

ANESTHESIOLOGY

■ Heparinase I Compared with Protamine for Heparin Reversal after Coronary Artery Bypass Graft. Stafford-Smith *et al.* (page 229)

Reversing anticoagulant effects of heparin with protamine after coronary artery bypass graft results in a 2.6% incidence of adverse events, ranging from hemodynamic instability to respiratory complications and even cardiovascular collapse. To see if heparinase I, a heparin-degrading enzyme with a 5.5- to 18-min half-life in cardiac surgery patients, might provide a safer alternative, Stafford-Smith *et al.* compared it to protamine in a randomized, double-blind, double-dummy trial.

The investigators recruited 167 on- and off-pump coronary bypass graft surgery patients, who were randomized to receive either heparinase I (maximum 35 $\mu\text{g/kg}$) or protamine (maximum 650 mg) for heparin reversal. For all doses, the study drug was administered as a combination of bolus (heparinase I or saline placebo) and infusion (protamine or saline placebo) in a double-dummy fashion. Two mandatory and two optional doses of study drug were available as part of the heparin-reversal protocol. If residual heparin effect was suspected after available doses of drug were administered, the investigators could use an open-label protamine and the subject was considered a treatment failure.

The primary efficacy measurement was postoperative hemorrhage, measured and recorded at hourly intervals. The secondary efficacy endpoint was hemodynamic stability, determined by a composite of systolic arterial blood pressure drop (≥ 30 mmHg) or pulmonary artery systolic pressure rise (≥ 40 mmHg with an increase of at least 10 mmHg from baseline) within 30 min of study drug dosing. The use of heparinase I was associated with an increased level of chest tube drainage compared with protamine, although this difference did not exceed the study's predefined noninferiority threshold for 12-h cumulative mediastinal chest tube drainage. There were no significant differences in the incidences of hemodynamic instability between the two drugs. When the study was one-quarter complete, an inferior safety profile for heparinase I emerged, prompting the Data Safety Monitoring Board to recommend that the study be halted. Patient enrollment was discontinued at that point, although data analysis did continue, yielding the results reported in this month's issue. The authors conclude that because of its safety risks, heparinase I is not suitable as a

replacement for protamine for heparin-reversal after coronary artery bypass graft.

■ Patient Simulator Used to Assess Nontechnical Skills of Anesthesia Residents. Yee *et al.* (page 241)

Using the Anesthetists' Non-Technical Skills scoring system, Yee *et al.* assessed if repeated exposure to simulated anesthesia crises effected improvement in nontechnical skills of 20 anesthesia residents. All subjects attended an orientation session composed of a 1-h didactic period (during which crisis evolution, patient simulation, and anesthesia crisis resource management principles were discussed) and a hands-on familiarization with the simulator mannequin, monitors, and operating room environment. The scoring system was not discussed before the simulator sessions, which consisted of three different scenarios. In groups of three, study participants cycled between the roles of primary anesthesiologist, secondary anesthesiologist remaining in a second room, and passive observer. Sessions were videotaped, mock anesthesia records were kept, and surgeon and nurse roles were played according to a script.

Study participants were kept in the same groups throughout the study, participating in nine different anesthesia crisis scenarios, but as primary anesthesiologist in only three. The scenarios ranged from blocked endotracheal tube to difficult airway in a burn victim to malignant hyperthermia. The Anesthetists' Non-Technical Skills scoring system is designed to assess participants' cognitive and interpersonal skills, and study authors found a significant improvement in residents' nontechnical skills from their first to second session and from their first to third session. However, when comparing scores from the second to third session, there was no significant improvement observed. The authors believe their results demonstrated that such simulation-based education is beneficial and does improve decision-making and crisis management skills.

■ Effects of Propofol on Long-term Potentiation of Synaptic Transmission in Rats. Nagashima *et al.* (page 318)

To study the possible mechanisms underlying memory disruption by propofol, Nagashima *et al.* conducted a series of experiments monitoring synaptic transmissions

in rat hippocampal slices before and after administration of propofol or delivery of tetanic stimulation. Extracellular recordings were obtained from the apical dendritic layer of the CA1 region. Evoked synaptic responses were elicited with 0.1 to 0.2 ms constant current pulses through an electrode placed in the Schaffer collateral pathway. Another set of experiments compared the effects of propofol and pentobarbital on paired pulse inhibition.

To induce long-term potentiation (LTP), the investigators used θ -burst stimulation (10 bursts of 4 pulses at 100 Hz, applied at 5 Hz). Low-frequency stimulation (1 Hz \times 900 pulses) was delivered to induce long-term depression. Higher-frequency stimulation (10 bursts of 4 pulses at 200 Hz, applied at 5 Hz) in the presence of the *N*-methyl-D-aspartate receptor antagonist MK-801 was used to examine propofol's effects on the *N*-methyl-D-aspartate receptor-independent form of LTP.

At 30 μ M, propofol inhibited LTP induction produced by θ -burst stimulation, but had less effect on LTP maintenance. When LTP was induced by 200 Hz in the presence of MK-801, propofol also blocked LTP induction. In the presence of picrotoxin, a specific antagonist of γ -aminobutyric acid type A receptors, propofol failed to block LTP induction. There may be other factors, besides the modulation of aminobutyric acid type A receptors, that account for propofol's effects on synaptic plasticity.

■ Does Bedside Screening Predict Difficult Intubation? Shiga *et al.* (page 429)

To ferret out the usefulness of bedside screening techniques in predicting difficult intubations, Shiga *et al.*

conducted a meta-analysis of reports and trials that investigated a variety of predictive tests. After a search of both MEDLINE and the Cochrane Central Register of Controlled Trials, two of the investigators independently reviewed and selected relevant trials. Thirty-five studies representing a total of 50,760 patients met the following inclusion criteria: that the study was prospective; had used at least one bedside diagnostic test; had reported absolute numbers of true-positive, false-negative, true-negative, and false-negative results that could be derived from the data; and had used a standard laryngoscope. The screening tests included the Mallampati oropharyngeal classification, thyromental distance, sternomental distance, mouth opening, and Wilson risk score.

The overall incidence of difficult intubation was 5.8% for the total patient population, 6.2% for normal patients, 3.1% for obstetric patients, and 15.8% for obese patients. The authors found that a combination of the Mallampati test and thyromental distance most accurately predicted difficult intubation, whereas each test alone yielded poor-to-moderate sensitivity and moderate-to-fair specificity. Their meta-analysis does not answer the ongoing debate about the usefulness of attempting to predict difficult intubations before anesthesia and surgery. In the absence of accurate predictive tests, the authors argue that work should focus on techniques used to cope with difficult intubations when they arise.

Gretchen Henkel