Anesthetic potency of sevoflurane with and without nitrous oxide in mechanically ventilated Dumeril monitors

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Objectives—To determine the minimum alveolar concentration (MAC) of sevoflurane and assess the sevoflurane-sparing effect of coadministration of nitrous oxide in mechanically ventilated Dumeril monitors (Varanus dumerili).

Design—Prospective crossover study.

Animals—10 healthy adult Dumeril monitors.

Procedure—Anesthesia was induced with sevoflurane in 100% oxygen or sevoflurane in 80% nitrous oxide (N2O) with 24% oxygen, delivered through a face mask. Monitors were endotracheally intubated, and end-tidal and inspired sevoflurane concentrations were measured continuously; MAC was determined by use of a standard bracketing technique. An electrical stimulus (50 Hz, 50 V) was delivered to the ventral aspect of the tail as the supramaximal stimulus. A blood sample for blood gas analyses was collected from the ventral coccygeal vessels at the beginning and end of the anesthetic period. An interval of at least 7 days was allowed to elapse between treatments.

Results—The MAC ± SDs of sevoflurane in oxygen and with N2O were 2.51 ± 0.46% and 1.83 ± 0.33%, respectively. There was a significant difference between the 2 treatments, and the mean MAC-reducing effect of N2O was 26.4 ± 11.4%. Assuming simple linear additivity of sevoflurane and N2O, the MAC for N2O was estimated to be 244%. No significant differences in blood gas values—with the predictable exception of oxygen pressure—were detected between the 2 groups.

Conclusions and Clinical Relevance—The MAC of sevoflurane in Dumeril monitors is similar to that reported for other species. The addition of N2O significantly decreased the MAC of sevoflurane in this species. (J Am Vet Med Assoc 2005;227:575–578)

Sevoflurane has shown promise as a rapid and safe alternative to isoﬂurane for inhalational anesthesia in reptiles. In humans and other animals, sevoflurane is a highly insoluble agent associated with rapid induction of and recovery from anesthesia. The cardiovascular changes are similar to those associated with isoﬂurane anesthesia. From the Toronto Zoo, 361A Old Finch Ave, Scarborough, ON M1B 5K7, Canada (Bertelsen, Crawshaw); and the Departments of Pathobiology (Bertelsen, Smith) and Clinical Studies (Mosley, Dyson), Ontario Veterinary College, University of Guelph, Guelph, ON N1G 2W1, Canada. Dr. Bertelsen’s present address is Center for Zoo and Wild Animal Health, Copenhagen Zoo, Søndre Fasanvej 79, DK-2000 Frederiksberg, Denmark. Dr. Mosley’s present address is Veterinary Teaching Hospital, College of Veterinary Medicine, Oregon State University, Corvallis, OR 97331. Supported by grants from the Toronto Zoological Society and the Ontario Veterinary College Pet Trust with additional support from Zoo Atlanta, Buffalo Zoo, Fort Worth Zoo, Philadelphia Zoo, and Michael Fost. Sevoflurane and the vaporizer were supplied by Abbott Canada. The authors thank Dr. Shannon Lee for technical assistance. Address correspondence to Dr. Bertelsen.
Anesthetic induction—A semiclosed circle anesthetic system with an out-of-circle, agent-specific precision vaporizer was used for induction and anesthetic maintenance. The vaporizer was dialed to achieve the maximum output (8%), and in each monitor, anesthesia was induced with the approximate gas mixture by use of a mask. Each monitor received sevoflurane in 100% oxygen or sevoflurane in a premixed combination of 66% nitrous oxide with 34% oxygen (1 L/min) in a randomized crossover study; an interval of at least 7 days was allowed to elapse between treatments. No other medication was administered.

After each monitor was completely relaxed, it was endotracheally intubated via the oral route by use of an uncuffed silicone tube of appropriate size (internal diameter, 2.5 to 3.5 mm); the tube was connected to the breathing circuit with a gas flow of 1 L/min. Mechanical ventilation was provided at 4 breaths/min with a tidal volume of 23 mL/kg (11.4 mL/lb) of body weight. The minute ventilation was 100 mL/kg (45.5 mL/lb), which was based on values obtained in clinically normal, unanesthetized, unventilated Savannah monitors.

Airway gas concentrations were continually assessed through a 3.5-F catheter introduced as far as the tip of the endotracheal tube through a T-piece at the base of the tube. The sevoflurane monitor was calibrated before each trial with the manufacturer’s recommended calibration gas.

Heart rate and rhythm were continuously monitored with lead II of a 3-lead ECG by use of alligator clips attached directly to skin folds on both forelimbs and the left hind limb of each monitor. A thermometer probe was inserted deep into the cloaca, and body temperature was maintained from 32° to 33° C (89.6° to 91.4° F) throughout the experiment by a relationship of simple linear additivity between sevoflurane and nitrous oxide; however, in 1 monitor, no apparent effect of nitrous oxide on the MAC was detected. Assuming that the reducing effect of nitrous oxide was 26.4% (95% CI, 18% to 36%). In 9 of the 10 monitors, the MAC of sevoflurane was decreased in the presence of nitrous oxide; however, in 1 monitor, no apparent effect of nitrous oxide on the MAC was detected. Assuming that a relationship of simple linear additivity between sevoflurane and nitrous oxide exists, the MAC for nitrous oxide is estimated to be 244%. The mean relative inspired-to-end-tidal sevoflurane concentration difference was 4.2 ± 3.3%.

Mean ± SD values for blood gas variables at the time of intubation and at the end of the experiment (lower MAC bracket) were calculated (Table 1). Compared with the values at intubation, a significant decrease in

<table>
<thead>
<tr>
<th>Variable</th>
<th>At intubation</th>
<th>At lower MAC bracket</th>
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<tr>
<td></td>
<td>100% O2</td>
<td>66% N2O and 34% O2</td>
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<tr>
<td>Blood pH</td>
<td>7.32 ± 0.15</td>
<td>7.32 ± 0.09</td>
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<tr>
<td>PCO2 (mm Hg)</td>
<td>40.3 ± 10</td>
<td>43.0 ± 7.7</td>
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<td>PO2 (mm Hg)</td>
<td>166.0 ± 85.4</td>
<td>85.8 ± 45.4</td>
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<td>HCO3⁻ (mmol/L)</td>
<td>25.2 ± 4.8</td>
<td>26.4 ± 5</td>
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<td>ABE (mmol/L)</td>
<td>−4.71 ± 7.3</td>
<td>−3.98 ± 5.6</td>
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*Value significantly (P < 0.05) different from the value at intubation. **Value significantly (P < 0.05) different from the value for sevoflurane in 100% oxygen at the same time point.

ABE = Adjusted base excess (calculated).
PCO₂ and significant increases in blood pH and HCO₃⁻ concentration were detected at the end of both experiments, whereas there were no changes in PO₂. There were no differences in any variable between the 2 treatment groups, with the predictable exception of PO₂, which was lower during treatment with sevoflurane in 66% nitrous oxide and 34% oxygen than during treatment in 100% oxygen.

Discussion

The MAC value of sevoflurane in Dumeril monitors at 32°C (90°F) was 2.51 ± 0.46%, a value that falls well within the range of values reported for mammals and birds. This value is also very close to the sevoflurane MAC value of 2.42% recently reported in radiated ratsnakes (Elaphe radiata). Nitrous oxide reduces the anesthetic requirement for sevoflurane in Dumeril monitors. The extrapolated MAC of nitrous oxide (244%) in mammals is similar to that estimated in dogs (222%), cats (255%), horses (205%), macaques (200%), and red-tailed hawks (220%) but is considerably higher than that estimated in humans (104%). The lower potency in these animals, compared with that in humans, is striking and has led researchers to question the usefulness of nitrous oxide as an adjunct to veterinary anesthesia. However, the reduction in sevoflurane requirement (26%) associated with administration of nitrous oxide determined in our study suggests a practical clinical application, which may decrease induction and recovery times as well as the extent of potentially deleterious cardiopulmonary effects of sevoflurane.

The sevoflurane and nitrous oxide concentrations on which the MAC estimate is based were measured by continuous sidestream sampling at the tip of the endotracheal tube, which was located about halfway down the trachea of each monitor. This location improves the accuracy of sampling in small subjects. The concept of MAC assumes that the end-tidal, alveolar, arterial, and brain anesthetic partial pressures are equal after a given time. In mammals, the end-tidal partial pressure is an accurate estimate of arterial partial pressure when only a small inspired-to-end-tidal difference exists. In humans, the difference between end-tidal and arterial partial pressure after 15 minutes of steady-state anesthesia is reported as being approximately one fifth the inspired-to-end-tidal difference. Assuming a similar relationship in the present study of monitors, during which at least 20 minutes was allowed for equilibration, the mean relative inspired-to-end-tidal isoflurane difference was 4%, indicating that the error of the estimate (ie, end-tidal-to-arterial difference) was < 1%.

The accuracy of MAC determinations, based on end-tidal gas sample analyses, could be seriously hampered by large differences between gas tensions in the lung and systemic arterial blood. In reptiles, gas tensions of the systemic arterial blood may be considerably different from the gas tension within the lungs. For example, in turtles and snakes breathing 21% oxygen, differences as great as 60 to 80 mm Hg have been reported, which are likely a result of intrapulmonary functional venous admixture and right-to-left intracardiac shunting. In contrast, the anatomic and physiologic features of the cardiovascular system of varanid lizards (characterized by notable pulmonary-to-systemic pressure separation, potential for high cardiac output, and high aerobic capacity) are more similar to mammalian systems and likely permit the application of standard techniques for MAC determination.

Results of analyses of blood gas variables in samples collected at the beginning and end of the experiments of the present study were highly variable. As the samples were collected from the ventral coccygeal vessels, there may have been contamination with lymph or arterial blood from adjacent vessels. The variability may have also reflected variations in the degree of intracardiac shunting or ventilation-perfusion mismatching among the monitors. A considerable decrease in PCO₂ and significant increases in blood pH, HCO₃⁻ concentration, and adjusted base excess developed over the course of the experiment with either anesthetic treatment. This respiratory alkalosis was a result of relative hyperventilation during mechanical ventilation. A minute ventilation of 100 mL/kg was excessive and should be decreased in a clinical setting. Assuming an inverse linear relationship between alveolar ventilation and PaCO₂, a minute ventilation of 75 mL/kg (34.1 mL/lb) might be more appropriate.

In the present study, sevoflurane requirement was not reduced as a result of coadministration of nitrous oxide in 1 monitor. It is unknown why this animal did not follow the response pattern of the others, but individual variation in sensitivity to nitrous oxide has been identified in cats, and it is conceivable that this particular monitor might be a so-called nonresponder to that agent.

Anesthesia in Dumeril monitors was induced and maintained in a smooth and reliable manner via inhalation of sevoflurane, both with and without coadministration of nitrous oxide, and no adverse reactions were encountered. The concurrent use of 66% nitrous oxide with 34% oxygen significantly reduced the requirement for sevoflurane, and the MAC values determined for sevoflurane in oxygen with and without nitrous oxide for Dumeril monitors provide a useful index for clinicians and researchers striving to provide effective, safe anesthesia in varanid lizards.

References