**Effect of Age on Minimum Alveolar Concentration (MAC) of Sevoflurane in Dogs**

Kazuto YAMASHITA¹, Yasunori IWASAKI¹, Mohammed A. UMAR¹ and Takaharu ITAMI¹

¹Department of Small Animal Clinical Sciences, School of Veterinary Medicine, Rakuno Gakuen University, Ebetsu, Hokkaido 069–8501, Japan

(Received 16 March 2009/Accepted 15 June 2009)

**ABSTRACT.** It is well known that the minimum alveolar concentration (MAC) of inhalation anesthetic decreases with increasing age. However, there is limited information regarding the effect of age on MAC in dogs. This study was designed to determine the effect of age on sevoflurane MAC in dogs. MAC was determined in 6 young (2 years old) and 6 old beagle dogs (8 to 10 years old) under artificial ventilation. Anesthesia was induced via mask induction and maintained with sevoflurane in oxygen, and MAC was determined by using a tail clamp method. The sevoflurane MAC for the older dogs was significantly less than that for the younger dogs (1.86 ± 0.29% vs 2.25 ± 0.15%, P=0.007). The MAC of sevoflurane is profoundly affected by age in dogs.

**KEY WORDS:** aging, anesthesia and analgesia, canine, minimum alveolar concentration (MAC), sevoflurane.

Sevoflurane is a volatile anesthetic agent with a relatively low blood/gas solubility coefficient resulting in rapid induction and recovery from anesthesia [28]. During the last decade, clinical use of sevoflurane has been spreading in veterinary species such as horses [3, 14, 24, 31], cats [15] and dogs [1, 2]. Sevoflurane is minimally metabolized and easily cleared in animals; however, it should be remembered that sevoflurane causes dose-dependent hypotension, hypoventilation, impaired cardiac contractility and hypothermia [21]. Because of these side effects, sevoflurane must be carefully titrated, and vigilant monitoring should be employed to avoid excessive anesthetic depth.

MAC has been defined as “the minimum alveolar concentration of anesthetic at 1 atmosphere that produces immobility in 50% of those animals exposed to a noxious stimulus” [5]. It has long been known that MAC decreases with age in humans [8, 20, 22, 26, 29]. In human medicine, anesthetists can rapidly determine the depth of anesthesia in age-corrected MAC units for volatile anesthetics by using a nomogram to estimate age-related MAC [16] and age-related iso-MAC charts [23]. In the recent practice of veterinary anesthesia, geriatric animals have become a significant proportion of the patient population. Attention to the unique physiology and particular requirements of individuals within this age group will contribute to the provision of safe and effective anesthesia [9, 19]. Veterinary practitioners believe that geriatric animals require a lower concentration of inhalation anesthetic to maintain anesthesia based on clinical experience. To the best of our knowledge, however, there are few reports on the relationship of MAC to age in veterinary species [11, 17]. Furthermore, the relationship of sevoflurane MAC to age has not been evaluated in dogs. The purpose of the study reported here was to determine the effect of age on sevoflurane MAC in dogs. The authors hypothesized that the sevoflurane MAC value would be inversely related to age in this species.

Six young beagles, 2 years of age (all male) and weighing from 9.7 to 11.8 kg (10.8 ± 0.9 kg of mean ± SD), and six old beagles, 8 to 10 years of age (9.7 ± 0.8 years old, 3 male and 3 female) and weighing from 8.8 to 15.4 kg (11.6 ± 2.6 kg), were used for this study. There was no consanguinity among these dogs. The dogs were judged to be in good to excellent health based upon a physical examination, complete blood cell count and serum biochemical analysis. Food and water were withheld from the dogs for 12 hr before the experiment. The dogs were owned by the university and cared for according to the principles of the “Guide for the Care and Use of Laboratory Animals” prepared by Rakuno Gakuen University. The Animal Care and Use Committee of Rakuno Gakuen University approved the study.

Anesthesia was induced by mask induction using sevoflurane (SevoFlo, Dainippon Sumitomo Pharma, Osaka, Japan) in oxygen. All dogs were orotracheally intubated with an endotracheal tube and anesthetized with oxygen-sevoflurane anesthesia in left lateral recumbency. The end-tidal partial pressure of CO₂ (PETO₂) was maintained between 35 and 40 mmHg by intermittent positive pressure ventilation (IPPV). All dogs were administered lactated Ringer’s solution at a rate of 10 ml/kg/hr intravenously through a 22-gauge catheter placed in the right cephalic vein. The esophageal temperature was maintained between 37.5 and 38.5°C using a heating pad and a warm air blanket.

Esophageal temperature (°C), heart rate (beats/min), cardiac rhythm, respiratory rate (breaths/min), PETO₂, end-tidal concentration of sevoflurane (ETSEV; %), indirect blood pressure (mmHg) and saturation of hemoglobin with oxygen (SpO₂; %) were monitored using a veterinary patient monitoring system (BP-508V, Omron Colin Co., Ltd., Tokyo, Japan). The esophageal temperature was measured using an electric thermometer probe placed orally into the thoracic esophagus. Heart rate and cardiac rhythm were
monitored by visual inspection of Lead II of the electrocardiogram. Blood pressure was determined by the oscillometric method. The SpO₂ was measured by pulse oximetry. A commercially available adaptor (Airway adaptor L-shape, Omron Colin Co.) modified with an 8-Fr feeding tube (Safed feeding tube, Terumo) was placed at the Y-piece of the breathing circuit. The tube passed through the endotracheal tube so that its tip rested in the thoracic portion of the trachea. A side-stream capnograph and anesthetic agent monitor were used to determine respiratory rate, PETCO₂ and ETSEV. The anesthetic agent monitor was calibrated immediately prior to each sevoflurane MAC determination.

The MAC of sevoflurane was determined by use of the tail clamp method [5], with minor modifications [32]. After the dogs were allowed to equilibrate for 30 min at ETSEV 2.4%, a standard Backhaus towel clamp was placed around the tail and closed to the third ratchet. The clamp was left in place for 60 sec or until gross purposeful movement was evident. Purposeful movement was defined as substantial movement of the head or extremities and did not include coughing, chewing, swallowing or increasing respiratory effort. When the dog exhibited purposeful movement, the ETSEV was increased by 10 to 20%, and the dog was retested after 20 min of re-equilibration. When the dog did not exhibit purposeful movement, the ETSEV was decreased by 10 to 20%, and the dog was retested after 20 min of re-equilibration. The MAC was determined as the mean of the ETSEV at which the dog did not demonstrate purposeful movement and next lower concentration tested (i.e., the highest concentration at which the dog demonstrated purposeful movement in response to tail clamping). The MAC for each dog was determined in triplicate by the same person (K.Y.), who was not aware of the age of the dogs. Cardiorespiratory data were collected immediately prior to tail clamping. The data are reported as means ± standard deviation (SD). The cardiorespiratory data and MAC were compared between the younger and older dogs. These data were analyzed by use of the Mann-Whitney U test. The level of significance was set at P<0.05.

It took 189.0 ± 51.5 min and 154.7 ± 44.7 min after induction of anesthesia to obtain the triplicate data for sevoflurane MAC in the young and old dogs, respectively (Fig. 1). There was no significant difference in the duration of MAC determination between the young and old dogs (P=0.262). Sevoflurane MAC was 2.25 ± 0.15% in the younger dogs and 1.86 ± 0.29% in the older dogs. The sevoflurane MAC for the older dogs was significantly less than that of the younger dogs (P=0.007). Throughout the present study, the heart rate and indirect mean blood pressure immediately prior to determination of sevoflurane MAC were within the normal values of dogs in all the dogs (Table 1). Normothermia, good oxygenation and eucapnia were achieved by incubation and IPPV. There were significant differences in heart rate (P=0.0002), indirect mean blood pressure (P=0.020) and SpO₂ (P=0.002) between the young and old dogs.

In the present study, the sevoflurane MAC for the young dogs was 2.25 ± 0.15%, which is quite similar to the MAC of sevoflurane reported by Kazama and Ikeda for a larger group of unmedicated dogs (2.36 ± 0.46%, n=18) [13]. As predicted, the sevoflurane MAC for the older dogs (1.86 ± 0.29%) was significantly less and represented a MAC reduction of approximately 17% compared with the younger dogs. It has been also reported that the MAC of isoflurane reduces with increasing age in dogs [17]. In this previous report, the isoflurane MAC was 1.82 ± 0.08% for young dogs (2 to 3 years old) and 1.45 ± 0.06% for old dogs (11 years old), indicating a MAC reduction of approximately 20% with increasing age. Our data reconfirm that dogs experience an increase in anesthetic potency with increasing age.
age, similar to humans [8, 20, 22, 26, 29].

It has been reported that no difference in MAC was found in women versus men anesthetized with desflurane, diethyl ether, halothane, methoxyflurane, sevoflurane or xenon [4, 12]. On the other hand, it has also been reported that elderly Japanese women given xenon or sevoflurane have a significantly lower MAC than Japanese men of the same age [4, 7]. Owing to the circumstances in the present study, the old group was composed 3 female and 3 male dogs, while the young group was composed all male dogs. The MACs of sevoflurane were 1.71 ± 0.37% for the 3 female and 2.01 ± 0.03% for the 3 male older dogs. The older male dogs seem to have a lower sevoflurane MAC than the young male dogs (2.25 ± 0.15%). Whether female dogs, particularly old female dogs, have a lower MAC than male dogs remains to be confirmed by further studies.

Sevoflurane has dose-dependent depressant effects on cardiorespiratory function in dogs [21]. In the present study, heart rate and indirect mean blood pressure were within the normal values for dogs during MAC determination. In addition, good oxygenation and eucapnia were achieved by IPPV. However, heart rate, indirect mean blood pressure and SpO2 were lower in the old dogs compared with the young dogs. The old dogs demonstrated mild to moderate cardiorespiratory depressions, although they were anesthetized with an equipotent titer of sevoflurane compared with the young dogs (i.e., around MAC). Decline of cardiorespiratory function has been well documented in aged dogs [6, 10, 18, 25, 27]. Therefore, cardiorespiratory function should be closely monitored during sevoflurane anesthesia in aged dogs.

In conclusion, the MAC of sevoflurane for dogs profoundly decreased with increasing age. Our data reconfirm that dogs experience an increase in anesthetic potency with declining age. Our data reconfirm anesthesia in aged dogs.

Sevoflurane has dose-dependent depressant effects on cardiorespiratory function in dogs [21]. In the present study, heart rate and indirect mean blood pressure were within the normal values for dogs during MAC determination. In addition, good oxygenation and eucapnia were achieved by IPPV. However, heart rate, indirect mean blood pressure and SpO2 were lower in the old dogs compared with the young dogs. The old dogs demonstrated mild to moderate cardiorespiratory depressions, although they were anesthetized with an equipotent titer of sevoflurane compared with the young dogs (i.e., around MAC). Decline of cardiorespiratory function has been well documented in aged dogs [6, 10, 18, 25, 27]. Therefore, cardiorespiratory function should be closely monitored during sevoflurane anesthesia in aged dogs.

In conclusion, the MAC of sevoflurane for dogs profoundly decreased with increasing age. Our data reconfirm that dogs experience an increase in anesthetic potency with declining age. Careful titration of inhaled anesthetics and vigilant monitoring should be employed to avoid excessive anesthetic depth in aged dogs.

REFERENCES

24. Ohta, M., Oku, K., Yamanaka, T. and Mizuno, Y. 2000. Anes-


