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# Comparison between Minimum Alveolar Concentration and Minimum Alveolar Concentration for Blunting Adrenergic Response after Administration of Sevoflurane in Cats

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## Abstract

**Objectives:** Minimum alveolar concentration (MAC) is defined as the alveolar concentration of anesthetic at 1 atmosphere that produces immobility in 50% of subjects exposed to a noxious stimulus. There is limited information regarding the MAC of sevoflurane required for blunting adrenergic responses (MAC-BAR) in cats. The aim of this study was to compare the MAC and MAC-BAR of sevoflurane required to prevent autonomic responses and purposeful movements in cats.

**Methods:** Six adult healthy domestic short-haired catswere anesthetized with sevoflurane. The MAC and MAC-BAR values for sevoflurane were determined by judging the cats' responses to a noxious electrical stimulus (50 V, 50 Hz, 10 msec) applied to the ventral side of the tail base.

**Results:** The difference between the MAC and MAC-BAR values for sevoflurane was not statistically significant.

**Conclusions and Relevance:** These results suggest that autonomic responses are prevented by anesthetic concentrations of sevoflurane at which purposeful movements are absent. Detrimental cardiovascular side effects, such as hypotension and impaired cardiac contractility, can occur easily in cat's anesthetized using sevoflurane.

**Keywords:** Anesthesia; Feline; Minimum Alveolar Concentration; Blunting Adrenergic Response; Sevoflurane

## Introduction

Sevoflurane is a volatile anesthetic agent with a relatively low blood/gas solubility coefficient that achieves rapid induction and recovery from anesthesia [1]. During the last decade, clinical use of sevoflurane has been increasing in animals, including in horses, dogs, and cats. 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 [2]. Because of these side effects, sevoflurane must be carefully titrated, and vigilant monitoring should be employed to avoid excessive anesthetic depth. Determination of an adequate level of anesthesia has traditionally relied on patient movement and/or the hemodynamic response to a surgical stimulus. MAC is defined as "the alveolar concentration of anesthetic at 1 atmosphere that produces immobility in 50% of subjects exposed to a noxious stimulus" [3]. As a guideline, most patients require approximately 1.2–1.4 MAC for an adequate level of surgical anesthesia [1]. However, it is well known that heart rate or arterial blood pressure may increase in response to surgical stimulation despite the absence of a motor response. The minimum alveolar concentration of blunting adrenergic responses (MAC-BAR) is the minimum concentration of inhalant anesthetic that prevents an autonomic response to a noxious stimulus and is a useful measure of the effects of an anesthetic agent on autonomic pathways in the spinal cord and brainstem [4,5]. However, information on MAC-BAR in cats is limited. The aim of this study was to determine the MAC-BAR in cats anesthetized with sevoflurane and compare it with the MAC.

## Materials and Methods

Six adult healthy domestic short-haired cats (3 male, 3 female, aged 1 year, mean weight 4.0 ± 0.6 kg) were anesthetized with sevoflurane on two occasions with a minimum 14-day washout period in between to determine the MAC and MAC-BAR for sevoflurane. The cats were judged to be in good to excellent health based on a physical examination, a complete blood cell count, and biochemical analysis. The cats were fasted for 12 hours before the experiment but had free access to water until just before the experiment. The cats 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 using sevoflurane in oxygen via a face mask (SevoFlo, Dainippon Sumitomo Pharma, Osaka, Japan). All cats were orotracheally intubated with an endotracheal tube and anesthetized using a semi-closed type of anesthetic delivery system.

Once the cats were positioned in lateral recumbency, a 22-gauge catheter was placed in the right cephalic vein and a 22-gauge or 24-gauge catheter was placed in the dorsal pedal artery. Arterial blood samples were collected anaerobically from this catheter into a syringe containing heparin to analyze the partial pressures of arterial $O_2$ and $CO_2$. Arterial blood pressure was measured directly by connecting this catheter to a pressure transducer (CDX-A90, Cobe Laboratories, Tokyo, Japan) placed and zeroed to open the transducer at atmospheric pressure and pressing the monitor's zero button at the level of the mid-sternum. During anesthesia, the respiratory rate was maintained at 24 breaths per minute and end-tidal $CO_2$ partial pressure ($PE'CO_2$) was maintained at 30–35 mmHg by intermittent positive pressure ventilation. All cats received Ringer's lactate solution at a rate of 10 mL/kg/hour intravenously through a 22-gauge catheter placed in the right cephalic vein. Esophageal temperature was maintained at 37.5°C–38.5°C using a heating pad and a warm air blanket in all cases. Heart rate, lead II of the electrocardiogram, and arterial blood pressure was recorded by a multi-parameter anesthetic monitoring system (DS-5300, Fukuda Denshi Co., Tokyo, Japan). The partial pressures of arterial $O_2$ and $CO_2$ were determined with a blood gas analyzer (GEM Premiere 3000, International Medical Intelligence Co., Saitama, Japan). Gas samples were drawn from the proximal end of the endotracheal tube using the feeding tube at a rate of 200 mL/min. A side stream capnograph and anesthesia monitor was used to determine respiratory rate and the end-tidal sevoflurane concentration (FE´Sevo). The anesthesia monitor was calibrated using commercially available calibration gases immediately prior to each sevoflurane MAC and MAC-BAR determination.

The MAC and MAC-BAR values for sevoflurane were determined by judging the cats' responses to a noxious electrical stimulus (50 V, 50 Hz, 10 msec) applied to the ventral side of the tail base [6]. The cats were allowed to equilibrate for 60 min at an FE´Sevo of 2.5%–3.0%, after which the electrical stimulus was applied for 10 sec using an electrical stimulator (SEN3301, Nihon Kohden Co., Tokyo, Japan). After determining the MAC for each cat, the MAC-BAR was determined. Positive response to the electrical stimulus for MAC determination was fixed a purposeful movement defined as substantial movement of

the head or extremities and did not include coughing, chewing, swallowing, or increasing respiratory effort [7]. Positive response for MAC-BAR determination was fixed an increase of either heart rate or mean arterial blood pressure more than 15% above the value recorded at 1 min before applying the electrical stimulus [8]. When there was a positive response from the cat, the FE´Sevo was increased by 10%–20%, and the cat was retested after 20 minutes of re-equilibration. When the cat did not show a positive response, the FE´Sevo was decreased by 10%–20%, and the cat was retested after 20 minutes of re-equilibration. The MAC and MAC-BAR were determined as the mean of the FE´Sevo at which the cat did not demonstrate a positive response, and the next lower concentration was then tested (i.e., the highest concentration at which the cat demonstrated a positive response to the electrical stimulus). The MAC and MAC-BAR for each cat were determined in triplicate by the same investigator (KY). Cardiorespiratory data were collected 1 min before applying the electrical stimulus.

All data are reported as the mean ± standard deviation. The parameters recorded immediately prior to determination of MAC and MAC-BAR were compared using the paired *t*-test. The MAC and MAC-BAR were also analyzed using the paired *t*-test. The level of statistical significance was set at $p < 0.05$.

## Results

The esophageal temperature and cardiorespiratory data recorded immediately prior to determination of MAC-BAR and MAC are summarized in Table 1. Normothermia was successfully maintained in all cats throughout the study by using a heating pad and air blanket. Good oxygenation and eucapnia were achieved by intermittent positive pressure ventilation. No statistically significant differences in any of the physiologic parameters were detected.

## Discussion

In this study, the MAC-BAR for sevoflurane in cats was 3.24% ± 0.41%, which is somewhat higher than the MAC-BAR for isoflurane (2.07%) recently reported in cats, and the difference between the MAC and MAC-BAR for sevoflurane was not statistically significant (Table 1, $p = 0.26$) [7]. These results were almost the same as those in a previous report for isoflurane in cats [1]. In contrast, the MAC-BAR for sevoflurane has been reported to be significantly higher than the MAC in dogs [9]. In a human study, Rosen et al. reported that a greater alveolar concentration of inhalant anesthetics was necessary to prevent autonomic adrenergic responses to a surgical stimulus (i.e., MAC-BAR) when compared with that necessary to merely prevent movements (i.e., MAC) [5]. MAC-BAR may provide an indirect assessment of the level of analgesia [5]. In a study in cats, MAC-BAR was comparable with the alveolar concentration of isoflurane necessary to prevent cortical arousal [8]. This finding is attributed to the widespread belief that most patients require a MAC of approximately 1.2–1.4 for an adequate level of surgical anesthesia and the cat was needed to approximately 3.50%–4.09% of the FE´Sevo. However, our present results for cats suggest that autonomic responses were prevented by anesthetic concentrations of sevoflurane at which purposeful movements are absent. Therefore, detrimental cardiovascular side effects, such as hypotension and impaired cardiac contractility, can easily occur in cats anesthetized using sevoflurane, and appropriate monitoring is warranted.

## Conclusion

The MAC-BAR for sevoflurane in cats was 3.24% ± 0.41% in this study, which is somewhat higher than the MAC-BAR for isoflurane in cats and significantly higher than the MAC in dogs. In cats, it is very important to check the “adequate” anesthetic depth to prevent purposeful movements and to keep normal range of cardiovascular conditions.

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## Conflicts of Interest

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article’.

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