◇ This Month in

ANESTHESIOLOGY

■ Risk Factors for Thromboembolic Events following Lower Extremity Arthroplasty. Mantilla *et al.* (page 552)

Using a case-control design, Mantilla *et al.* set out to pinpoint potential risk factors for perioperative thromboembolic events following primary elective hip or knee arthroplasty. Accessing the large Mayo Clinic patient database, they first identified all patients who had undergone the procedures within a 10-yr period, and then determined which patients had developed clinically relevant venous thromboembolism within 30 days postoperatively. The team also identified, from the same patient database, a pool of potential control patients who had undergone the same surgery with the same surgeon but who had experienced no postprocedure adverse events. To allow for the change in thromboprophylactic strategies (such as use of warfarin or low molecular weight heparin), the cases were separated into two time periods: 1986–1990 and 1991–1995.

The researchers found that of a total 9,791 who had undergone lower extremity arthroplasties from 1986 to 1995 at their institution, 116 persons had experienced one or more definite adverse thromboembolic events. Of those 116, 39 had received a total hip replacement, 49 a unilateral knee replacement, and 28 bilateral knee replacements. Of the 68 patients who had experienced deep venous thrombosis, 56 (82%) had developed the thrombosis in the surgically treated leg and 12 in the nontreated leg. Overall, 43 patients experienced the first venous thromboembolic event within 3 days of their surgery, 43 within 4–10 days after surgery, and 30 between days 11–30 after surgery. Fifty-six patients experienced pulmonary embolism following their arthroplastic procedure.

By analyzing patient characteristics and perioperative factors, the team found that an increased body mass index, an American Society of Anesthesiologists physical status of 3 or greater, and lack of thromboprophylaxis were found to independently increase the likelihood of postsurgical pulmonary embolism or deep venous thrombosis. Intraoperative use of invasive blood pressure monitoring *via* arterial cannulation was also associated with an increased risk of adverse thromboembolic events. In addition, the researchers found that the use of aspirin or subcutaneous heparin was as protective against the occurrence of clinically relevant pulmonary embolism or deep venous thrombosis within 30 days of elective hip or knee replacement surgery as was thromboprophylaxis with warfarin or low molecular weight heparin.

■ Spinal and General Anesthesia Compared during Cesarean Section in Preeclamptics with Fetal Compromise. Dyer *et al.* (page 561)

Is fetal outcome influenced by the method of anesthesia in preeclamptic women who require emergency cesarean section for a nonreassuring fetal heart trace? To answer this question, Dyer *et al.* randomized 70 women to receive either spinal or general anesthesia for cesarean section procedures. The diagnosis of preeclampsia in these women had been determined by diastolic blood pressure readings of 90 mmHg or higher on two separate occasions at least 4 h apart, after 20 weeks' gestational age, and proteinuria greater than or equal to 1 g or 2+ on urine dipstix at least 4 h apart or greater than or equal to 300 mg protein per 24 h. Severe preeclampsia was determined as systolic blood pressure of 160 mmHg or more and diastolic pressure of 110 mmHg on two separate occasions, including symptoms of imminent eclampsia, such as severe headache, visual disturbance, dizziness, or fainting. Patients with severe preeclampsia received seizure prophylaxis, which consisted of a 4-g intravenous loading dose of magnesium sulfate followed by 1 g hourly.

In the absence of labor, the following were considered indications for delivery by cesarean section: a baseline fetal heart rate of less than 100 or greater than 150 beats per minute, decreased or absent fetal heart rate variability (less than 5 beats per minute) of 60-min duration, and presence of repetitive decelerations. All women received 30 ml sodium citrate orally prior to initiation of surgery. Noninvasive monitoring consisted of electrocardiography, blood pressure reading, and pulse oximetry testing in both groups. The spinal anesthesia group received 1.8 ml of hyperbaric bupivacaine plus 10 μg of fentanyl at the L3/4 interspace. Hypotension was treated with ephedrine. The women in the general anesthesia group received thiopental, magnesium sulfate, and suxamethonium intravenously prior to intubation, followed by 50% nitrous oxide and isoflurane 0.75–1.5% and morphine postdelivery.

In both groups, hemodynamic measures remained within acceptable limits. Spinal anesthesia patients required more ephedrine, and maternal $Paco_2$ was lower. In neonates, 1-minute Apgar scores were lower after

general anesthesia than with spinal anesthesia. The neonatal umbilical arterial base deficit was greater and neonatal umbilical arterial pH was lower after spinal anesthesia. A retrospective analysis of starting values revealed that if maternal diastolic blood pressure on admission was over 110 mmHg, the neonatal base deficit was greater in those who had undergone spinal anesthesia. The clinical significance of these observed differences has yet to be established.

■ Reversing Rocuronium Neuromuscular Block with Org 25969. Epemolu *et al.* (page 632)

Org 25969 is a drug that may be able to reverse the actions of nondepolarizing relaxants, not by blocking acetylcholinesterase (as do traditional reversal agents) but instead by binding with the neuromuscular blocker itself. To investigate the effects of this new drug on the depth of neuromuscular blockade and rocuronium plasma levels, Epemolu *et al.* performed a series of experiments on 12 male guinea pigs following infusion of rocuronium. The animals were first cannulated during surgery and were allowed to stabilize for 30 min after surgery. Six were assigned to the Org 25969 treatment group and six to the saline control group. An infusion of rocuronium was started at the rate of 12 nmol/min and was subsequently increased to obtain a steady-state 90% neuromuscular block of gastrocnemius contractions. In protocol 1, a second infusion of saline was started 30 min after rocuronium was begun. After 30 min of saline infusion, the animals were killed with an overdose of anesthetic and the urine in the bladder was collected for later analysis. In protocol 2, the animals received a second infusion 30 min after rocuronium had begun, of Org 25969 at a rate of 50 $nmol \cdot kg^{-1} \cdot min^{-1}$. The animals were killed after 30 min and the urine was collected from their bladders.

Arterial blood samples were taken at 10-min intervals over the 60-min total infusion period. The blood samples were also collected for later analysis with mass spectrometry. In the saline-treated group, no significant changes in either twitch height or plasma levels of rocuronium occurred during the saline infusion period. In the Org 25969-treated group, there was a rapid reversal of twitch height within 10 min of the start of the infusion. In addition, the plasma level of rocuronium (free and complexed to Org 25969) doubled within the 30-min infusion period. There was a small increase of rocuronium concentration in the urine samples of the Org 25969-treated group compared to that detected in the saline-treated group, although the difference was not statistically significant.

The authors propose that the rapid reversal of neuromuscular blockade observed in this study is due to the capture of rocuronium by Org 25969. The increase in total plasma concentration of rocuronium is explained by the rapid transfer of free rocuronium from the effect compartment (neuromuscular junction) to the central compartment, where it is bound to Org 25969.

■ Is Inhaled Morphine Efficacious in Treating Postsurgical Pain? Thipphawong *et al.* (page 693)

To assess the safety, efficacy, and dose response of morphine delivered *via* a new pulmonary delivery system, Thippawong *et al.* enrolled 89 patients scheduled for bunionectomy surgery in their third-party blinded trial. During the consent process, participants were informed that they would receive their primary postsurgical pain medication *via* either the intravenous or inhaled route. The inhaled study drug was delivered using a portable, battery powered, handheld, microprocessor-controlled device that was breath-actuated. The device furnishes visual cues to patients to inhale deeply in the optimal range of inspiratory flow rates.

Patients who developed moderate-to-severe pain ($\geq$ 50 mm on a 100-mm visual analog scale) within 6 h after surgery were randomized to one of six treatments: intravenous morphine, three inhalations of morphine, one inhalation of morphine, intravenous saline, three inhalations of water, or one inhalation of water. Nurses who had prepared the study drug were not involved in administering the drugs or in assessing patients during the study.

All study participants were observed for 8 h and assessed at regular intervals for levels of pain relief. They were encouraged to avoid remedication for at least 60 min after the first dose of study drug; after that time, they were allowed to remedicate as frequently as every 15 min, according to need. At any time in the study, patients were allowed to receive 2 mg intravenous morphine, up to three times an hour, as rescue medication. All inhalations were self-administered without nursing assistance. At the end of the study, the authors found that three inhalations of morphine and 4 mg intravenous morphine provided comparable single and multi-dose analgesia. One inhalation of morphine was statistically indistinguishable from placebo.

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