◇ This Month in

ANESTHESIOLOGY

■ Effect of Surgical Stimuli on Desflurane-induced Electroencephalographic Changes. Röpcke *et al.* (page 390)

Röpcke *et al.* recruited 24 female patients scheduled to undergo abdominal surgery to investigate the effect of surgical stimuli on the concentration–response relation of desflurane-induced electroencephalographic changes. Oral midazolam, 7.5 mg, was administered to all patients 2 h before surgery, and anesthesia was induced with 2 mg/kg propofol. A 45-min waiting period was allowed for dissipation of the effects of the induction dose of propofol; during this time, 1.0 MAC desflurane was administered to the patients.

The team used 12 patients as controls to determine the desflurane–electroencephalographic effect relation without noxious stimulation. With the desflurane concentration administered during the waiting period serving as a starting point, half the patients were assigned randomly to administration of a decreased desflurane concentration initially, whereas the other half were assigned to administration of an increased amount. Desflurane was increased or decreased in incremental steps, and concentrations did not exceed 1.6 MAC to avoid a high percentage of burst suppressions. Data were collected for at least 30 min.

In the other 12 patients, desflurane vaporizer settings were increased or decreased after opening of the peritoneum. Decreasing the desflurane vaporizer settings was terminated if an end-tidal desflurane concentration of 0.5 MAC was achieved or if the attending anesthesiologist deemed the depth of anesthesia inadequate. Raw signals from electroencephalographic monitors were filtered and digitized. The median power frequency (the frequency below which 50% of the power lies) and spectral edge frequency 95 (the frequency below which 95% of the power lies) were calculated for each epoch. The Bispectral Index was computed from the bilateral frontal channels on a second electroencephalographic monitor. Desflurane effect-site concentrations and the concentration–effect curves for spectral edge frequency 95, median power frequency, and Bispectral Index were determined by simultaneous pharmacokinetic and pharmacodynamic modeling.

The researchers found that surgical stimulation caused a shift in desflurane concentration–electroencephalographic effect curves for spectral edge frequency 95, median power frequency, and Bispectral Index toward higher desflurane concentrations. In the unstimulated group of patients, 2.2 ± 0.74 vol% desflurane was necessary to achieve a Bispectral Index of 50, whereas in the group monitored during surgery, 6.8 ± 0.98 vol% was required. Although all study participants underwent the same type of procedure (gynecologic laparotomy), the researchers concede that the level of noxious stimulation might not have remained constant throughout the data collection period. However, their results showed that surgical stimulation affects the cortical electrical activity measured by univariate electroencephalographic parameters.

■ Lidocaine, Ropivacaine, and Dyclonine Compared for Ability to Attenuate Histamine-induced Bronchospasm. Groeben *et al.* (page 423)

To assess the relation between attenuation of histamine-evoked bronchoconstriction and topical anesthesia, Groeben *et al.* compared the effects of aerosolized lidocaine, ropivacaine, and dyclonine in 15 volunteers with bronchial hyperreactivity. At initial screening visits, lung function measurements were performed, including baseline vital capacity, forced expiratory volume in 1 s, and maximal inspiratory flow at 50% of the vital capacity. Volunteers also underwent inhalational challenge with histamine to confirm bronchial hyperreactivity.

On each of 4 study days, baseline lung function was assessed again. In random order, volunteers inhaled lidocaine (4%), ropivacaine (1%), dyclonine (1%), or saline (0.05 ml/kg). Lung function was assessed immediately after inhalation, and then histamine challenges were repeated. To effect the challenge, the team used starting concentrations of histamine diphosphate of 0.075 mg/ml and then trebled that on each subsequent challenge up to a dose of 18 mg/ml. Venous blood also was drawn at 5-min intervals for analysis of plasma concentrations of the anesthetics.

At the screening evaluations, the inhaled histamine concentration necessary for a 20% decrease of forced expiratory volume in 1 s was 7.0 ± 5.0 mg/ml. Lidocaine and ropivacaine significantly increased it to 16.1 ± 12.9 and 16.5 ± 13.6 mg/ml, respectively. Despite producing profound topical anesthesia, dyclonine did not attenuate histamine-induced bronchospasm. In addition, dyclonine also might be considered contraindicated even as a

topical anesthetic in patients with bronchial hyperreactivity because it also caused significant airway irritation. Although the mechanisms for attenuating histamine-induced bronchospasm are unclear, effects on airway smooth muscle or neural structures may explain partially the effects of lidocaine and ropivacaine seen in this study.

■ Researchers Compare Diffusion of Xenon and Nitrous Oxide into the Bowels of Pigs during Anesthesia. Reinelt *et al.* (page 475)

A well-known side effect of nitrous oxide anesthesia is its diffusion into air-filled spaces, such as the bowel. Parameters that define the amount of gas diffusion are well-known for nitrous oxide but not for xenon, an inert gas with a blood–gas partition coefficient of 0.12[1]–0.14[2]. Accordingly, Reinelt *et al.* randomly assigned 21 pentobarbital-anesthetized pigs to administration of xenon–oxygen, nitrous oxide–oxygen, or nitrogen–oxygen, all in mixtures of 75/25. After median laparotomies, four segments of small intestine, 15 cm long in each animal, were isolated and occluded with elastic rubber bands. Pressure in each of the bowel segments was monitored for 1 h before the start of the experiments to exclude possible gas losses. During the 4-h anesthesia periods, arterial blood pressure and pressure in the bowel were measured continuously and were recorded every 30 min. Pressure and volume values of the four bowel segments were averaged for each animal at corresponding measuring points.

There were no detectable gas leaks before or after the test period. Nitrous oxide and xenon both led to an increase of the intraluminal gas volumes compared with the nitrogen–oxygen control group, although the volumes were greatest in the nitrous oxide group. The median volume of bowel gas in animals to which inhalational nitrous oxide was administered was 88.0 ml, compared with 39.0 ml for xenon anesthesia and 21.5 ml in the nitrogen–oxygen group. Xenon has a relatively low blood solubility, an important factor influencing its diffusion into air-filled cavities.

■ Effects of Endocannabinoids on Referred Hyperalgesia in the Rat Investigated. Farquhar-Smith and Rice (page 507)

Using an established model of turpentine-induced urinary bladder inflammation, Farquhar-Smith and Rice investigated the effect of administration of the endocannabinoids anandamide and palmitoylethanolamide on referred hyperalgesia in the rat. The investigators first measured limb withdrawal latencies to thermal stimulus (baseline) in 50 female Wistar rats. Bladder inflammation was provoked by instillation of turpentine (0.5 ml, 50% in olive oil) *via* urethral catheters. Then, the rats were assigned randomly to 1 of 10 groups. Twenty animals divided into four groups of five were assigned to administration of 25 mg/kg anandamide, an equivalent volume of soya emulsion vehicle control, 25 mg/kg palmitoylethanolamide, or an equivalent volume of a 2:3 vehicle control of dimethyl sulphoxide–saline *via* the intraperitoneal route. Two other groups (five animals each) were assigned to administration of 10 mg/kg of either anandamide or palmitoylethanolamide, also *via* the intraperitoneal route. The last four groups of animals (n = 5) were assigned to administration of higher doses of either endocannabinoid coadministered with one of two receptor antagonists.

Latencies to withdrawal of hind limbs to thermal stimuli were recorded 2, 4, 6, 8, and 24 h after removal of turpentine, with the forepaw latencies of each animal serving as control measurements. At doses of 10 and 25 mg/kg, both anandamide and palmitoylethanolamide attenuated the referred hyperalgesia in the hind limbs of the rats after bladder inflammation. The CB_1 receptor antagonist SR14176A reduced the antihyperalgesic effect of anandamide, but the CB_2 antagonist SR144528 did not. Coadministration of SR141716A with palmitoylethanolamide did not affect the antihyperalgesic effect but was reduced by SR144528. CB_1 and CB_2 receptors, the investigators state, are situated strategically to influence the nerve growth factor–driven referred hyperalgesia associated with inflammation of the urinary bladder.

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