

## ANESTHESIOLOGY

### ■ Sugammadex: A Safe Alternative for Reversing Neuromuscular Blockage? Sparr *et al.* (page 935)

In three centers, Sparr *et al.* investigated the efficacy and safety of sugammadex in reversing rocuronium-induced neuromuscular blockade. The primary objective of the study was to establish time to recovery of train-of-four (TOF) ratio to 0.9. The study's secondary objectives included evaluation of the safety, pharmacokinetic profile, and pharmacokinetic-pharmacodynamic relation of single doses of sugammadex.

Ninety-eight adult male study participants were anesthetized with propofol and fentanyl and then randomly assigned to receive sugammadex (1, 2, 4, 6, or 8 mg/kg) or placebo at 3, 5, or 15 min after administration of 0.6 mg/kg rocuronium. Control values for TOF ratios, determined using supramaximal stimulation, were recorded immediately before administration of the neuromuscular blocking agent. Neuromuscular monitoring was continued for at least 60 min after the administration of sugammadex or placebo. Blood samples were collected for pharmacokinetic analysis. Urine samples were obtained from patients at only one of the trial sites.

The time from end of the study drug administration until recovery of the TOF to a ratio of 0.7, 0.8, and 0.9 was assessed. After administration of placebo, the mean time to recovery of the TOF ratio to 0.9 after dosing at 3, 5, and 15 min decreased from 52.1, 51.7, and 35.6 min. After administration of 8 mg/kg sugammadex, recovery to commensurate TOF ratios was 1.8, 1.5, and 1.4 min. Sugammadex was safe and well-tolerated, but 20.4% of patients showed signs of inadequate anesthesia after its administration. Based on analysis of urine samples obtained from one group of participants, sugammadex enhanced renal excretion of rocuronium; its clearance is about one third that of rocuronium.

### ■ Impact of Recruitment Maneuvers Examined in Patients with Acute Respiratory Distress Syndrome. Constantin *et al.* (page 944)

Patients with acute respiratory distress syndrome have impaired alveolar fluid clearance. Constantin *et al.* designed a study to assess alveolar fluid clearance after a recruitment maneuver in patients with acute respiratory distress syndrome. For their study, they enrolled 15 consecutive, unselected patients who met American Eu-

ropean Consensus Conference acute respiratory distress syndrome criteria. They excluded those with chronic respiratory insufficiency, intracranial hypertension, bronchopleural fistula, and unstable hemodynamics.

Patients were orally intubated, sedated with sufentanil and midazolam, given cisatracurium, and ventilated. Pulmonary edema fluid and plasma protein concentrations were measured before and after a recruitment maneuver (RM), accomplished by maintaining positive end-expiratory pressure 10 cm H<sub>2</sub>O above the lower inflection point of the pressure-volume curve for 15 min. During RM, the maximum peak airway pressure was limited to 50 cm H<sub>2</sub>O. In case of severe arterial hypotension or severe hypoxemia, the team immediately discontinued the RM. Investigators classified a positive response to RM as a 20% increase in Pao<sub>2</sub> 1 h after RM. After the RM, patients were ventilated with initial ventilator settings. Bronchoalveolar fluid was collected at 1 and 4 h after RM for measurement of protein concentrations.

All patients in the study initially had severe hypoxemia with a Pao<sub>2</sub>/Fio<sub>2</sub> ratio of 163 ± 64 mmHg, a mean chord compliance of 31 ± 5 ml/cm H<sub>2</sub>O, and a mean alveolus/plasma protein ratio of 1.16 ± 0.46. After the RM, eight patients were considered responders—Pao<sub>2</sub> increased by 181% and 185% at 1 and 4 h after RM. Seven patients were nonresponders—there was a 9% decrease in Pao<sub>2</sub> 1 h after RM, returning to baseline values 4 h later. In the responders, alveolar concentrations of proteins increased by 26% 1 h after RM and by 40% 4 h after RM. Net alveolar fluid clearance and significant alveolar recruitment were observed in the responding patients. Further studies will be necessary to assess whether the beneficial effects of RM observed in this study influence lung fluid balance over several hours or days.

### ■ Epinephrine Compared with Arginine Vasopressin to Treat Anaphylactic Shock in Rats. Dewachter *et al.* (page 977)

In a rat model of anaphylactic shock, Dewachter *et al.* explored the use of alternatives to epinephrine to treat anaphylactic shock. Four groups of six rats were sensitized by subcutaneous administration of grade VI chicken egg albumin. After surgery for instrumentation placement, hemodynamic values were allowed to stabilize. Then anaphylactic shock was induced by injecting 1 mg ovalbumin diluted in 500 µl of saline solution over 1 min. Rats were randomly allocated into four groups. The

control group received no added therapy (saline only) after induction of shock, while one group received epinephrine alone. A third group received arginine vasopressin (AVP) alone and the fourth group received an epinephrine bolus followed by AVP continuous infusion. Investigators noted the average dose per minute of vasoconstrictor drugs, the duration of drug infusion, and weight evolution in surviving rats. The animals who survived the experiment were killed on day 7.

The group of rats receiving saline all died, as did those who received AVP alone. There was an 84% survival rate in the rats who received epinephrine alone, but 100% of the rats who received epinephrine + AVP survived. The mean average weight loss in the epinephrine-only group on day 7 was 23%, whereas the weight loss for rats treated with epinephrine + AVP averaged 16%. Based on these results, epinephrine must still be considered the first-line therapy for anaphylactic shock. Further studies will be necessary to determine whether administration of a continuous small dose of AVP added to epinephrine could be clinically relevant.

### ■ What Contributes to Chronic Pain after Hysterectomy? Brandsborg *et al.* (page 1003)

Combining clinical data from a national registry, the Danish Hysterectomy Database, Brandsborg *et al.* identified 1,299 women who had undergone hysterectomies for benign indications. They mailed questionnaires to patients who were 12.3–15.2 months postprocedure to assess the incidence and characteristics of posthysterectomy pain. Respondents were asked to report whether

they had had pain in the pelvic region within the last 3 months. Other questions included those on the intensity, frequency, and location of pain before their hysterectomies and at the time of surgery.

Just more than 90% (1,173) of the women returned their questionnaires. After discarding incomplete and blank questionnaires, the authors were able to evaluate a total of 1,135 (87.4%). Overall, most questionnaires were complete, with a median question response rate of 98.6%. In most of the women, undergoing hysterectomy had improved their pain complaints. However, 31.9% (362) still had pelvic pain 1 yr after surgery, and 14.9% of women currently experiencing chronic postsurgical pain had not had pain prior to their procedures. Analysis of the questionnaire data revealed several risk factors for chronic pain. Women with preoperative pain were 3.25 times more likely to have postoperative pain, and those who had had cesarean deliveries previously were 1.54 times more likely to have posthysterectomy pain. Other risk factors for chronic pain included pain as the main indication for their surgery and pain problems elsewhere. The risk of having posthysterectomy chronic pain was not associated with the surgical approach: women undergoing vaginal or total abdominal hysterectomies had similar risks of chronic pain. Of interest to anesthesiologists, spinal anesthesia was associated with a lower frequency of chronic pain. A prospective study of spinal anesthesia in women with a high risk of developing chronic postsurgical pelvic pain could further elucidate this finding.

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