CORRESPONDENCE

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No Difference between Remifentanil and Fentanyl in Patients Undergoing Craniotomy

To the Editor:—I read with interest the excellent clinical investigation of remifentanil and fentanyl in patients undergoing craniotomy for supratentorial space-occupying lesions, although I am troubled by the authors recommendations that "remifentanil appears to be a reasonable alternative to fentanyl" and "appears appropriate" in such cases.

The authors report that induction hemodynamics, intracranial pressure, and cerebral perfusion pressure were similar, as was the median time to extubation. There was no difference in the incidence of nausea or neurologic sequelae. Anesthetic recovery, as evaluated by anesthesiologists, was not significantly different, although one patient in the remifentanil group exhibited emergence delirium. Also, postoperative systolic blood pressure and analgesic requirements were greater in the remifentanil group. The only negative association with fentanyl was the frequency of naloxone utilization.[1] I would thus conclude that presently there is no indication to use remifentanil instead of fentanyl. This does not even consider the extensive experience that exists with fentanyl and neurosurgery patients or the issue of cost.[2,3]

As has been discussed recently in the literature, physicians should decide whether the relationship between investigators and sponsor affected interpretation of the results.[4] This study has an acknowledged relationship with Glaxo Wellcome, Inc., which produces remifentanil, and raises this issue.

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In Reply:—We are grateful for comments regarding the execution of our protocol.[1] The goal of that study was to examine the efficacy and safety of remifentanil in neuroanesthetic practice. The study was designed when factors such as cumulative effects of long-term remifentanil infusions (which would occur during complex craniotomies) were unknown. We generally agree with the characterization of our results with one exception. Remifentanil-treated patients required postoperative analgesia earlier than did those receiving fentanyl, but incidence of postoperative analgesic requirement did not differ between groups.

New drugs have been and will continue to be introduced into the practice of anesthesia. Specific examination of the pharmacokinetic and pharmacodynamic properties of any new drug should be obtained in patient populations having unique anesthetic requirements. All anesthetics carry risk. Therefore, interpretation of the effects of a new drug should be made in the context of properties of established agents. This explains our choice of fentanyl-based anesthesia as the comparator group.

Remifentanil proved to be efficacious during neuroanesthesia (a fact unknown before the execution of this protocol). Outcome, to the extent that it was measured, was generally similar for the two opioids. The only logical conclusion is that remifentanil (when administered appropriately) can be substituted for fentanyl with an apparently similar efficacy and safety profile in this patient population. A Phase IV trial examining a far larger population of neurosurgical patients is being conducted to confirm this with respect to relative frequency of adverse events.

Numerous factors other than safety are involved in the decision to select one agent over another. Such factors include cost, convenience, reliability, tradition, and familiarity with the agent. Those factors were not examined in our trial because of practical limitations (*e.g.*, difficulty in quantifying those end-points) and because we believed those factors to be of secondary importance during an initial investigation. In reality, the final verdict regarding appropriate use of a compound does not occur during highly structured clinical trials but rather during routine use by regular anesthesiologists who weigh the above factors and actually make the selection. We hope that we have contributed a scientific basis to that process.

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The editorial review for these letters was conducted by Lawrence J. Saidman, M.D.

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The Risks of Central Neuraxial Anesthesia

To the Editor: — Ho *et al.*[1] report on the successful use of combined spinal and epidural anesthesia for the management of labor and delivery in a patient with idiopathic hypertrophic subaortic stenosis (IHSS).

Idiopathic hypertrophic subaortic stenosis, or hypertrophic obstructive cardiomyopathy (HOCM) as it also is known, is a cardiomyopathy characterized by asymmetric septal hypertrophy, and dynamic left ventricular outflow tract (LVOT) obstruction, which worsens with hypovolemia, increased left ventricular contractility, and vascular dilation.[2] The diagnosis is confirmed with two-dimensional echocardiography, and the LVOT gradient is quantified by Doppler echocardiography. Provocative testing with inhaled amyl nitrate is used to accentuate the gradient.

In the current case, the diagnosis of IHSS was made several years before pregnancy, but we are given no details regarding its severity; specifically, no mention is made of a "provoked" gradient at diagnosis. Without this information, the reader has no way of knowing what the severity of the condition was and therefore no way of knowing the risks of sympathetic blockade with neuraxial anesthesia. For the patient with the potential for severe LVOT obstruction, the risks of central neuraxial anesthesia are profound and should never be underestimated.

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In Reply: — We thank Dr. Oxorn for his interest in our report. During pregnancy, our patient's mild limitation of exercise tolerance remained essentially unchanged, and echocardiography showed a left ventricular outflow tract gradient of 15 mmHg. Although the response to amyl *nitrite* may provide some measure of severity, its use is not universal, it is not commonly used in our institution, and there are few data to support its safe use in pregnancy. We concur with Dr. Oxorn that hypovolemia, in-