Pulmonary Airway Resistance Compared after Insertion of Endotracheal Tube and Laryngeal Mask Airway. Kim et al. (page 391) and Berry et al. (page 395)

Endotracheal intubation produces reflex irritation and increased respiratory system resistance (Rs) that is reversed by inhaled bronchodilators. The laryngeal mask airway (LMA) is less likely to lead to bronchoconstriction and has already proven to cause less coughing during emergence from anesthesia, less postoperative sore throat, and less interference with mucociliary clearance. However, the effect of the LMA on airway reactivity has not been studied to date. In this issue, two teams of researchers present Rs measurement data obtained immediately after airway placement with either LMA or endotracheal tube (ETT).

In the first of the two studies, Kim et al. recruited 52 patients (45 men, 7 women) scheduled for elective surgery, excluding from participation patients with active upper respiratory tract infections or who were taking bronchodilators. Baseline peak expiratory flow was assessed while subjects were seated and awake. They were then randomly assigned to placement of either an ETT or LMA. Women received a 7.5-mm ETT, and men received an 8.0-mm ETT. In the LMA group, women received a size 4, and men received a size 5. Anesthesia was induced with 2 µg/kg of fentanyl and 5 mg/kg of thiopental. Placement of the airway device was facilitated with 1 mg/kg of succinylcholine.

After ensuring that a seal of than 20 cmH2O existed after airway placement, the team measured Rs, blood pressure, and heart rate. Rs was measured under identical conditions after an end-tidal concentration of inhalational isoflurane had been achieved and maintained for 10 min. The initial Rs was significantly lower in patients who received the LMA (9.2 ± 3.3 compared with 13.4 ± 9.6 in the ETT group). After 10 min of isoflurane administration, the resistance declined to 8.6 ± 3.6 in the ETT group but remained stable in the LMA group (9.1 ± 3.3). Blood pressure and pulse after airway placement were also significantly lower in the LMA group than in the ETT group.

The second study, authored by Berry et al., measured peak airway pressure and mean airway resistance at three different tidal volumes (5, 10, and 15 ml/kg) in 36 patients who randomly received either a size 4 LMA or ETT (men received a 9.0-mm ETT, whereas women received an 8.0-mm ETT). To obtain the measurements, the team used a CP-100 pulmonary monitor with flow transducer and esophageal balloon.

Anesthesia was induced with fentanyl, 1 µg/kg, and propofol, 2.5 mg/kg, and was maintained with isoflurane, 1.5%, and 33% oxygen in N2O until all measurements were completed. Measurements began 5–10 min after induction of anesthesia and were repeated 10 times at each ventilator setting, with the distal end of the ETT or LMA open to atmosphere. Two patients in the LMA group who had a leak at or above 3% at 15 ml/kg and two patients in the ETT group who could not be ventilated at 15 ml/kg (peak inspiratory pressure was more than 40 cmH2O) were excluded from the analysis. For the others, peak airway pressure, mean airway resistance, device resistance, and pulmonary airway resistance were all lower in the LMA group than in the ETT group.

Both studies conclude that the LMA triggers fewer incidents of bronchoconstriction than the ETT, and that this may have implications for the anesthesia treatment of patients at risk for airway reactivity and for reducing the risk of atelectasis and pulmonary infection.

Can a Diluted Solution Prevent Transient Neurologic Symptoms after Spinal Lidocaine? Pollock et al. (page 445)

Speculations about the causes of transient neurologic symptoms (TNS) after spinal lidocaine administration have included local anesthetic toxicity, needle trauma, neural ischemia resulting from sciatic stretching, patient positioning, muscle spasm, early mobilization, and many others. In light of manufacturer’s recommendations, Pollock et al. designed a randomized, double-blind prospective trial to test the hypothesis that diluting lidocaine solutions for spinal anesthesia may reduce the risk of postoperative TNS.

They recruited 109 American Society of Anesthesiologists physical status I or II patients scheduled for outpatient knee arthroscopy and randomly assigned them to receive 50 µm hyperbaric spinal lidocaine as 2.0%, 1.0%, or 0.5% concentrations. Patients and the investigator who conducted postoperative telephone interviews with them were blinded as to which concentration of lidocaine they received, but the anesthesiologist performing the spinal anesthetic was not. Spinal anesthesia was performed at the L2–L3 or L3–L4 interspace with either a 22-gauge (for patients aged more than 60 yr) or a 25-gauge needle (for patients aged less than 60 yr).
with patients lying in the lateral decubitus position. Patients received supplemental oxygen and were monitored with electrocardiography, automated blood pressure, and pulse oximetry. Further intraoperative sedation was provided as needed with midazolam or as a continuous infusion of 0.2% methohexital or propofol. Four surgical attendings performed the arthroscopic surgeries, so some variation in surgical techniques was present and may have had some influence on the results. The mean duration of surgery was 40 min.

Patient participants were contacted on the third postoperative day by the blinded investigator and questioned about their postoperative recovery. The investigator asked specific questions regarding presence of headache, backache, pain radiating into the buttocks or legs, difficulty walking, degree of activity, and pain control. For purposes of this study, TNS were defined as pain in one or both buttocks or legs, beginning within 24 h of surgery. Back pain that did not radiate into the buttocks or legs was not considered TNS. Pain was rated on a 0–10 verbal pain rating scale. Patients who reported TNS were evaluated for 2 weeks.

Of the 20 patients who reported TNS, 18 complained of bilateral symptoms and 2 of unilateral pain. All of them also reported having low back pain. The incidence of TNS did not differ between patients receiving 2.0%, 1.0%, or 0.5% lidocaine. The dilution of spinal lidocaine, therefore, does not appear to have clinical usefulness for decreasing the incidence of TNS.

- Roles of Spinal Muscarinic and Nicotinic Receptors in Mediating Antiallodynic Effects of Cholinesterase Inhibitors. Hwang et al. (page 492) and Pan et al. (page 509)

Two groups of authors in the present issue have used the rat model of neuropathic pain to explore the mediating effects of spinal muscarinic and nicotinic receptors on the antiallodynic effects of cholinesterase inhibitors. Both suggest that cholinergic mechanisms and agents may have an important future role in the management of chronic neuropathic pain.

Hwang et al. replicated the rat model of neuropathy according to the methods of Kim and Chung, ligating the left L5 and L6 spinal nerves and then allowing 7 days for postoperative recovery. Intrathecal catheters were implanted if rats showed a withdrawal threshold of 4.0 g or less. Experiments began no sooner than 5 days after catheters were implanted. Mechanical threshold testing (using von Frey hairs of logarithmically incremental stiffness) and assessment of motor weakness were conducted at 15, 30, 45, 60, and 90 min after intrathecal administration of edrophonium chloride (3, 10, 30, or 100 μg) and at 120 and 180 min after intrathecal administration of neostigmine (in doses of 0.3, 1, 3, or 10 μg). Both drugs produced a dose-dependent antagonism of touch-evoked allodynia.

Pretreatment with intrathecal atropine produced complete antagonism of the effects of the cholinesterase inhibitors. Mecamylamine (a nicotinic receptor antagonist), however, did not produce this result. In another set of experiments, the team compared the action of subtype antagonists by administering the M1 muscarinic receptor antagonist pirenzepine, the M2 antagonist methoctramine, the M3 antagonist 4-DAMP, and the M4 antagonist tropicamide before injection of either edrophonium or neostigmine. The antiallodynia produced by 100 μg of edrophonium was reversed by pretreatment with all four muscarinic subtype antagonists. However, only pirenzepine (the M1 subtype) had a moderate effect on reversal of allodynia seen in rats receiving 10 μg of neostigmine. The team observed a significant magnitude of difference for reversal of antiallodynic effects between atropine and selective muscarinic antagonists.

Pan et al. produced allodynia in rats using the identical model and allowed them to recover for 5–7 days before intrathecal cannulation. Then, placing rats in six groups of 6–8 each, they conducted a series of pharmacologic experiments within 3–4 weeks after spinal ligation because tactile allodynia typically develops within 1 week after surgery and lasts for 6–8 weeks. The effects of intrathecal injections of saline, two muscarinic receptor antagonists (atropine and scopolamine), and two nicotinic receptor antagonists (mecamylamine and hexamethonium) on the antiallodynic action of 20 μg of intrathecal clonidine were assessed.

The nicotinic receptor antagonists partially weakened the clonidine’s effect, whereas blockade with the spinal muscarinic receptors almost abolished clonidine’s antiallodynic effect entirely. The results indicate that activation of spinal muscarinic receptors is important for manifestation of the analgesic action of intrathecal clonidine in neuropathic pain.

- Pharmacodynamics of Remifentanil and GR90291 Compared in a Rat EEG Model. Cox et al. (page 535)

High concentrations of the metabolite GR90291 have been observed after administration of remifentanil in
patients undergoing elective inpatient surgery. Because the metabolite cannot be given to patients to determine its relative potency and activity. Cox et al. compared the short-acting opioid and its metabolite in a rat electroencephalographic (EEG) model. They devised an integrated pharmacokinetic–pharmacodynamic approach to determine the interactions of remifentanil and GR90291 and the mechanisms of their differences in potency.

One week before experiments began, EEG electrodes were implanted in the skulls over the cortex area in three groups of male Wistar rats. One day before experiment, four indwelling cannulas were implanted. Cannulas in the right jugular vein were used for administration of opioids and midazolam, whereas the femoral vein cannula was utilized for administration of vecuronium bromide. Serial collection of blood samples was accomplished through the femoral artery cannula. Thirty minutes after the start of the midazolam infusion (given at a rate of 5.5 mg · kg⁻¹ · h⁻¹ to prevent opioid-induced seizures), the rats received either remifentanil, GR90291, or saline according to a stepwise decreasing infusion scheme. The maximum infusion rate for remifentanil was 50 µg · kg⁻¹ · min⁻¹ and for GR90291 was 4 mg · kg⁻¹ · min⁻¹. Arterial blood samples were taken at set time intervals. Output from two bipolar EEG leads was continuously recorded and concurrently digitized. The digitized signal was fed into a computer and then stored on disk for off-line analysis.

Administration of remifentanil resulted in concentration ranges from 0 to 1.2 ng/ml of remifentanil and from 0 to 850 ng/ml of GR90291. When the metabolite was given alone, its concentration was in the range of 0–220 µg/ml, with no measurable concentrations of remifentanil observed. The relative free concentration in the brain, determined on the basis of the cerebrospinal fluid-to-total blood concentration ratio at steady-state, was 25 ± 5% for remifentanil and 0.11% for GR90291.

Concentration–EEG–effect relationships were characterized on the basis of the sigmoidal E_max pharmacodynamic model. There was a significant difference (11.000-fold) in EC₅₀ values between remifentanil and GR90291. Values of E_max, EC₅₀, and Hill factor for remifentanil were 109 ± 12 mV, 9.4 ± 0.9 ng/ml, and 2.2 ± 0.3, respectively. For GR90291 the values of EC₅₀ and the Hill factor were 103,000 ± 9,000 µg/ml and 2.5 ± 0.4, respectively. The low clearance of GR90291 and its low relative concentration may be explained by its low affinity to the µ-opioid receptor in combination with a poor brain penetration.

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