

## ANESTHESIOLOGY

### ■ Testing Alternatives to Bispectral Index as Measures of Sevoflurane Drug Effect. Ellerkmann *et al.* (page 1275)

In 16 participants scheduled for minor surgery, Ellerkmann *et al.* analyzed the performance of a new electroencephalographic monitor designed for measuring depth of anesthesia and compared its performance to the Bispectral Index as a measure of sevoflurane drug effect. The new monitor calculates two different spectral entropy indicators: state entropy, which is computed over the frequency range from 0.8 to 32 Hz, reflecting the electroencephalographic-dominant part of the spectrum; and response entropy, computed over the frequency range of 0.8 to 47 Hz.

All participants in the study were American Society of Anesthesiologists physical status 1 or 2. Anesthesia was induced by sevoflurane inhalation only, and patients were mechanically ventilated *via* facemask to an end-tidal carbon dioxide of 35 mmHg. Sevoflurane concentrations were decreased and increased systematically two to four times to achieve end-tidal concentrations between 1 and 4 vol%. Measurements were then stopped and patients were intubated for surgery. The performance of state entropy, response entropy, and Bispectral Index to predict the estimated sevoflurane effect site concentration, obtained by simultaneous pharmacokinetic and pharmacodynamic modeling, was compared by calculating the correlation coefficients and the prediction probability. The investigators demonstrated a close correlation of state entropy and response entropy with sevoflurane effect site concentrations. Both measures detected increasing and decreasing sevoflurane concentrations as well as the BIS<sup>®</sup> monitor (Aspect Medical Systems, Newton, MA). The authors believe that the new model can be useful as a monitor for measuring increasing and decreasing sevoflurane concentrations over the entire range of observed anesthetic depth. They urge further investigation, however, to determine whether response entropy yields an advantage in revealing electromyographic activation, leading to faster response in patient arousal.

### ■ Does Genetic Testing Add to Predictive Value of Preoperative Cardiac Risk Assessment? Faraday *et al.* (page 1291)

Between June 1997 and May 2002, 196 patients who underwent elective infrainguinal surgery, abdominal aor-

tic surgery, or descending thoracic aortic surgery were enrolled in a study conducted by Faraday *et al.* The object of the study was to determine whether platelet genotype would furnish additional useful information for preoperative cardiac risk assessment. Clinical risk factors for perioperative myocardial ischemia were obtained from patient interviews and review of their medical records, and participants gave their permission for genetic testing to determine platelet genotype.

Patients' DNA was genotyped for the Leu33Pro polymorphism of GPIIIa and the Thr145Met polymorphism of GPIIb. The myocardial ischemic outcomes for the study were defined as the occurrence of one of the following within 30 days of surgery: cardiac death; myocardial infarction; elevated surveillance troponin I; or prolonged myocardial ischemia on automated ST-segment analysis. There were 65 patients from the group (33%) who suffered one or more ischemic endpoints: 2% died; 5% suffered myocardial infarction; 20% had elevated troponin I levels; and 22% exhibited prolonged myocardial ischemia on automated ST-segment analysis.

Multivariate regression identified five factors that were independently associated with the main ischemic outcome measure: diabetes mellitus, abdominal aortic surgery, thoracic aortic surgery, Pro33 genotype, and Met145 genotype. The greatest risk of perioperative myocardial ischemia was associated with the operative procedure: thoracic aortic surgery is greater than abdominal aortic surgery is greater than infrainguinal surgery. The investigators constructed a final model to predict the primary ischemic outcome measure, assigning a numeric value to each risk factor and calculating a summary risk score. Addition of platelet genotype to the clinical risk factors improved the model's predictive ability by likelihood ratio testing. The relationship between platelet genotype and the secondary outcome measure (defined as clinical myocardial infarction or elevated troponin I only) was weaker. The authors caution that results of this study should be considered preliminary; if reproduced by others, their findings could be considered clinically useful.

### ■ Volatile Anesthetics and Protection against Renal Ischemia-Reperfusion Injury in Rats. Lee *et al.* (page 1313)

Lee *et al.* designed a set of experiments to determine whether volatile anesthetics can protect against renal

ischemia-reperfusion injury, as has been demonstrated in cardiac ischemia-reperfusion injury, and if so, what the mechanisms of protection might be.

The team anesthetized rats with equipotent doses of volatile anesthetics (desflurane, halothane, isoflurane, or sevoflurane) or injectable anesthetics (pentobarbital or ketamine). Each animal was subjected to midline laparotomy, right nephrectomy and sham operation, or 45 min left renal ischemia during anesthesia. After the procedure, pentobarbital- or ketamine-treated animals were returned to their cages to recover from anesthesia. Animals that received volatile anesthetics were allowed to breathe identical anesthetic concentrations spontaneously for an additional 3 h.

In another set of experiments, the team tested whether a 1-h pretreatment with a volatile anesthetic provided protection against renal ischemic injury during intraperitoneal pentobarbital anesthesia. In addition, the team pretreated rats with 6 mg/kg intravenous glibenclamide, a  $K^+_{ATP}$  channel antagonist, 30 min before sevoflurane anesthesia. The latter experiment was designed to determine whether volatile anesthetics mediate renal protection through activation of  $K^+_{ATP}$  channels.

Within 24–72 h after injury, the rats treated with volatile anesthetics had lower plasma creatinine levels and less renal necrosis compared with rats anesthetized with pentobarbital or ketamine. Desflurane demonstrated the weakest reduction in plasma creatinine of the four volatile anesthetics tested. The investigators believe the protection against renal ischemic injury was due mainly to the antiinflammatory effects of the anesthetics: the renal cortices from rats treated with volatile anesthetics demonstrated reduced expression of intercellular adhesion molecule-1 protein and messenger RNA, as well as messenger RNAs encoding proinflammatory cytokines and chemokines. Glibenclamide failed to block renal protection, demonstrating that  $K^+_{ATP}$  channels are not involved in the mechanisms of renal protection.

### ■ Nicotine Nasal Spray Assessed for Analgesic Activity Postsurgery in Women. Flood and Daniel (page 1417)

Flood and Daniel conducted a randomized, double blind, placebo-controlled trial to assess the analgesic efficacy of

a single 3 mg dose of nicotine nasal spray in 20 healthy women set to undergo uterine surgery. All patients were given standardized anesthetic premedication consisting of fentanyl and vecuronium. Anesthesia was induced with propofol and succinylcholine. After reversal of the muscle relaxant, as the surgeon was closing the fascia, the anesthesiologist was given an opaque sealed container with either nicotine nasal spray or saline nasal spray (placebo). The nasal spray was administered as three jets in each nostril at a 45-degree angle.

Patients were asked to report their pain (0 to 10 on the Visual Analogue Scale) at 5 min intervals for 1 h after extubation, and at 2 and 24 h postsurgery. Patient-controlled analgesia pumps were programmed to deliver 1 mg doses of morphine, with a lockout interval of 6 min and a maximum dose during 1 h of 10 mg. Rescue doses of 3 mg morphine administered by a nurse, up to a maximum of 12 mg every 4 h, were allowed if the patient's pain score was greater than 3 of 10. If the patient had a respiratory rate of less than 8 breaths per minute or was determined by the nurse to be oversedated, rescue doses were not given. Blood pressure and heart rate were monitored continuously for the first hour. The investigator recording data and the nurse were blinded as to treatment group assignment.

Patients in the placebo group (nasal saline spray) reported more postoperative pain than did the patients treated with nicotine nasal spray. Peak pain scores in the placebo group were 7.6 at 25 min after extubation, whereas peak pain scores in the nicotine-treated group were 5.3 at approximately 35 min after surgery. The patients in the nicotine group still reported lower pain scores 24 h after surgery, and their morphine utilization was less (6 mg *versus* 12 mg in the placebo group). Blood pressure and heart rate were not affected by nicotine nasal spray; in fact, systolic blood pressure was actually lower in the study drug-treated group. The investigators do not know whether this treatment will be equally effective in men. In addition, the ideal dose and administration paradigm for nicotinic analgesia in the postoperative period remains to be developed.

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