where nine out of 30 consecutive fetuses of mothers that received the CSE technique for labour analgesia developed a bradycardia immediately after the spinal injection of fentanyl 50 µg. In five of the nine cases there was uterine hypertonus associated with the bradycardia. Seven of the nine cases resolved either spontaneously or after giving terbutaline. However, two patients had emergency Cesarean deliveries. Fortunately neonatal and maternal outcome was excellent in every case.

Further evidence that there is an association between labour analgesia and fetal bradycardia was provided by Gambling *et al.*⁶ They compared the CSE technique with *iv* meperidine for labour analgesia. The authors found that eight of the 400 patients (2%) of the CSE patients had emergent Cesarean deliveries for fetal bradycardia within one hour of the spinal injection component of the CSE. None of the meperidine patients needed an emergent Cesarean delivery. Presumably, there would be a higher incidence of fetal bradycardia with the CSE technique because *iv* meperidine would not provide enough analgesia to set the proposed mechanism by which labour analgesia causes fetal bradycardia into motion.

When effective labour analgesic techniques are used for labour, there seems to be a significant incidence of fetal bradycardia (3–20%).^{2,3,7} There does not appear to be any significant difference in the incidence of fetal bradycardia with regard to analgesic technique. In three studies that had comparable groups of patients, the incidence of fetal bradycardia was not different whether the patient had a CSE technique or an epidural technique for labour analgesia.^{2,3,7}

How do we treat fetal bradycardia after performing a CSE?

Should we be concerned with this association between labour analgesia, fetal bradycardia and emergency Cesarean delivery? If I believed that there truly was a 2 to 5% risk of emergent Cesarean associated with the use of the CSE technique (e.g., the study by Gambling *et al.*⁶ or the case series by Clarke *et al.*¹), I would be against its use. However, I believe the labour analgesic techniques such as epidurals and combined spinal techniques are safe. The key is managing the fetal heart rate changes appropriately if they occur.

Albright and Forster⁸ reviewed their practice and found that out of 1,240 CSE they performed for labour analgesia, not one patient required an emergent Cesarean delivery within 90 min of the induction of analgesia. In the three studies comparing CSE and epidural techniques^{2,3,7} there were no Cesarean deliv-

eries performed within one hour of induction of analgesia. I believe this experience mirrors what happens in most practices.

Why were all these centres able to avoid performing any emergent Cesarean deliveries after performing all these blocks that have a relatively high incidence of fetal bradycardia? Most likely because there was proper treatment. In the face of a fetal bradycardia, I recommend the following treatment:

- Uterine displacement. Remember this any time there is significant fetal or maternal resuscitation! Practitioners often forget about uterine displacement.
- Correct any hypotension. I give ephedrine if the systolic blood pressure is less than baseline.
- Supplemental oxygen. This may increase the supply to the fetus.
- Turn off oxytocin. May help relax the uterus.
- Fetal scalp stimulation.
- Change maternal position.
- Nitroglycerin 200 to 400 µg *iv* or *sl*. It's quick, easy, few side effects, and labour will quickly return to normal after giving it. However, if it does not work quickly (two to four minutes) I give terbutaline.
- Terbutaline 0.25 mg *sc*

All of the above interventions are standard for resuscitation of the fetus except for nitroglycerin. Nitroglycerin has been used for acute uterine relaxation in a number of circumstances (e.g., retained placenta, uterine inversion, etc.).⁹ However, clinical evidence that nitroglycerin actually relaxes the uterus is limited to case series and observational studies. Despite this, the American Society of Anesthesiologists has recommended its use for uterine relaxation for removal of a retained placenta.¹⁰ Mercier *et al.*¹¹ conducted a prospective, observational study and determined that nitroglycerin was effective for acutely relaxing the uterus in the circumstance of fetal bradycardia after labour analgesia. Therefore, the use of nitroglycerin in this circumstance is well supported by experts in the field.

Why use nitroglycerin instead of terbutaline for acute uterine relaxation? The main advantage of nitroglycerin is that it will acutely relax the uterus, but then its effects are short-lived. The parturient will return to a normal labour pattern quickly. With terbutaline, labour can be slowed for 30 to 60 min. Terbutaline also causes a prolonged tachycardia that can be distressing for some women.

Summary

Labour analgesia induction can result in fetal heart rate changes and even severe fetal bradycardia. This is

most likely due to uterine hypertonus secondary to an acute drop in circulating epinephrine. If the uterus is quickly relaxed and fetus properly resuscitated, this should not affect the outcome of the delivery or neonatal health.

References

- 1 Clarke VT, Smiley RM, Finster M. Uterine hyperactivity after intrathecal injection of fentanyl for analgesia during labour: a cause of fetal bradycardia? (Letter). *Anesthesiology* 1994; 81: 1083.
- 2 Palmer CM, Maciulla JE, Cork RC, Nogami WM, Gossler K, Alves D. The incidence of fetal heart rate changes after intrathecal fentanyl labour analgesia. *Anesth Analg* 1999; 88: 577–81.
- 3 Nielsen PE, Erickson JR, Abouleish EI, Perriatt S, Sheppard C. Fetal heart rate changes after intrathecal sufentanil or epidural bupivacaine for labour analgesia: incidence and clinical significance. *Anesth Analg* 1996; 83: 742–6.
- 4 Cascio M, Pygon B, Bennett C, Ramanathan S. Labour analgesia with intrathecal fentanyl decreases maternal stress. *Can J Anaesth* 1997; 44: 605–9.
- 5 Segal S, Csavoy AN, Datta S. The tocolytic effect of catecholamines in the gravid rat uterus. *Anesth Analg* 1998; 87: 864–9.
- 6 Gambling DR, Sharma SK, Ramin SM, *et al.* A randomized study of combined spinal-epidural analgesia versus intravenous meperidine during labor: impact on cesarean delivery rate. *Anesthesiology* 1998; 89: 1336–44.
- 7 Eberle RL, Norris MC, Eberle AM, Naulty JS, Arkoosh VA. The effect of maternal position on fetal heart rate during epidural or intrathecal labor analgesia. *Am J Obstet Gynecol* 1998; 179: 150–5.
- 8 Albright GA, Forster RM. Does combined spinal-epidural analgesia with subarachnoid sufentanil increase the incidence of emergency cesarean delivery? *Reg Anesth* 1997; 22: 400–5.
- 9 Riley ET, Cohen SE, Chitkara U. Intravenous nitroglycerin: a potent uterine relaxant for emergency obstetric procedures. Review of literature and report of 3 cases. *Int J Obstet Anaesth* 1996; 5: 264–8.
- 10 Hawkins JL, Arens JF, Bucklin BA, *et al.* Practice Guidelines for Obstetrical Anesthesia: a report by the American Society of Anesthesiologists Task Force on Obstetrical Anesthesia. *Anesthesiology* 1999; 90: 600–11.
- 11 Mercier FJ, Dounas M, Bouaziz H, Lhuissier C, Benhamou D. Intravenous nitroglycerin to relieve intrapartum fetal distress related to uterine hyperactivity: a prospective observational study. *Anesth Analg* 1997; 84: 1117–20.