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 21 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⁻¹·min⁻¹. 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 cli-
ician 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 vol-
unteers (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 activ-
ation of platelet GPIIb-IIIa, a surface receptor that
when activated binds fibrinogen (and PAC-1) and facil-
tates aggregation. P-selectin expression was also mea-
sured. 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 hypother-
ic 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 expres-
sion 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) dramati-
cally increased GPIIb-IIIa activation at hypothermic tem-
peratures. The results indicate that hypothermia in-
creases the ability of platelets to respond to activating
stimuli. However, the experiment involved a relatively
short period of hypothermia (only 30 min), so extrap-
olating results to clinical conditions, in which hypother-
mia 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 Eagle’s minimal essential
medium, maintaining cultures in a humidified 5% CO2/
95% air atmosphere at 37°C, changing the growth me-
dium 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 be-
fore each experiment.

After first equilibrating cells at physiologic tempera-
ture and pH, the team abruptly replaced isotonic solu-
tion perfusate 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 indi-
cated 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 sud-
den 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 furose-
mide experiments was significantly inhibited in the
presence of furosemide.

Osmotherapy with mannitol is commonly used in neu-
roanesthesia 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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