

Title: VENTILATORY AND MENTAL EFFECTS OF ALFENTANIL AND FENTANYL

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Introduction. The ventilatory and mental effects of alfentanil, a new synthetic narcotic, were compared to those of fentanyl.

Methods. Forty healthy young volunteers were randomly divided into five groups, each of whom received one of the following treatments: 7.5 $\mu\text{g}/\text{kg}$ alfentanil (A1), 15 $\mu\text{g}/\text{kg}$ alfentanil (A2), 1.5 $\mu\text{g}/\text{kg}$ fentanyl (F1), 3 $\mu\text{g}/\text{kg}$ fentanyl (F2), and Saline (P). Treatments were administered intravenously over a two minute period in a double blind fashion. Prior to treatments, subjects were trained in the ventilatory and mental tests and baseline data were obtained. The ventilatory test consisted of a Read rebreathing CO_2 challenge where subjects breathed to-and-fro into a 5 Liter reservoir bag charged with 7% CO_2 and 50% O_2 . Flow and end tidal CO_2 (PECO_2) were monitored and a hybrid computer was utilized to calculate breath-by-breath minute ventilation (VE) and perform a linear regression of VE on PECO_2 for the approximately 80 breaths for each test. From the regression equation, the PECO_2 for a VE of 30 L/min (CO_230) was calculated from each CO_2 response curve. The test was repeated at 4, 20, 30, 50, 80, and 120 minutes post-treatment. The mental and psychomotor tests consisted of an immediate and delayed free recall task, a tapping task, a symbol cancellation test, and a subjective questionnaire. The tests were repeated at 10, 40, 100, 130, and 180 post-treatment. From the two high treatment dose groups, blood for analysis of drug levels was drawn at baseline, 20, 30, and 60 minutes post-treatment and every hour for 8 hours. Concentrations were determined by radioimmunoassay. Data were analyzed by an analysis of variance.

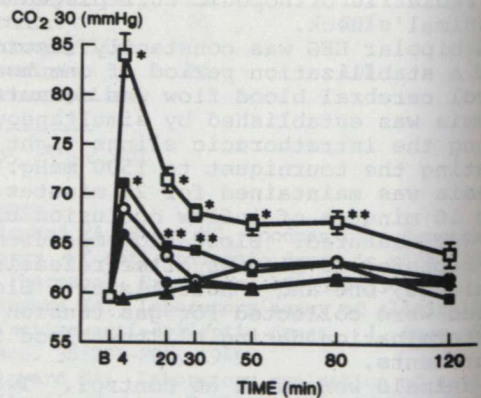
Results. F2 caused an increase in CO_230 up to 80 minutes, F1 up to 20 minutes, A2 only at 4 minutes and A1 was not different from placebo ($p < .001$) (Fig.). The ratio of respiratory depression for F2/A2 was $2.6 \pm .2$ (mean \pm SE). Immediate and delayed recall were not affected ($p > .06$), tapping rate was impaired by F2 ($p < .001$) and volunteers who received F2 reported impairment on subjective scales measuring mental ability e.g. mentally slow vs quick-witted. The mean $t_{1/2}$ of elimination of fentanyl was 4.5 ± 0.6 hours and volume of distribution at steady state was $2.2 \pm .21/\text{kg}$. Kinetic analysis of alfentanil was not possible because of inability to measure drug concentrations for an adequate time following treatment. Four subjects after F1 became nauseated, 7 after F2 became nauseated and 4 vomited, 4 after

A2 became nauseated and 1 vomited and none after A1 had these effects.

Discussion. Fentanyl produced a longer and more intense respiratory depression than that of alfentanil. Fentanyl was more potent by a factor of 2.6 and since we used a dose of alfentanil 5 times larger, alfentanil is about 13 times less potent as a respiratory depressant. If alfentanil is only 1/3 less potent as analgesic than fentanyl, alfentanil seems to spare the ventilation more. A linear regression of the respiratory depression and plasma levels of fentanyl revealed that respiratory depression is predicted to disappear at a plasma level of 0.5 ng/ml at 206 minutes. Subjects reported decreased mental ability after F2 although their learning, recall and cognition were different from P. There was no sedation or tranquility with any treatment. Subjects who received fentanyl were 3 to 4 times more liable to suffer nausea and vomiting than those who received alfentanil. It is concluded that alfentanil may be valuable for out-patient anesthesia and short operation when rapid recovery is desirable.

References.

- de Castro J, Vande Water A, Wouters L, et al: Comparative study of cardiovascular, neurological and metabolic side-effects of eight narcotics in dogs. Acta Anesthesiol Belg 30:5-99, 1979.



Respiratory responses to CO_2 reported in terms of CO_230 .

●—● A1, ○—○ A2, ■—■ F1, □—□ F2, ▲—▲ P

* $P < .001$, ** $P < .001$ to $< .01$.