Naloxone Reversal of Diazepam Effects

To the Editor: —Christensen and Hütte1 are to be commended for their carefully designed and conducted study of the effects of naloxone on diazepam-induced sedation. Unfortunately, they did not report the mean consciousness scores for the naloxone and placebo groups, but simply stated that "statistical analysis showed no difference (P = 0.02)." I cannot understand why Drs. Christensen and Hütte have concluded that there was "no difference", since the P value of 0.02 indicates a 98 per cent probability that whatever difference existed between the mean consciousness scores did not occur by chance.

If their studies showed a greater mean consciousness score in the naloxone-treated group, with P = 0.02, I would interpret that to indicate an incomplete, but detectable, effect of naloxone in reversing diazepam-induced sedation. The patient I described2 had received a much larger dose of diazepam (estimated 15 mg/kg) than those in the study of Christensen and Hütte (approximately 0.5 mg/kg). The child was in coma, and responded dramatically to 0.1 mg naloxone. Toxicologic analysis of blood and urine failed to detect any of the drugs that are known to be reversible with naloxone. Perhaps the difference in response is related to the dose of diazepam. I hope Drs. Christensen and Hütte will share additional details of their results with us.

Edward F. Bell, M.D.
Assistant Professor
Department of Pediatrics
University of Iowa
Iowa City, Iowa 52242

REFERENCES

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[Editor's note: The P value was incorrect as stated in the letter of Christensen and Hütte. The error was corrected in an erratum, Anesthesiology 52:334, 1980.]

Influence of Anesthetic Technique on Nitroprusside Requirements

To the Editor: —In their recent article, Marsh et al. demonstrated that during the reduction of arterial blood pressure in cats with intracranial hypertension, the rate of administration of sodium nitroprusside (SNP) and the arterial blood oxygen and carbon dioxide tensions affect the amount of change in intracranial pressure.1 The mean doses of SNP used in this study, 440 ± 25 and 470 ± 30 µg/kg/min, are much greater than the usual initial clinical doses of 0.5–1.5 µg/kg/min.2 The authors did not suggest a reason for the large dose of SNP needed to produce a decrease in blood pressure in their test animals, but felt that it was consistent with their findings in previous studies.

The cats in this model of intracranial hypertension were anesthetized with a single dose of pentobarbital (30 mg/kg) prior to the insertion of intravascular catheters and two intracranial balloons. Previous data from sodium-replete dogs anesthetized with the same dose of pentobarbital demonstrated that any noxious stimulus produced a large increase in blood pressure.3 The hypertensive response was mediated through the sympathetic nervous system, since the systemic hypertension could be blocked with hexamethonium. In the model of intracranial hypertension, the initial mean blood pressure of the cats in each group was about 135 torr. Large doses of SNP were necessary to decrease the blood pressure as a result of the initial hypertension from stimulation of the sympathetic nervous system.

In assessing the results and clinical implications of animal studies, it is necessary to evaluate the methods used in the experiment. The anesthetic technique for patients with increased intracranial pressure should decrease the response of the sympathetic nervous system to surgical stimuli and decrease the SNP dosage necessary to produce a decrease in blood pressure. If the authors had selected a different
anesthetic technique for their model, SNP requirements might have been consistent with those used clinically.

ARNOLD J. BERRY, M.D.
Assistant Professor of Anesthesiology
Department of Anesthesiology
Emory University School of Medicine
1364 Clifton Road N.E.
Atlanta, Georgia 30322

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In reply: In our cat studies describing the effects of sodium nitroprusside on ICP, pentobarbital was used exclusively as our sedative–hypnotic. Inspired gases included room air or variations of oxygen and carbon dioxide tensions. Baseline blood pressures were high and, consequently, excessive doses of nitroprusside were also high. In applying the model to the clinical setting, Doctor Berry’s point is well taken: excessive doses of sodium nitroprusside are reduced when combined with adequate general anesthesia. However, it is worth mentioning two practical circumstances in which higher doses and the described administrative caution may pertain: first, in the ICU patient with Cushing’s triad of elevated ICP, elevated blood pressure, and reduced heart rate who is perhaps not a candidate for general anesthesia but needs blood pressure control and, second, in a similar patient with suspected but unmeasured intracranial hypertension who must undergo anesthetic induction (with endotracheal intubation) but also needs prior blood pressure control. In both circumstances the effective doses of sodium nitroprusside will be predictably higher than those in the comparable anesthetized state.

M. LOU MARSH, M.D.
12916 Via Latina
Del Mar, California 92014

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The Consequences of Not Applying Sensory Decision Theory

To the Editor: — The recent editorial, “On the Possible Painful Consequences of Misapplying Signal Detection Theory,” by Ominsky,1 provides a clear description of the sensory decision theory model as applied to pain perception. He correctly points out that the model provides more information about the response to painful stimulation than does the traditional psychophysical threshold measure. We concur, particularly since the traditional pain threshold may also be computed from sensory decision data.

However, he concludes his editorial by wondering whether this added information will predict the clinical usefulness of analgesic drugs, or will be a hindrance or even misleading. By addressing only the problem of analgesics and possible changes in but one of the parameters of sensory decision theory, discriminability, the reviewer has skirted the major contribution of our study.2 We were particularly concerned with the combined use of the discriminability and the pain report criterion indices to evaluate drugs such as diazepam that may possess both mood-altering and analgesic properties. Our study demonstrated that the increased morphine threshold was caused by a combination of reduced discriminability (the neurosensory component) and raised pain report criterion (the psychological component). In contrast, the increased diazepam threshold was largely due to a change in the pain report criterion. However, there also was a decrease in discriminability, which was masked in the threshold measure.

The discriminability measure P(A) is independent of the report of “pain.” Thus, sensory decision theory represents the sole approach to the study of those drugs which influence both the subject’s mood and his pain sensation. It is well known that a decrease in anxiety will decrease the incidence of pain reports. Thus, a raised pain threshold following the administration of an antidepressant or an