◇ This Month in

ANESTHESIOLOGY

■ Relation between Circadian Rhythm and Duration of Action for Epidural Anesthetics Investigated. Debon *et al.* (page 542)

In dental and skin anesthesia, a relation between hour of administration and duration of action for local anesthetics has been demonstrated. Debon *et al.* hypothesized that the duration of action for ropivacaine, when injected epidurally, might also be related to circadian rhythms. From June to September 2000, the team enrolled 194 nulliparous and multiparous women, all of whom were in the first stage of labor (less than 5 cm dilated) and required epidural anesthesia. The women were assigned to one of four groups based on the time of day that epidural analgesia was initiated. The 14-ml epidural injection consisted of 12 ml ropivacaine, 0.2%, plus 2 ml saline injected over a 1-min period. Blood pressure and heart rate were monitored before injection, every 5 min for the first 30, and then every 15 min thereafter.

The study protocol and data collection were terminated when participants requested additional anesthesia. The duration of analgesia (the period from time of study drug administration until additional anesthesia was requested) was recorded. The women were also asked to rate their pain intensity on a 100-mm visual analog scale. Analgesia durations were as follows: group 1 (1:01 AM to 7:00 AM), 94 ± 23 min; group 2 (7:01 AM to 1:00 PM), 110 ± 25 min; group 3 (1:01 PM to 7:00 PM), 117 ± 23 min; and group 4 (7:01 PM to 1:00 AM), 91 ± 23 min. The greatest difference in analgesia duration among groups was 26 min between groups 3 and 4, representing a 28% longer duration of analgesia between 1:00 PM and 7:00 PM. None of the participants in the study required ephedrine for transient hypotension. The authors note that failure to include chronobiologic parameters in studies of analgesia duration may create bias and that further studies in the field of epidural obstetric anesthesia should include this factor.

■ Does Epidural Analgesia Increase Incidence of Cesarean Deliveries? Sharma *et al.* (page 546)

The increased use of epidural analgesia during labor in the past 20 yr, coupled with a concomitant increase in the cesarean delivery rate, has prompted some controversy about a suspected association between the two. Various design flaws, including retrospective analyses rather than randomized trials, small sample sizes, and inclusion of both nulliparous and parous women have clouded results of studies performed to assess a possible causal effect. Sharma *et al.* performed a randomized trial to compare epidural analgesia during labor with intravenous meperidine. All of the 459 women recruited for this study were nulliparous and were randomly assigned to receive either epidural analgesia with bupivacaine or intravenous meperidine. Protocol violations, including some women in the meperidine group who crossed over to epidural analgesia, occurred in 38 women.

Epidural analgesia was initiated with 0.25% bupivacaine and maintained with 0.0625% bupivacaine and 2 μg/ml fentanyl at 6 ml/h with 5-ml boluses every 15 min as needed using patient-controlled analgesia. Women in the intravenous analgesia group received 50 mg meperidine with 25 mg promethazine hydrochloride as an initial bolus, followed by 15 mg meperidine every 10 min as needed. Women who received epidural analgesia reported lower pain scores during the first and second stages of labor than did women in the intravenous analgesia group, although the epidural analgesia tended to prolong these stages when compared with the intravenous analgesia group. In addition, there were more forceps deliveries in the epidural group. However, there was no increase in cesarean deliveries due to use of epidural analgesia, and the researchers also found that none of the neonates of mothers in the epidural group required naloxone for depressed respiration, whereas 6% of those from meperidine-treated women did. Queried 24 h after delivery, 95% of the women in the epidural group reported excellent or good satisfaction levels with their analgesia, as compared with 69% of those in the intravenous meperidine group.

■ Short-term Vasopressin *versus* Norepinephrine Compared in Patients with Severe Septic Shock. Patel *et al.* (page 576)

Although α-adrenergic agonists have been the primary vasopressors for cardiovascular management in septic shock, their use presents potential adverse effects, such as increased oxygen demand and decreased renal flow. Patel *et al.* conducted a randomized trial in the intensive care units of two hospitals to test whether a short-term vasopressin infusion would produce a vasopressor-sparing effect while maintaining hemodynamic stability and adequate end-organ perfusion. Informed consent was obtained from the next of kin of 24 patients in severe

septic shock, and patients were randomized to receive a 4-h infusion of either norepinephrine or vasopressin.

All patients were treated using norepinephrine infusion before the study period. After baseline measurements of arterial pressures, urine output, and gastric mucosal partial pressure of carbon dioxide, the prestudy vasopressor agent (norepinephrine) was titrated down while maintaining constant mean arterial pressures. Patients randomized to norepinephrine went from a median prestudy norepinephrine infusion of 20.0 μg/min to a blinded infusion of 17.0 μg/min at 4 h. Those randomized to vasopressin infusion went from a median prestudy norepinephrine infusion of 25.0 μg/min to 5.3 μg/min.

After a 4-h infusion period, the requirement for vasopressor use was significantly diminished in the group receiving vasopressin. Additionally, vasopressin substantially increased both urine output and creatinine clearance. Although the study's findings were positive for the use of vasopressin, the authors caution that the study period was brief and that larger sample sizes are required to demonstrate a survival benefit and clinical safety for this use of vasopressin.

■ Role of Spinal Glutamatergic Receptors in Secondary Tactile Allodynia in Rats. Nozaki-Taguchi and Yaksh (page 617)

Nozaki-Taguchi and Yaksh implanted intrathecal catheters in nearly 400 male rats, allowed them 5 days' recovery, and then determined baseline paw withdrawal thresholds to mechanical and thermal stimuli. They then induced thermal injury on one hind paw of each rat. A variety of *N*-methyl-D-aspartate (NMDA) receptor and α-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid–kainate (AMPA–KA) receptor antagonists were administered either 5 min before or 30 min after injury. Tactile withdrawal thresholds were assessed every 30 min for 3 h after the injury, and thermal withdrawal latencies were assessed 30, 45, 60, 90, and 120 min after inducing injury. Any motor dysfunction due to drug administration was also noted.

After the thermal injury, the median paw withdrawal threshold to mechanical stimulation with von Frey filaments at an off-injury site decreased in control group animals receiving saline and water pretreatment, an indication of the development of secondary allodynia. Both pretreatment and posttreatment with intrathecal MK-801 or AP5, two of the NMDA receptor antagonists, had only modest effects on the secondary tactile allodynia after thermal injury. However, pretreatment with intrathecal AMPA–KA receptor antagonists reduced secondary tactile allodynia. The intrathecal NBQX (34 nmol) pretreatment prevented thermal injury–evoked secondary tactile allodynia, and posttreatment administration of the same drug at the same dose significantly reversed secondary allodynia. Similarly, NBQX (34 nmol) and CNQX (36 nmol) showed a significant blockade of primary thermal hyperalgesia when administered before injury. In the dosages used during testing, NMDA antagonists provoked a high incidence of motor deficits, which lasted more than 30 min but were reversible. The authors concluded that spinal AMPA–KA receptors have a major role in the initiation of secondary tactile allodynia, whereas spinal NMDA receptors have only a minimal role. The results indicate a possible clinical role for the AMPA–KA antagonists in pretreatment for hyperalgesia and allodynia after acute tissue injury, such as postoperative pain.

Gretchen Henkel