Parecoxib Evaluated for Opioid-Sparing and Pain Relief Effects after Major Gynecologic Surgery. Tang et al. (page 1305)

Tang et al. designed a randomized controlled trial to test the ability of parecoxib, a water-soluble prodrug of valdecoxib available for intravenous administration, to produce a postoperative opioid-sparing effect in women undergoing major gynecologic procedures. Fifty-five of 60 patients recruited completed the entire study. After surgery, using standardized general anesthetic techniques, the women were randomly assigned to one of three groups. Group 1 (control) received normal saline; Group 2 received parecoxib 20 mg; and Group 3 received 40 mg parecoxib. Initial doses of study medication were administered when patients first requested pain medication in the postanesthesia care unit. Subsequent doses of the same medication were administered 12 and 24 h later. All study and placebo solutions had been prepared by the hospital pharmacist in identical plastic syringes to ensure blinding.

All patients were given access to a PCA device programmed to deliver 1 to 2 ml boluses of morphine with a minimum lock-out interval of 6 min and a total dose not to exceed 20 mg morphine during a 4 h period. Patients’ blood pressure, heart, and respiratory rates were recorded just before administration of study medication and at 1, 2, and 4 h intervals after the first dose. Adverse events and need for supplemental medications, such as antiemetics, were recorded throughout the 36 h study period. Patients were asked to rate their pain intensity before receiving the study drug and at regular intervals afterwards. Their global evaluation of the analgesic efficacy of the study medication was also obtained at 12 and 24 h using a 4-point satisfaction scale.

After administration of the study medication, the cumulative doses of morphine were significantly decreased at the 6, 12, and 24 h assessment intervals for patients receiving parecoxib 20 mg and 40 mg intravenously. However, there were no significant differences in patients’ global evaluations of study drug effectiveness between those who received parecoxib or saline. The postoperative pain scores and side effect profiles were similar in all three treatment groups. These results suggest that parecoxib may be more effective in the prevention—as opposed to treatment—of acute pain. Additional studies using an active nonsteroidal antiinflammatory drug (NSAID) comparator (such as ketorolac) and furnishing data on blood loss during the perioperative period may reveal more information on the effects of parecoxib in postoperative pain.

Does Density of Cerebrospinal Fluid Influence Extent of Spinal Block? Schiffer et al. (page 1325)

In efforts to explain the unpredictability of the extent of spinal block, Schiffer et al. recruited 67 patients scheduled for peripheral orthopedic surgery under spinal anesthesia with plain bupivacaine. Before initiation of spinal anesthesia, 2 ml of cerebrospinal fluid (CSF) were obtained via lumbar puncture at the L3-L4 level with a 25-gauge needle, with patients in the lateral decubitus position. Spinal injection of 3 ml plain bupivacaine 0.5% with the needle aperture directed toward the nonoperated side was then performed over 10 s. Patients were turned supine and remained in the horizontal position through the end of the study. Both the CSF samples and the remaining 2 ml of bupivacaine solution were frozen at −30°C for later density measurements.

Extent of sensory block was assessed by loss of cold sensation elicited by ether drops, and motor block assessed on the nonoperated side by the modified Bromage scale. The maximal sensory block level achieved, time to sensory regression to L4, time to complete motor recovery, and maximal decrease in mean arterial pressure during the first 60 min after spinal injection were all recorded. These data, as well as hemodynamic parameters, were recorded by the anesthesiologist during surgery and by the recovery room nurse postoperatively. Fluid samples were later unfrozen and density measurements conducted at 37°C. Determination of CSF protein, glucose, and electrolyte concentrations were also performed. The relationship between maximal sensory block level and CSF density, protein, glucose, sodium, and chloride was calculated. The correlation between maximal sensory block level and CSF density was highly significant but poorly predictive. Men in the study had significantly higher values of CSF densities, protein, and glucose concentrations compared with women. Since it is not practical to measure CSF density in everyday practice, the findings about CSF density may not be clinically useful. However, the authors did note that upper sensory block extent varied by 13 segments (T1-L1) with median values higher than necessary (T5) for lower limb surgery. Accordingly, they recommend that plain local anesthetic solutions and the supine position be avoided in favor of hyperbaric solutions and a 30° elevated torso.
position. Based on results from this and other work, sensory block levels achieved during plain bupivacaine can be expected to vary between subgroup patient populations in which CSF density differs (i.e., higher CSF density in men vs. women, postmenopausal vs. premenopausal women, nonpregnant vs. pregnant women).

- Cognitive Function Measured in Middle-aged Patients after Noncardiac Surgery. Johnson et al. (page 1351)

In a multicenter study, Johnson et al. assessed, through objective measures and subjective reports, the incidence of postoperative cognitive dysfunction (POCD). The team recruited 508 patients and 183 control subjects between the ages of 40 and 59. Using methods similar to their earlier studies in an elderly population, they administered neuropsychologic tests before the patients' scheduled elective procedures; at 7 days and 3 months postoperatively; and compared changes from baseline with results of identical tests also given to the control group. Tests included a Visual Verbal Learning test, the Concept Shifting test, the Stroop Colour Word Interference test, and the Letter Coding test. The inclusion of age-matched control subjects allowed the investigators to control for learning effect and patient variability, including educational levels, background, and cultural differences.

Patients' moods were determined preoperatively and after 3 months by using the Geriatric Depression Scale. A Subjective Cognitive Functioning questionnaire, which assesses memory, concentration, vitality, and ability to sustain mental burden, was given to both patients and controls at the 3-month follow-up. Instrumental Activity of Daily Living (IADL) scores were also determined for patients and controls.

Results were evaluable from 463 patients tested 1 week after surgery, and 422 retested at 3 months. Performed a median of 6 days after surgery, the results of the 1-week cognitive assessment revealed dysfunction in 89 of 463 patients (19.2%). Given a median of 102 days postoperatively, the second test found 6.2% of patients had cognitive dysfunction. In the control population, cognitive dysfunction was revealed in 4.0% at 1 week and 4.1% at 3 months. Early POCD (at the 1-week testing) correlated with a decline in the IADL score reported by patients' relatives. Depression was associated with subjective but not objective measures of cognitive dysfunction. Supplementary epidural analgesia and peroperative avoidance of alcohol were associated with a higher risk for POCD. The association between epidural analgesia and POCD may be related to local anesthetic toxicities. This should be evaluated in further studies, which, if they included more frequent postoperative testing, could also establish the exact duration of acute POCD.

- Neuroprotective Effects of Xenon Investigated in In Vitro and In Vivo Rat Models. Wilhelm et al. (page 1485)

As opposed to other anesthetics with N-methyl-D-aspartate (NMDA) receptor antagonist properties, xenon does not appear to induce neurotoxicity. Wilhelm et al. conducted a series of in vitro and in vivo experiments to determine whether xenon confers neuroprotection in subanesthetic concentrations. In cortical glial cell cultures prepared from early postnatal mice, the investigators induced neuronal injury by exposure to either NMDA or glutamate, or by oxygen deprivation. They coadministered increasing concentrations of either xenon or nitrogen until injury was confirmed by the release of lactate dehydrogenase (LDH) into the culture medium. For the second set of experiments, one group of female Sprague-Dawley rats received saline subcutaneously (n = 6, control group); another group, N-methyl-DL-aspartate (NMA), 100 mg/kg subcutaneously (n = 7); and a third group, 75% xenon in oxygen (n = 5). Animals in group 4 were further divided into four treatment subgroups and exposed to a range of xenon concentrations (20–75%) before subcutaneous injection of 100 mg/kg NMA. Three hours after treatment was initiated, the animals were killed and their brains removed. Sections midway between the rostral and caudal boundaries of the arcuate nucleus were stained for microscopic evaluation.

Results of the in vitro testing revealed that xenon exerted a concentration-dependent protective effect against neuronal injury induced by NMDA, glutamate, and oxygen deprivation. In the in vivo model, xenon also produced a concentration-dependent protective effect. At the highest xenon concentration tested (75% atm), brain injury was reduced by 45%. It is not known, however, whether a decrease in brain temperature may have contributed to this effect, as brain temperature was not monitored during the experiments. Since xenon is a rare gas, its extraction renders it too expensive for widespread clinical applications. The authors believe that xenon may prove useful administered preemptively in well-defined settings such as cardiopulmonary bypass, where the need for neuroprotection would justify its cost.