

TITLE: SUFENTANIL, ALFENTANIL AND FENTANYL: IMPACT ON CSF PRESSURE IN PATIENTS WITH BRAIN TUMORS

AUTHORS: W. MARX, M.D., N. SHAH, M.D., C. LONG, M.D., E. ARBIT, M.D., J. GALICICH M.D., C. MASCOTT, M.D., K. MALLYA, M.D., R. BEDFORD, M.D.

AFFILIATION: DEPARTMENT OF ANESTHESIOLOGY AND CRITICAL CARE MEDICINE, AND THE NEUROLOGICAL SURGICAL SERVICE, MEMORIAL SLOAN-KETTERING CANCER CENTER AND CORNELL UNIVERSITY MEDICAL COLLEGE, 1275 YORK AVENUE, NEW YORK, NY 10021

Introduction: Narcotic-based anesthetic techniques combined with hyperventilation are often regarded as optimal for patients with brain tumors and other space-occupying lesions. Recently, however, a canine study documented that Sufentanil caused profound increases in CBF without evidence of an increase in cerebral metabolic rate for oxygen. The authors concluded that Sufentanil was acting as a cerebral vasodilator and that it may be contraindicated in patients with compromised intracranial compliance.¹ Because of the clinical importance of these observations, we initiated the following study comparing the CSF pressure (CSFP) effects of Sufentanil and Alfentanil with those of Fentanyl in patients with brain tumors.

Methods: The subjects were 30 adult patients undergoing elective excision of supratentorial tumors. General anesthesia was induced with a thiopental-N₂O-vecuronium sequence and mechanical ventilation was instituted to maintain a constant end-tidal CO₂ tension between 30 and 35 mm Hg (Criticare POET). With the patients in lateral decubitus position, a lumbar subarachnoid catheter was inserted and CSFP was continuously monitored via a calibrated transducer. Mean arterial pressure was recorded via a radial artery catheter. After obtaining control CSFP, hemodynamic values and blood gas tensions, the level of anesthesia was deepened with an IV bolus injection of either: 1) Sufentanil, 1 µg/kg, 2) Fentanyl, 5 µg/kg, or 3) Alfentanil, 50 µg/kg followed by an infusion of 1 µg/kg/min. CSFP and cardiovascular parameters then were recorded for 10 minutes. Throughout the study period external sensory stimuli were carefully avoided and end-tidal CO₂ tension was held constant. Mean arterial pressure (MAP) was calculated as 1/3 of the arterial pulse-pressure difference; Cerebral Perfusion Pressure (CPP) was derived from MAP-CSFP. Statistical comparisons were performed using Student's t-test for paired and non-paired data as appropriate. P<.05 was regarded as significant.

Results: The peak changes recorded for each individual during the 10-minute observation period are summarized in figures 1 & 2. Mean control CSFP for Fentanyl, Sufentanil and Alfentanil were 12.3 ± 3.1, 9.1 ± 1.8 and 12.6 ± 1.8 (mm Hg ± SE), respectively; mean arterial CO₂ tension for the three groups (mm Hg ± SE) were as follows: Fentanyl = 35.6 ± 1.1, Sufentanil = 35.2 ± 1.5, Alfentanil = 36.9 ± 1.2.

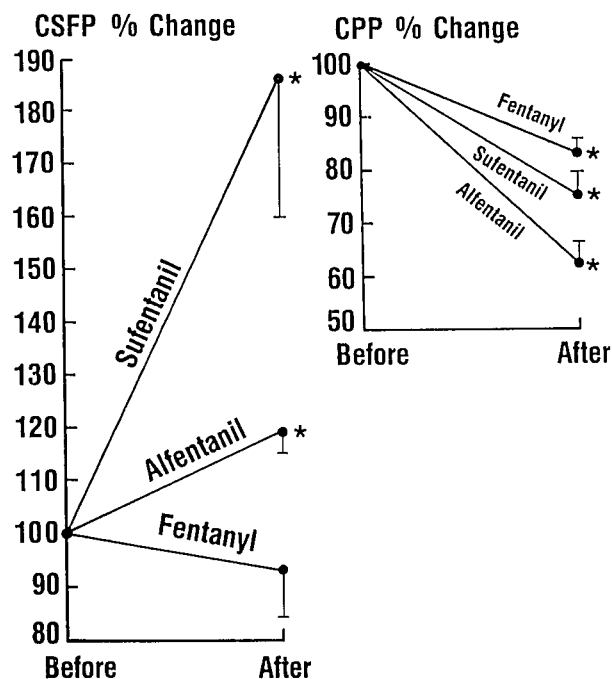
As expected, Fentanyl had negligible effect on CSFP, and its effect on CPP was the least of the three agents examined. In contrast, Sufentanil resulted in the greatest increases in CSFP. Alfentanil produced minimal increases in CSFP, but the greatest reduction in CPP, primarily due to a significant fall in MAP in these unstimulated patients.

Discussion: We believe these clinical findings regarding Sufentanil are compatible with the results of the canine study described above. The fact that CSFP increases even as arterial pressure is decreasing suggests that Sufentanil acts as a cerebral vasodilator in humans. Interpretation of the Alfentanil data is more problematic because MAP fell so markedly. An increase in CSFP despite a reduction in MAP, however, suggests that Alfentanil might also act as a cerebral vasodilator. While hyperventilation and concomitant administration of agents known to increase cerebral vascular resistance may modify these responses, we conclude that Fentanyl is the preferred opioid among these three for potentiating N₂O-O₂ anesthesia in patients with compromised intracranial compliance.

Reference: 1. Milde LN, Milde JH. The cerebral hemodynamic and metabolic effects of sufentanil in dogs. *Anesthesiology* 67:A570, 1987.

Fig 1

Fig 2



Figures 1 & 2: Peak changes in cerebrospinal fluid pressure (CSFP) and cerebral perfusion pressure (CPP) induced by Fentanyl, Sufentanil and Alfentanil during N₂O-O₂-vecuronium anesthesia expressed as percent change from control. All values: mean ± SE. Asterisks indicate p<.05 versus control value.