

CORRESPONDENCE

Anesthesiology
1998; 88:271
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No Difference between Remifentanyl and Fentanyl in Patients Undergoing Craniotomy

To the Editor:—I read with interest the excellent clinical investigation of remifentanyl and fentanyl in patients undergoing craniotomy for supratentorial space-occupying lesions, although I am troubled by the authors' recommendations that "remifentanyl 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 remifentanyl group exhibited emergence delirium. Also, postoperative systolic blood pressure and analgesic requirements were greater in the remifentanyl 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 remifentanyl 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 acknowl-

edged relationship with Glaxo Wellcome, Inc., which produces remifentanyl, and raises this issue.

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(Accepted for publication August 6, 1997.)

Anesthesiology
1998; 88:271-2
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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 remifentanyl in neuroanesthetic practice. The study was designed when factors such as cumulative effects of long-term remifentanyl infusions (which would occur during complex craniotomies) were unknown. We generally agree with the characterization of our results with one exception. Remifentanyl-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.

Remifentanyl 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 remifentanyl (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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