Determining Placental Transfer of Remifentanil Used As an Adjunct to Epidural Anesthesia. Kan et al. (page 1467)

Kan et al. included 19 parturients eligible for routine epidural anesthetic for non-emergent cesarean sections in their study to determine the extent of placental transfer of remifentanil and any possible side effects on mothers and neonates. The women first received 30 ml of a nonparticulate antacid orally and a 1- to 2 ml intravenous crystalloid bolus before anesthetic administration. After placement of epidural catheters (using loss-of-resistance technique followed by 2% lidocaine test doses), patients received epidural solutions of 2% lidocaine with epinephrine in divided doses to establish a sensory level around T4. Intravenous infusions of remifentanil were administered after dosing of the epidural catheter with lidocaine at a dose of 0.1 μg·kg<sup>−1</sup>·min<sup>−1</sup>. Skin incisions were timed for 15 min after initiation of the intravenous infusions, which were continued until skin closure.

Participating anesthesiologists were allowed to use clinical judgment to increase the intravenous remifentanil infusion or to administer additional 2% epidural lidocaine or an intravenous bolus of remifentanil. Two reductions in the intravenous infusion dose, each halving the existing rate, were allowed before discontinuation of the infusion. Each patient received 3-5 mg of epidural morphine and oxygen, 3-5 l/min by mask, after delivery.

Maternal arterial and umbilical venous and arterial samples were obtained for analysis of blood gases and concentrations of remifentanil and remifentanil acid after delivery. Neonates were evaluated by Apgar scores at 1, 5, 10, and 20 min and using Neurologic and Adaptive Capacity Scores (NACS) at 30 and 60 min and were observed for side effects until 24 h after delivery. Likewise, maternal side effects were monitored for 24 h after delivery. Maternal blood pressure, heart rate, oxygen saturation, and respiratory rate were recorded continuously, and pain and sedation scores were recorded 15 min. before and after initiation of intravenous infusion and at several other predetermined points during and after the cesarean sections.

The researchers recorded a mean remifentanil umbilical vein/maternal arterial (UV/MA) ratio of 0.88 ± 0.78, suggesting a significant degree of placental transfer. The mean remifentanil umbilical artery/umbilical vein (UA/UV) ratio of 0.29 ± 0.07 was low, suggesting a rapid distribution of the drug in the fetus. However, these results are limited by the single sampling of blood (at delivery only) and may not accurately reflect levels of the drug in newborns. All babies scored over 7 on the Apgar score at 5 min after delivery, so the neonates did not appear to be adversely affected. Intravenous infusion rates were decreased in 3 of 17 parturients before delivery because of transient hypotension (n = 1) and subjective excessive sedation (n = 2). After delivery, five parturients also required a decrease in their infusions because of dizziness and excessive sedation. Because of these side effects and some respiratory depression, remifentanil use as an obstetric analgesic must be evaluated further.

How Reliable Is Aspiration in Detecting Intravascular Placement of Epidural Catheters? Norris et al. (page 1495)

Norris et al. used 20-gauge, multiholed epidural catheters in 1,029 of 1,624 women requesting neuraxial labor analgesia. At the discretion of the anesthetist, patients received either epidural or combined spinal epidural (CSE) anesthesia. After insertion of the catheters, the initial testing was performed according to a defined protocol: (1) catheters were observed and gently aspirated for return of blood or cerebrospinal fluid; (2) if negative, 2 ml of local anesthetic (0.25% bupivacaine or 0.2% ropivacaine) was administered to rule out intrathecal placement; (3) 10-15 ml local anesthetic ± opioid in divided doses was administered to patients receiving epidural analgesia, and infusions of 0.083% bupivacaine with 0.33 mg/ml sufentanil at 10-15 ml/h were begun for patients receiving CSE analgesia.

Most of the catheters yielding blood or CSF were removed and reinserted, although management was left to the clinician’s discretion. Data sheets kept on each epidural catheter included patient demographics, depth of catheter insertion, anesthetic technique, presence of blood or cerebrospinal fluid, results of the intrathecal local anesthetic test, and whether the catheter was judged to be “positive” (presence of bilateral sensory change and effective analgesia), “negative” (no sensory change) or “equivocal” (inadequate analgesia despite some sensory change within 2 h of intrathecal drug injection).

Using aspiration and observation, the team detected 60 intravenous catheters. Most were simply replaced and reinserted. Six catheters initially within vessels were with-
drawn until aspiration was negative and then dosed. Four of these catheters were judged positive, whereas two were still intravascular. Two other catheters may have been intravenous despite negative aspiration. Although this is the largest study to date examining aspiration alone as a method to detect intravascular catheters, the degree of accuracy depended on using multiholed catheters and incrementally administered doses of low concentrations of the local anesthetics. The results of any test of catheter location, the authors caution, should never lead the clinician to administer a bolus injection of large and potentially toxic doses of local anesthetics.

**Effect of Hypothermia on Platelet Function Studied In Vitro. Faraday et al. (page 1579)**

To clarify the effect of temperature on platelet function, Faraday et al. collected blood from 36 healthy volunteers (aged 20–45 yr; 24 men and 12 women). The blood was anticoagulated with 3.8% sodium citrate (9:1) and then placed into multiple plastic cuvettes. The team used three methods (platelet aggregation, platelet fibrinogen binding, and PAC-1 binding) to assess the activation of platelet GPIIb-IIIa, a surface receptor that when activated binds fibrinogen (and PAC-1) and facilitates aggregation. P-selectin expression was also measured. Measurements were taken under conditions of normothermia (37°C), moderate hypothermia (33°C), and profound hypothermia (22°C).

ADP and collagen-induced platelet aggregation and fibrinogen binding were greater at 22°C and 33°C than at 37°C (normothermia). Platelet binding of PAC-1 and P-selectin antibodies also were greater during hypothermic conditions. In another 10 experiments, samples were kept at either 22°C, 33°C, or 37°C for 30 min. The cooler samples were rewarmed to 37°C and then analyzed for aggregation responses. In this series the aggregation responses were indistinguishable from those maintained at normothermia, revealing a rapid reversal of increased platelet reactivity when normal temperatures were reestablished.

Platelet GPIIb-IIIa activation and P-selectin expression were enhanced at hypothermic temperatures, but the effects depended on the platelet agonist used. Increased aggregability was clearly demonstrated for ADP, but was not apparent for collagen. Platelet stimulation using TRAP (thrombin receptor activating peptide) dramatically increased GPIIb-IIIa activation at hypothermic temperatures. The results indicate that hypothermia increases the ability of platelets to respond to activating stimuli. However, the experiment involved a relatively short period of hypothermia (only 30 min), so extrapolating results to clinical conditions, in which hypothermia is likely to last much longer, may be difficult.

**Response of Rat Astroglial Cells to Hypertonic Mannitol. McManus et al. (page 1586)**

McManus et al. investigated the volume response of astroglial cells exposed to hypertonic mannitol. They cultured rat C6 glioma cells in Eagles's minimal essential medium, maintaining cultures in a humidified 5% CO2/95% air atmosphere at 37°C, changing the growth medium every 48 h. Experiments were conducted when cultures reached 80–90% confluence (about 3–5 days). The researchers confirmed the cells were healthy, with normal morphology, in microscopic examination before each experiment.

After first equilibrating cells at physiologic temperature and pH, the team abruptly replaced isotonic solution perfunctuate with hypertonic experimental solutions. They used laser light scattering to observe and measure changes in relative cell volume in real time. Decreases in cell volume were detected by increases in laser light scattering and PMT voltage outputs. Conversely, decreased light scattering and PMT voltage outputs indicated increases in cell volume.

The team also conducted four to six experiments exposing cells to a furosemide and mannitol solution (+40 mOsm) after first equilibrating them in an isotonic buffer containing furosemide. Results showed that sudden exposure to hypertonic mannitol caused cells to shrink rapidly. However, after only a brief lag time, cell volume returned to baseline at a mean initial rate of 1.7 ± 0.36%/s and then increased beyond baseline. Cells stabilized in a swollen state for the remainder of the 30-min observation period. This rebound swelling was concentration-dependent and in the separate furosemide experiments was significantly inhibited in the presence of furosemide.

Osmotherapy with mannitol is commonly used in neuroanesthesia and critical care settings. The results of this study, although preliminary, seem to suggest that entry of mannitol into the brain might contribute to cerebral edema.

Gretchen Henkel

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