Determination of the Minimum Alveolar Concentration (MAC) of Aliflurane in Dogs

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The minimum alveolar concentration (MAC) of aliflurane was measured in ten dogs. A value of 1.84 volumes per cent was determined, which correlates well with predictions based on lipid solubility. Induction of anesthesia and recovery were rapid, as would be anticipated with an agent of relatively low solubility in blood (blood–gas partition coefficient = 1.7). Circulatory responses over a relatively narrow range of aliflurane concentrations (0.8 to 1.4 MAC) remained stable, but the development of tachypnea, irregular ventilatory patterns, and increased muscle tone were frequently encountered during aliflurane anesthesia. (Key words: Anesthetics, volatile: aliflurane. Potency, anesthetic: MAC.)

This investigation with dogs was undertaken to determine the minimum alveolar concentration (MAC) of the new experimental inhalational anesthetic, aliflurane (1-chloro-2-methoxy-1,2,3,3-tetrafluorocyclopropane, compound 26-P). Studies by Holaday, Jardins and Greenwood indicate that satisfactory anesthesia is achieved in man with inspired aliflurane concentrations ranging from 1.4 to 1.6 per cent. However, no quantitative data regarding anesthetic potency are available, and they are important to know, since aliflurane is flammable in nitrous oxide–oxygen (60/40) in concentrations above 3.0 per cent. The clinical usefulness of aliflurane would be greatly enhanced if its potency (MAC) were substantially less than its lower limit of flammability. Knowledge of aliflurane potency in dogs also would allow prediction of anesthetic potency in man.

In addition to the determinations of anesthetic potency, we measured blood-gas and pH values, respiratory rate, tidal volume, heart rate, and blood pressure at various end-tidal aliflurane concentrations. We also observed the degree of motor tone and salivation during anesthesia and the rate of recovery from anesthesia.

Methods

The MAC of aliflurane was determined by use of the tail-clamp technique described by Eger et al. Ten

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15 min. We tested four to seven end-tidal alifurane concentrations in each animal (at least two above and two below MAC) until the highest concentration allowing and the lowest concentration preventing a positive muscular response were obtained. MAC is defined as the concentration midway between these two values.2

**Results**

Induction of anesthesia was rapid when 4.0 to 4.5 per cent alifurane was inhaled. However, establishment of an adequate level of anesthesia for the performance of endotracheal intubation was often accompanied by tachypnea (to the point of panting), irregular ventilatory patterns (alternating tachypnea and apnea), and increased muscle tone. The latter frequently made laryngoscopy and endotracheal intubation difficult. Continuous salivation was notable during induction of and recovery from anesthesia. After a mean exposure of three hours (range 2.5–3.5 hours), recovery from alifurane was rapid. In every instance, the end-tidal alifurane concentration decreased to 0.25 to 0.20 of the value during alifurane inhalation within 60 sec after return to air breathing. Animals were able to stand and move around their cages 5 min later.

MAC values with corresponding blood-gas, pH, and base-excess values and cardiorespiratory responses taken for each animal just prior to the final tail-clamping are shown in table 1. The ratio of end-tidal to inspired concentration difference ($F_1 - F_{ET}/F_1 \times 100$) was relatively low (mean ± 3.4 SD ± 3.3 per cent), indicating that nearly complete equilibration had occurred and assuring that there was a minimal possibility of contamination of end-tidal alifurane concentrations by higher inspired concentrations. In spite of the wide variations in respiratory rate and minute ventilation (table 1), $P_{aco_2}$ values were relatively constant and within a range indicating that adequate alveolar ventilation was maintained.

Quantitation of cardiorespiratory responses cannot be made, since control measurements were not performed. However, the relationships of heart rate, systolic blood pressure, respiratory rate, and level of $P_{aco_2}$ to end-tidal alifurane concentrations (n = 47) were analyzed by linear regression over the range of alifurane concentrations studied. No statistically significant correlation was found for any of these responses over alifurane concentrations ranging from 1.49 to 2.50 per cent (mean ± SD, 1.88 ± 0.21 per cent). Cardiac arrhythmias other than sinus tachycardia were not observed at any time.

**Discussion**

Induction of alifurane anesthesia was as rapid as would be anticipated for a volatile agent of relatively low blood solubility (blood–gas partition coefficient $= 1.70$, W. R. Grace and Co.) and at inspired concentrations greater than its anesthetic potency.6 Recovery from prolonged alifurane anesthesia was rapid. However, the accompanying disturbances in ventilatory patterns and the lack of muscle relaxation during induction and maintenance of anesthesia make alifurane less desirable, in our experience, than other agents such as halothane, enflurane and isoflurane. The rate of induction could be made more rapid with alifurane if concentrations higher than 4.5 per cent were inspired, and it is possible that some of these disadvantages might be overcome if a greater depth of anesthesia were achieved prior to endotracheal intubation. The use of higher alifurane concentrations would, of course, be accompanied by a greater risk of flammability.

A prediction of anesthetic potency can be derived from the equation oil–gas partition coefficient times MAC equals a constant of potency. Eger and colleagues7 measured the potencies of 11 inhalational anesthetic agents in dogs and found a mean constant of potency of 2.14. Our determination of MAC for alifurane correlates well to its relationship to lipid solubility. Using gas chromatography, we determined an alifurane oil–gas partition coefficient (37°C) of 124, a value similar to the 117 reported by W. R. Grace and Co. Therefore, we would predict alifurane MAC to be 1.73 per cent (2.14/124 × 100). We determined alifurane MAC to be 1.84 ± 0.21 volumes per
cent (mean ± SD). Since our laboratory in Gainesville is near sea level (average barometric pressure 760 torr), no correction factor was applied. Therefore, the value of 1.84 volumes per cent is equivalent to a MAC value of 0.0184 atmospheres. The coefficient of variation (one standard deviation as a percentage of the mean) of our MAC value is relatively low (11.4 per cent) compared with a mean coefficient value of 20 per cent determined for other agents.

A prediction of anesthetic potency in man is also possible by use of the mean constant of 1.43 derived from human studies. Extrapolation of our aliflurane MAC value in dogs would predict a MAC value of 1.22 per cent in man. This value is similar to the aliflurane concentration that Holaday, Jardinis and Greenwood found to produce light levels of anesthesia in human subjects. Aliflurane is more potent than nitrous oxide, cyclopropane, fluoroxene, diethyl ether, and enfurane, and less potent than halothane and methoxyflurane.

The lower flammability limits (LFL) of aliflurane in oxygen and in nitrous oxide–oxygen (60/40) are 3.2 and 3.0 per cent, respectively (W. R. Grace and Co.). With an allowance for 20 per cent overpressure, the ratio of inspired aliflurane concentration to the value of LFL would give a twofold margin of safety (LFL/MAC). As with fluoroxene, halothane and other halogenated agents, it is possible that the use of aliflurane in combination with nitrous oxide and narcotic drugs would decrease the aliflurane requirement significantly and thereby increase the ratio of LFL/MAC. The effects of nitrous oxide and narcotics on the anesthetic requirements for other anesthetics suggest that aliflurane MAC under these conditions might be decreased to 0.5 per cent or less. However, this concentration value refers to maintenance levels of anesthesia only; the use of overpressure during induction would still require the use of aliflurane concentrations within the flammable range.

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References