Title: NARCOTIC INHALATION ANESTHESIA

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Introduction: Because of their water solubility and potency, some of the new ultra-potent synthetic narcotics may enable anesthesia to be induced in a novel way, via inhalation of a mist of the compound in a croup or mist tent. In this study we evaluated the speed, safety and simplicity of induction and maintenance of anesthesia utilizing nebulized carfentanil, a cogener of fentanyl. Carfentil is 40 times as potent as fentanyl (8000 times as potent as morphine) and has a therapeutic index (LD_{50}/ED_{50}) which is 30 and 115 times greater than fentanyl and morphine, respectively.

Methods: The experimental subjects were six mongrel dogs (20±2kg) and four Rhesus monkeys (2.1±2kg). All of the animals were placed in a specially designed air-tight plexiglass box with dimensions of 2'x3'x4'. The box is equipped with four ports, two at the top for the introduction of gases and two at the bottom for the evacuation of effluent gases. To introduce carfentanil, two Intec 2010 Fanjet nebulizers were attached to air and oxygen flowmeters. Each nebulizer was loaded with 5 ml of carfentanil in distilled water (concentration = 1 mg/ml). Oxygen (50%) in air was introduced to the chamber via the nebulizers at a total flow of 20 l/min. A continuous vacuum with ambient access was employed during and for 5 min after nebulization. Nebulization was continued for 5 min in all dogs and for 5 and 2 min and 30 and 15 sec in the four monkeys, respectively. Heart and respiratory rates were measured before and at 5 min intervals for one hour after beginning nebulization in all animals. Time for beginning of ataxia (difficulty in standing), leaning (balancing against the box wall), and lying down (collapsed on floor), were also measured. When the animals had collapsed a surgical clamp was applied to a full clamp position on the tail (dogs) or the abdominal wall (monkeys) every 15 min for an hour, to test for surgical analgesia. No movement or vocalization was considered evidence of surgical analgesia. Data were analyzed for statistical significance utilizing Students paired t-test, analysis of variance and the chi-square test.

Results: Times for ataxia, leaning and collapse averaged 2.0, 3.1 and 4.2 min, respectively, in the dog and were of a similar magnitude in the monkey irrespective of exposure time. No animal became rigid and all animals had surgical analgesia 10 min following exposure. Forty-five minutes after exposure 50% of the dogs and the 15 and 30 sec exposure monkeys responded to painful stimulation. All animals except the monkey exposed to carfentanil for 5 min responded to painful stimulation one hour after anesthetic induction. Dogs experienced a significant decrease in heart rate but no significant change in respiratory rate. All monkeys except the 15 sec exposure experienced a decrease in respiratory rate but none had a change in heart rate. Peak heart and respiratory rate depression occurred 15 min following exposure and gradually returned to pre-exposure values after one hour. No dog required or was given mechanical respiratory assistance. Monkeys exposed for 5 and 2 min were intubated 30 min after exposure and mechanically ventilated for one hour and 30 min respectively because of respiratory rates which persisted below 8 breaths/min. An average of 3.9 mg of carfentanil was delivered over the 5 min exposure period in the dogs and proportionately less during the shorter periods of exposure in the monkeys.

Discussion & Conclusion: These data indicate that short-term nebulization of carfentanil in a close space is a rapid, safe and simple method of inducing anesthesia in uncooperative subjects. No physical contact between patient and anesthetist is required and, with the exception of long exposure insensitive subjects (monkeys) no respiratory support is required. Anesthesia of 30-45 min duration was obtained in dogs with a 5 min exposure to nebulized carfentanil and anesthesia of similar magnitude with exposures of 2 min or less in monkeys. Unfortunately, longer exposures than 30 sec in monkeys produced sufficient respiratory depression to necessitate mechanical assistance. However, even in these situations, significant respiratory depression never recurred until 10 min after carfentanil exposure. Our findings suggest that further studies with nebulized carfentanil and/or perhaps topical application are indicated. In addition, our results demonstrate that the new ultra-potent synthetic narcotics deserve further investigation as anesthetics or anesthetic adjuvants in man.