Effects of Nitrous Oxide and Fentanyl Anesthesia on Fetal Heart-rate Variability
Intra- and Postoperatively

ERIC S. JOHNSON, M.D.,* AND PETER S. COLLEY, M.D.†

Loss of fetal heart rate (FHR) variability is often used as an indicator of fetal hypoxia in the awake parturient in labor. Decreased FHR variability presumably could also be used as an indicator of fetal hypoxia in the pregnant patient undergoing a surgical procedure. There is little information, however, as to the effects of general anesthesia on FHR variability. Katz et al.¹ have reported the operative courses of two pregnant patients anesthetized with halothane and nitrous oxide in whom FHR variability was normal except when it decreased in the presence of fetal hypoxia. Their report suggests that general anesthesia itself has little or no effect on FHR variability. The following case report suggests that anesthesia with nitrous oxide and fentanyl can cause loss of FHR variability in the absence of fetal hypoxia.

REPORT OF A CASE

A 28-year-old woman, gravida 3, para 1, abortus 1, weighing 57 kg, had a 28-week intrauterine pregnancy. She sought treatment for headaches and menimngismus. A computed tomographic (CT) brain scan and cerebrall angiography were consistent with an avascu lar tumor of the third ventricle producing hydrocephalus. A left frontal craniotomy was scheduled. The only other medical problem was neurofibromatosis, the diagnosis based on numerous café au lait spots.

The patient was brought to the operating room unpremedicated. A towel roll was positioned beneath the right hip, producing left uterine displacement. Peripheral and central intravenous catheters and a radial-artery catheter were placed. The FHR was recorded with a Hewlett-Packard 8300-A Cardiotocograph* with the ultrasonic Doppler transducer applied externally to the abdomen. Maternal blood pressure was 100/50 torr, pulse rate, 100/min, and FHR, 130/min, with normal "long-term" FHR variability (fig. 1, 0800 hr). Arterial blood-gas values during breathing of room air were pH 7.47, PaO₂ 82 mmHg, PaCO₂ 29 mmHg, and HCO₃⁻ 22 mmol/l.

The patient was given droperidol, 2.5 mg; fentanyl, 0.05 mg, and diazepam, 5 mg, iv, for sedation, with no change in maternal or fetal vital signs. A ventriculostomy was placed using local anesthesia, and the intracranial pressure (ICP) measured 2 cm H₂O.

Induction of anesthesia followed, with a sequence of voluntary hyperventilation, thiopental, 250 mg, pancuronium, 7 mg, controlled hyperventilation, laryngoscopy, and orotracheal intubation. The patient was mechanically ventilated with a tidal volume of 700 ml at a rate of 10/min, with an inhaled mixture of nitrous oxide and oxygen (60:35). Two minutes after induction and tracheal intubation maternal blood pressure decreased to 80/50 torr, and FHR slowed from 140 to 100/min, without loss of long-term FHR variability. Ephedrine, 5 mg, iv, raised the blood pressure to 95/50 torr, and FHR increased to 130/min. Arterial blood-gas values at an inspired fraction of oxygen (F io₂) of 0.33 were pH 7.36, PaO₂ 75 torr, PaCO₂ 43 mmHg, and HCO₃⁻ 24.5 mmol/l. The endotracheal tube was withdrawn 2 cm, and the results of a repeat arterial blood-gas analysis, without alteration of the ventilator or F io₂, were pH 7.48, PaO₂ 102 torr, PaCO₂ 33 mmHg, and HCO₃⁻ 25 mmol/l. Maternal blood pressure stabilized at 100/60 torr.

The FHR continued at 130/min with normal long-term variability until 20 min after induction, during which time, fentanyl, 200 μg, had been given iv in divided doses. The FHR variability then became minimal (heart rate changes from 0 to 3/min), and remained this way throughout the operative period (six hours) (fig. 1, 1100 hr).

A grade 2 astrocytoma was partially excised from the left lateral ventricle. Intraoperatively, maternal blood pressure, pulse and temperature were maintained at normal levels, and urinary output averaged 75 ml/hr (mannitol was not given). Representative arterial blood-gas values at F io₂ 0.33 were pH 7.46, PaO₂ 100 torr, PaCO₂ 29 torr, and HCO₃⁻ 20.7 mmol/l. Anesthesia was maintained with nitrous oxide and fentanyl; pancuronium was given for paralysis. Elevation of blood pressure and maternal heart rate were indications for additional doses of fentanyl. A total of 19 ml fentanyl (0.05 mg/ml) and 15 mg pancuronium was given iv. The endotracheal tube was removed in the operating room. The patient immediately opened her eyes and followed simple commands.

The preanesthetic pattern of normal long-term FHR variability did not return until two hours after completion of the operation (fig. 1, 1515 hr and 1700 hr). During that interval the patient received no medication.

The patient was discharged from the hospital six days after operation with no neurologic dysfunction. She returned eight weeks later for cesarean section and tubal ligation. With lumbar epidural anesthesia, a 3,290-g female infant with Apgar scores of 8 and 9 at 1 and 5 min, respectively, was delivered. Three weeks post partum the patient received a course of brain irradiation. Six months after

* Resident.
† Assistant Professor.

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Address reprint requests to Dr. Johnson.
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Fig. 1. Loss of fetal heart-rate variability (long-term) is demonstrated by comparing fetal rhythm strips at 0800 and 1100 hours. The gradual return of normal variability postoperatively is shown at 1515 and 1700 hours (each division is equal to 1 cm, the recorder rate is 3 cm/min).

the craniotomy, both she and her daughter were free of any neurologic impairment.

DISCUSSION

Fetal heart-rate variability is of two types: beat-to-beat or "short-term" variability, which describes changes in the interval between successive pairs of heart beats, and "long-term variability," which is somewhat rhythmic fluctuations in rate occurring two to six times per minute with a normal amplitude of change in rate of 6–10/min. Both types of variability tend to change in the same direction, and both are often decreased with fetal hypoxia. Long-term variability is also suppressed during fetal sleep. The external Doppler ultrasound fetal monitor may artifactually increase short-term variability, and is more reliable in detecting loss of long-term variability. Katz et al. reported a case in which external monitoring detected fetal tachycardia and loss of FHR variability in a hypoxemic patient anesthetized with halothane and nitrous oxide. With resolution of the hypoxemia, however, the fetal heart rate and variability returned to normal, despite the continuation of halothane–nitrous oxide anesthesia. In the same report, the authors also noted the persistence of normal FHR variability in a second patient during anesthesia with halothane and nitrous oxide. The lack of effect of halothane–nitrous oxide anesthesia on fetal variability is contrary to the prolonged loss of FHR variability in our patient during anesthesia with nitrous oxide and fentanyl. The absence of maternal hypotension, hypoxemia, acidosis, and vasoconstriction in our patient makes the possibility of an inadequate supply of oxygen to the fetus an unlikely cause of the fetal rhythm change.

Both diazepam and thiopental were administered to our patient, and these drugs have been reported to decrease FHR variability. There was, however, no loss of FHR variability in our patient until 20 min following induction, when anesthesia was being maintained with nitrous oxide and fentanyl. The effects of fentanyl on FHR variability have not been reported, but Petrie et al. found that a single sedative dose of both morphine and meperidine, iv, reduced FHR variability in approximately 55 per cent of pregnant patients, and that this effect lasted more than 30 min.

From studies of the effects of narcotics on FHR variability, we conclude that the intraoperative and postoperative loss of FHR variability in the case of our patient was probably secondary to the direct effects of fentanyl alone, or the combination of nitrous oxide and fentanyl, on the fetus. The prolonged loss of FHR variability does not appear to have had any long-term detrimental effects on the fetus. The normal birth and development of the infant indicate that a loss of FHR variability due to fetal drug effects is not necessarily an ominous sign, as is the loss of variability due to fetal hypoxia.

REFERENCES