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Title : VENTILATORY DEPRESSION BY FENTANYL IN ANESTHETIZED PATIENTS

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Fentanyl (F) is considered to be a short-acting narcotic analgesic that is used to supplement general anesthetics. Studies in enflurane-anesthetized dogs demonstrated that both the intensity and duration of F effects were proportional to the dose, and that there was a progressive recovery from its ventilatory depressant effects.[1] Comparable studies have not been done in patients, but there are reports of recurrent ventilatory depression attributable to F.[2] We examined the ventilatory depressant effects of F in anesthetized patients.

METHODS. Twenty-nine patients (18-43 yrs) undergoing elective extremity or vaginal surgery gave informed consent to this study which was approved by the Human Investigations Committee. A single 100mg dose of pentobarbital was administered the night before surgery and was the only drug the patients received in the 24 hours prior to anesthesia. Anesthesia was induced with thiopental (3-4mg/kg) followed by the inhalation of 3-4% enflurane in 60% N_2O in O_2 via a Bain circuit at 10L/min flow. Succinylcholine (1mg/kg) was given to facilitate endotracheal intubation. The enflurane concentration was reduced to 1 to 2% 30 to 45 min after induction and maintained at a constant level for the remainder of the study. Fifteen minutes later, control measurements of frequency (f), tidal volume (TV), minute ventilation ($\dot{V}_E$), arterial and end-tidal CO_2 were made. The response to CO_2 was determined by decreasing the fresh gas flow to 1 L/min resulting in rebreathing. These measurements were repeated and the average taken as the control value. Then the patient was given an iv bolus dose of one of four drugs 30 min or less before the end of surgery: 1)fentanyl 50, 100 or 100 µg/70kg; 2) droperidol, 5mg/70mg; 3)Innovar 2cc/70kg (i.e., 5mg droperidol + 100µg fentanyl/70kg); 4)saline 2cc/70kg. Ventilatory measurements were repeated periodically until they had returned to control levels or 2 hours had passed after administration of the drug.

RESULTS. The onset of respiratory depression was evident within 30 sec after the injection of F as f and TV decreased. Patients receiving the largest dose of F became apneic; they were given a 10cc/kg breath every 30 sec until spontaneous ventilation resumed, and their PaO_2 remained above 100 torr throughout the study. TV recovered to greater than control levels as CO_2 accumulated to peak values. The recovery of f and $\dot{V}_E$ toward control values was initially rapid and then more gradual (Figure). Both the intensity and duration of ventilatory depression were proportional to log-dose of F (r=0.9). These changes in spontaneous ventilation paralleled alterations in the ventilatory response to rebreathing. The CO_2-response line was shifted to the right and its slope decreased by F in a dose-dependent fashion. There was a progressive recovery of the response to CO_2 at a rate inversely related to dose. There was no evidence of recurrent ventilatory depression by any measure in any patient at a stable level of enflurane-N_2O anesthesia. Saline and droperidol alone had no significant effect on any ventilatory variable. The ventilatory depressant effects of Innovar were essentially the same as those produced by the same dose of F alone.

DISCUSSION. Pharmacokinetic studies of F in dogs and human volunteers predicted that both the intensity and duration of ventilatory depression by F would be proportional to the dose.[1,3] The present study confirmed those predictions and demonstrated that there was a progressive recovery from the ventilatory depressant actions just as there was a progressive decline of F concentrations in plasma following a single intravenous dose.[3] Although recurrence of ventilatory depression was not evident in this study, the clinician should be alert to the possibility of long lasting ventilatory effects of fentanyl, especially after larger doses.

REFERENCES. 1)Hug CC, Jr., Murphy MR: Fentanyl disposition in cerebrospinal fluid and plasma and its relationship to ventilatory depression in the dog. Anesthesiology 50:342-349, 1979.
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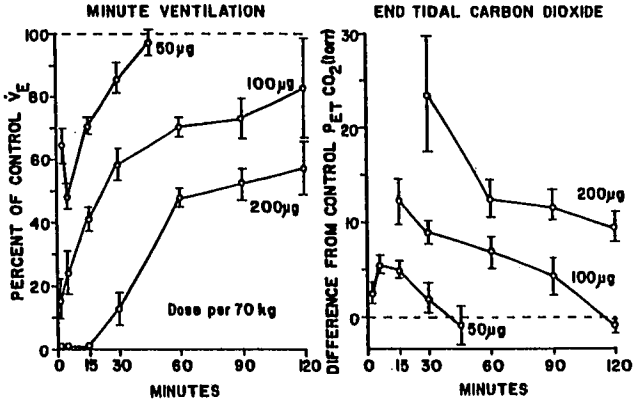

Figure. Dose-dependent ventilatory depression induced by fentanyl in anesthetized patients. Values are means ± SEM.