

**TITLE:** NARCOTIC CONCENTRATION-RESPIRATORY EFFECT CURVES IN MAN  
**AUTHORS:** DENNIS L. FUNG, M.D. AND JOHN H. EISELE, M.D.  
**AFFILIATION:** DEPARTMENT OF ANESTHESIOLOGY  
 UNIVERSITY OF CALIFORNIA, DAVIS  
 DAVIS, CALIFORNIA 95616

Introduction:

It is frequently stated that the relative potencies of the narcotics as analgesics parallels their relative potencies as respiratory depressants. There are few studies that have attempted to measure relative potencies of narcotic-induced respiratory depression. One experimental difficulty in performing such a study is obtaining enough dose-effect points to draw a convincing line or curve. In this study multiple concentration-effect points for estimating relative potency were obtained in each subject by serial measurements of plasma narcotic concentration and respiratory effects after a single intravenous injection of narcotic. The concentration-effect lines for three narcotics were constructed in this manner, and the relative potencies were estimated.

Method:

Prospective subjects were interviewed to exclude those with a history of smoking, recent hepatitis, recent exposure to medication and possible pregnancy. Informed consent was obtained from 21 healthy, young subjects. Narcotic induced respiratory effects were assessed by the ventilation response to CO<sub>2</sub> rebreathing. After consistent control CO<sub>2</sub> responses were obtained each subject received a single injection of either fentanyl, alphaprodine, or meperidine administered intravenously over two minutes. Arterial blood samples were drawn using an indwelling radial artery Teflon catheter. Serum was analyzed for fentanyl by radioimmunoassay.<sup>1</sup> Plasma was analyzed for chromatography.<sup>2</sup> The CO<sub>2</sub>-ventilation response slopes are expressed as a percent of each subjects control slope. The mean percent slopes and mean narcotic concentrations for each group were plotted and a logistic curve was fitted to the data in order to estimate the EC<sub>50</sub>, the narcotic concentration when ventilation slope was 50% of control.

Results:

The results for each group of subjects is shown in table 1. The ratios of EC<sub>50</sub> for fentanyl:alphaprodine:meperidine were 1:225:430.

Discussion:

There are limited data with which our results can be compared. Morphine has been the standard for comparison. Using the horizontal shift to the CO<sub>2</sub>-ventilation

response line and two dose levels, the respiratory potency ratio for alphaprodine and morphine was 2.8 to 1.<sup>3</sup> Using ventilation at an alveolar PCO<sub>2</sub> of 46 mmHg, two doses of meperidine, and three doses of morphine, the respiratory potency ratio for meperidine to morphine was 5.4 to 1.<sup>4</sup> Although different respiratory measurements were used in the above studies, the relative potency of 1.9 to 1 for alphaprodine to meperidine agrees exactly with our results. In another study the peak effect of 75 mgs meperidine was bracketed by the<sup>5</sup> peak effects of 0.1 and 0.2 mgs fentanyl. From these values a respiratory potency ratio for fentanyl to meperidine can be estimated between 375:1 and 750:1. Our potency ratio for fentanyl to meperidine is 430:1. In summary, the method of estimating relative potencies from concentration-effect lines yielded results for the respiratory effect of fentanyl, alphaprodine, and meperidine which are comparable to the respiratory potency ratios obtained by traditional methods. There are advantages to this method which will be discussed.

Drug	Dose (µg/kg)	Number	EC <sub>50</sub> (µg/ml)	Slope
Fentanyl	4	9	.0046	1.11
Alphaprodine	500	6	.66	1.08
Meperidine	1430	6	1.26	1.11

Table 1

References:

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