Determination of the Minimum Alveolar Concentration (MAC) of Isoflurane and Sevoflurane in *Callithrix penicillata*

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ABSTRACT

Background: The minimum alveolar concentration (MAC) is a measure of quantitative anesthetic potency and has become the standard index for the evaluation and comparison of volatile anesthetics, in addition to guiding dose administration. Black-tufted marmosets (*Callithrix penicillata*) are primates present in the clinical and surgical routine of veterinary hospitals, as well as experimental models, especially in neuroscience. Few studies have evaluated the potency of the main volatile anesthetics in this species. This study aimed to determine the MAC of isoflurane and sevoflurane in *C. penicillata* using the up-and-down method and to evaluate the effects of these drugs on the quality of anesthetic induction, maintenance, and recovery.

Materials, Methods & Results: Twenty-four animals of undetermined age were used. All marmosets were healthy according to hematological and physical evaluation. The animals were randomly divided into 2 groups: ISO_{MAC} and $SEVO_{MAC}$. Each animal was induced to general anesthesia in an anesthetic box with oxygen (5 L/min) and sevoflurane at 7% in the $SEVO_{MAC}$ group or isoflurane at 5% in the ISO_{MAC}. Upon reaching lateral decubitus, orotracheal intubation was performed. General anesthesia was maintained with isoflurane or sevoflurane diluted in oxygen (0.8 L/min) using a non-rebreathing delivery system under spontaneous ventilation. As defined in the pilot study, the first animal from ISO_{MAC} started the maintenance of anesthesia with 2.6% isoflurane, while the first animal in $SEVO_{MAC}$ received 4% sevoflurane. After finishing the instrumentation to assess heart rate, respiratory rate, systolic blood pressure, pulse oximeter oxygen saturation, end-tidal carbon dioxide concentration, and rectal temperature, a 15-min wait to reach anesthetic equilibrium was allowed, and then an electrical noxious stimulation (50 mA and 50 Hz) was performed on the lateral aspect of the thigh (a faradic current of 3 consecutive single stimuli, followed by 2 continuous stimuli). The animals' responses to the electrical stimulus were observed. The presence of a positive response (gross movement of the limbs, head, or vocalization) or a negative response (absence of gross movements) determined the increase or reduction, respectively, of the inhalation anesthetic concentration by 10% in the subsequent marmoset. The quality of anesthetic induction and recovery from anesthesia was evaluated using a scale that measured the intensity of agitation, coughing, nausea, and vomiting. Physiological variables were recorded before (M0) and after (M1) applying the nociceptive stimulus. Isoflurane and sevoflurane MAC values in *C. penicillata* were 2.29 ± 0.10% and 3.93 ± 0.61 % respectively. Physiological parameters, quality of anesthetic induction and recovery did not differ significantly between groups. However, isoflurane caused irritation of the airway and ocular mucous membranes, more coughing episodes, and tearing at induction. There was no difference between groups for time to extubation and recovery time to regain sternal position.

Discussion: Previous studies in primates found lower MAC values for both anesthetics, except for *Lemur catta*. Those findings may be explained by the use of different nociceptive stimuli and the MAC determination method employed, although no differences in MAC values have been described between bracketing or up-and-down methods in human primates and dogs. It is unlikely that the stimulus and technique alone are the determining factors for the high concentration of isoflurane and sevoflurane observed in the present study since MAC was high with both halogenates, indicating that dose extrapolation from other species can lead to the wrong anesthetic dosage.

Keywords: *Callithrix penicillata*, marmoset, anesthetic potency, volatile anesthetic, anesthetic dosage, halogenates.

INTRODUCTION

Callithrix penicillata, also known as the black-tufted-ear-marmoset, star tamarin, or cerrado tamarin, is a primate species native to the Brazilian cerrado [23,44]. This species is also found in institutions such as zoos, veterinary hospitals specializing in exotic animals, and neuroanatomy research centers due to its similarity to humans, especially regarding the forebrain [13,20,34]. For this reason, marmosets are routinely anesthetized for clinical examination and surgical procedures [21].

In 1965, Eger *et al.* [11] developed the concept of minimum alveolar concentration (MAC) for gaseous and volatile anesthetic agents as a means of evaluating and comparing their potency. This quantitative measure of potency has become useful and reproducible in any species and is the standard indicator for evaluating and comparing volatile anesthetics, besides guiding the dose to be administered in different species [4,33].

Since the beginning of the use of inhalational anesthesia, only 4 anesthetic agents have been widely used in veterinary medicine. Nowadays, isoflurane followed by sevoflurane, 2 anesthetics from the halogenated group, stand out in the daily routine of veterinarians and are indicated for induction and maintenance of anesthesia in small primates [41,49].

Given the scarcity of information on the use of halogenates in small primates which results in the extrapolation of doses from other species, this study aimed to determine the MAC of isoflurane and sevoflurane in *C. penicillata* and to evaluate the effect of these drugs on the anesthetic induction, maintenance, and recovery.

MATERIALS AND METHODS

Animals

Seven families of *C. penicillata*, totaling 24 animals (11 females and 13 males) of undetermined age and from the same captivity, were used. Animals were randomly allocated to 2 groups according to the inhalation anesthetic used: ISO$_{MAC}$ and SEVO$_{MAC}$.

All marmosets were considered healthy by means of physical, hematological, and biochemical evaluation. The identification of any impairment in those assessments determined the animal to be excluded from the study.

Food but not water was withdrawn for 4 h previously to the experimental procedures.

Instrumentation and anesthesia

After 5 min of preoxygenation (5 L/min), anesthesia was induced with 5% isoflurane[1] in ISO$_{MAC}$ and 7% sevoflurane1 in SEVO$_{MAC}$ delivered through an induction chamber consisting of a transparent anesthetic box (capacity for 16.6 L) until reaching lateral recumbency. Then, animals were positioned in dorsal recumbency at a 45° angle and oral-tracheal intubation was conducted with an over-the-needle intravenous catheter according to Thomas *et al.* [42]. The number of tracheal intubation attempts was registered.

The anesthetic plane was maintained with isoflurane or sevoflurane diluted in oxygen at 100% (0.8 L/min) in a non-rebreathing system through a precision vaporizer for each of the halogenates used [33]. Additionally, isoflurane and sevoflurane concentrations were measured using an infrared gas analyzer from the multiparametric monitor[2] by sampling airway gases from a port located between the proximal end of the endotracheal tube and the breathing system. Both vaporizers were calibrated using the FI-21 equipment[3]. A standard gas mixture[4] was used to calibrate the gas analyzer before each animal was anesthetized. In addition, the vaporizers were calibrated for gas flow with a gas flow analyzer[5]. The entire calibration process was performed in a room controlled for humidity and temperature using a thermohygrometer equipment[6].

The quality of the anesthetic induction was always assessed by the same qualified evaluator by using a scale developed for this purpose. Signs of coughing, agitation, nausea, and vomiting were assessed from the beginning of the anesthetic inhalation until lateral recumbency was reached and the animal was unresponsive to stimulus. Coughing, agitation, and mimics of vomiting/ vomiting were classified as 1 (absent), 2 (mild), 3 (moderate - 2 to 3 events), and 4 (high - 4 or more events), while nausea was categorized as yes or no.

From the orotracheal intubation to the end of the procedures, oxygen saturation by pulse oximetry (SpO$_2$), electrocardiography, heart rate (HR), respiratory rate (RR), rectal temperature (RT), end-tidal carbon dioxide concentration (EtCO$_2$), FE'Iso, and FE'Sevo were measured by using a vital sign monitor[2]. Non-invasive systolic blood pressure (SBP) was assessed by a vascular Doppler[7], which probe was placed

on the palmer surface of the forelimb (Figure 1). All physiologic parameters were continuously monitored and registered at M0 (the moment immediately after 15 min following the orotracheal intubation) and M1 (immediately after the supramaximal noxious stimulus).

Figure 1. *Callithrix penicillata* after orotracheal intubation and under anesthetic monitoring with multiparametric monitor, ultrasonic Doppler, and electrical neurostimulator.

Supramaximal noxious stimulation and MAC determination

ISO_{MAC} and $SEVO_{MAC}$ were determined using the up-and-down method. The end-tidal isoflurane (FE′Iso) and sevoflurane (FE′Sevo) concentrations administered in the first animal from each group were established as 2.6% in ISO_{MAC} and 4% in $SEVO_{MAC}$ based on a pilot study using one marmoset per group. This end-tidal concentration was maintained for 15 min (equilibration period).

In order to apply the noxious electrical stimulus, a neurostimulator[8] was employed. The electrical stimulus was applied in the tibia region using a pair of hypodermic needles (25x0.7 mm) placed intramuscularly and connected to the electrical stimulator. The electrical stimulus (50 mA and 50 Hz) consisted of 3 short stimuli with an interval of 5 s between them, followed by 2 long stimuli of 5 s duration. The response to the noxious stimulus was classified as negative when movements of the tail, head, contralateral limb to the stimulus, and vocalization were absent after the stimulus. The presence of these events was considered a positive response. When a negative response was observed, the FE′Iso and FE′Sevo to be tested in the subsequent animal were decreased by 10%. This procedure was performed until an animal showed a positive response to the painful stimulus, then the end-tidal concentration of the halogenate was increased by 10% for the next primate. Crossover events were recorded when a negative response was followed by a positive response or vice versa. Four events were required to determine MAC.

Following the MAC determination experiment, the animals were submitted to sterilization surgery. Females underwent bilateral partial salpingectomy according to the Parkland techniques, while males were submitted to double ligation of the vas deferens during vasectomy. Butorphanol[9] was administered as perioperative analgesia added to locoregional anesthesia with lidocaine[1] (3 mg/kg) injected in the incision line in females and the scrotal incision in males.

At the end of the surgery, inhalation anesthesia was discontinued, and the quality of the anesthetic recovery was assessed by scoring signs of coughing, agitation, nausea, vomiting, and the time until gaining the sternal position. The total time of anesthesia (from the beginning of the anesthetic administration up to the extubation), and the time of anesthetic recovery (from the discontinuation of the halogenate until the animal regained sternal posture) were recorded.

Dipyrone[10] (25 mg/kg), meloxicam[11] (0.2 mg/kg), and enrofloxacin[12] (5 mg/kg) were administered subcutaneously at the end of the final evaluation.

Statistical analysis

The partial minimum alveolar concentration was calculated using the Dixon up-and-down technique, and the average of the crosses was calculated according to Monteiro [26], by using Microsoft Excel Statistical Analysis System for each of the analyses. Subsequently, the results were corrected to 1 atm [49] to obtain the MAC value.

Statistical tests were performed using the GraphPad Prism software[13]. Values of physiological variables were compared between M0 and M1 by Student's paired *t*-test and are shown as mean ± standard deviation. Differences between ISO_{MAC} and $SEVO_{MAC}$ regarding the physiological variables were examined using a two-way analysis of variance (ANOVA) followed by Bonferroni post hoc test. The quality of anesthetic induction and recovery was analyzed using the chi-square test. Associations between the isoflurane and sevoflurane concentrations with physiological parameters at M0 and M1 were assessed by Pearson's correlation (r) test. Differences were considered statistically significant at $P < 0.05$.

RESULTS

Three animals were excluded - 2 females due to pregnancy and 1 male weighing less than 200 g, characterized as in an inadequate nutritional status. Therefore, 22 animals completed the study (ISO_{MAC}, n=9 and $SEVO_{MAC}$, n=12). ISO_{MAC} was composed of 4 females and 5 males, while $SEVO_{MAC}$ contained 5 females and 7 males. There was no statistical difference concerning the average weight of the animals between ISO_{MAC} (0.392 ± 0.079 kg) and $SEVO_{MAC}$ (0.400 kg ± 0.103 kg; *P* = 0.882).

The total time of anesthesia was statistically similar between ISO_{MAC} (116 ± 47 min) $SEVO_{MAC}$ (112 ± 30 min; *P* = 0.840).

Determination of the minimum alveolar concentration of isoflurane and sevoflurane

The MAC of isoflurane in *C. penicillata*, evaluated by the average of 4 crossovers without repeating animals, was 2.30 ± 0.10% at 0.903 atm. When corrected for sea level (1 atm), the isoflurane MAC was 2.295 ± 0.10%. MAC values for sevoflurane were 3.94 ± 0.61% at 0.903 atm and 3.931 ± 0.61 V% at 1 atm after correction.

Physiological variables

Values of physiological parameters of ISO_{MAC} and $SEVO_{MAC}$ before (M0) and after (M1) applying the noxious stimulus are in Table 1. HR (ISO_{MAC}, *P* = 0.0018 and $SEVO_{MAC}$, *P* = 0.0002) and RR (ISO_{MAC}, *P* = 0.0030 and $SEVO_{MAC}$, *P* = 0.0015) increased significantly from M0 to M1 in both groups, although no statistical difference was observed between groups (HR: M0, P = 0.0620 and M1, *P* = 0.0750; RR: M0, *P* = 0.8611 and M1, *P* > 0.9999). SBP values did not differ significantly between groups (M0, *P* = 0.6586 and M1, *P* > 0.9999) or between M0 and M1 (ISO_{MAC}, *P* = 0.9919 and $SEVO_{MAC}$, *P* = 0.0818). Likewise, there was no significant difference between groups or time points of evaluation for $EtCO_2$, SpO_2, and RT (*P* > 0.05).

A strongly negative and significant correlation (r = -0.85; *P* = 0.003) was observed between FE′Iso and SpO_2. FE′Sevo was negatively and significantly correlated with RR (r = -0,73; *P* = 0,004) and $EtCO_2$ (r = - 0,60; *P* = 0,02).

Table 1. Mean ± standard deviation of physiological variables of heart rate (HR) in beats per minute (bpm), respiratory rate (RR) in movements per minute (mpm), systolic blood pressure (SBP in mmHg), end-expiratory carbon dioxide concentration ($EtCO_2$ in mmHg), peripheral oxygen saturation (SpO_2) and rectal temperature (RT, ºC), pre and post - electrical stimulus (M0 and M1), in *Callithrix penicillata* under isoflurane or sevoflurane anesthesia.

Variables	Isoflurane		Sevoflurane		Reference values
	M0	M1	M0	M1	
HR (bpm)	225.4 ± 35.54	245.6 ± 24.17 A	193.5 ± 36.85	214.8 ± 31.94	240 a 350*
RR (mpm)	44.8 ± 4.44	51.0 ± 4.58 A	47.1 ± 7.37	52.7 ± 8.15 C	20 a 50*
SAP (mmHg)	86.6 ± 33.26	86.3 ± 17.68	73.3 ± 18.60	82.1 ± 10.54	100-145**/90 - 145***
SpO_2 (%)	97.3 ± 1.80	95.6 ± 2.13 C	95.9 ± 1.75	95.9 ± 1.95	94 a 99***
$EtCO_2$ (mmHg)	34.1 ± 10.88	34.7 ± 12.34	29.2 ± 2.35	30.8C ± 2.74	35 a 45***
RR (°C)	37.0 ± 1.61	37.2 ± 1.68	37.1 ± 0.92	37.0 ± 0.99	35.4 a 39.7*

*Reference by Verona and Pissinatti [48] for unanesthetized *Callithrix*. **Reference by Mietsch and Einspanier [25]; Schnell and Wood [35] for unanesthetized *Calithrix*. ***Haskins [18] for anesthetized small animals. A- Indicates difference from M0 after paired *t*-test. C- Indicates a negative and significant correlation between the MAC of the anesthetic agent and the variable evaluated according to Pearson's correlation.

Quality of induction of anesthesia

The mean duration of induction of anesthesia was 84 ± 44 s in ISO_{MAC} and 203 ± 90 s in $SEVO_{MAC}$.

Coughing was significantly higher (*P* = 0.004) in ISO_{MAC}, in which it was classified as moderate (between 2 and 3 events of coughing), in comparison to $SEVO_{MAC}$ which did not show coughing at anesthesia induction.

Salivation, mimics of vomiting or vomiting were not observed during the induction of anesthesia in either of the groups (*P* > 0.05). Mild agitation was identified in both ISO_{MAC} and $SEVO_{MAC}$ without a statistical difference between them (*P* = 0.077). Tearing was observed in all animals in ISO_{MAC} during the anesthetic induction.

All animals were successfully intubated, however, a median of 2 (1 - 6) attempts were needed for adequate orotracheal intubation in ISO_{MAC} against 1.5 (1 - 3) attempts in $SEVO_{MAC}$ (*P* = 0.2048).

Anesthetic recovery assessment

Voluntary extubation occurred 9.33 ± 5.11 min and 9.41 ± 7.27 min after discontinuing the administration of isoflurane and sevoflurane ($P = 0.9626$), respectively. Mean time from the extubation to regaining sternal position was 16.46 ± 8.00 min in ISO_{MAC} and 15.00 ± 8.22 min in $SEVO_{MAC}$ ($P = 0.6242$). No animal presented agitation, mimics of vomiting or vomiting during the anesthetic recovery. However, both groups showed 2 to 3 coughing events following extubation ($P = 0.1825$).

DISCUSSION

In this study, it was chosen to research the induction, maintenance, and recovery of anesthesia in *Callithrix penicillata* due to the importance of this species as an experimental model [13,20]. In addition, *C. penicillata* is found in several areas of the Brazilian territory and, currently, faces overpopulation issues, besides being a commercial species of marmoset [44]. Isoflurane and sevoflurane were chosen to be studied in this work because of the safety associated with their administration, besides being the most used halogenates [28].

Besides animals being randomly allocated into each group, seven families were used to avoid genetic interferences in the study. Although the mean weight of the animals did not differ significantly, there was a disparity in sex distribution between groups. However, MAC is not influenced by sex [14].

Total blood count was within normal values for the species in captivity, according to the literature [48]. Additionally, in the physical evaluation, no alterations suggesting disease, electrolyte disturbance, or body temperature alterations were identified. Anemia, hyperthermia, hypothermia, hyponatremia [31,41], and hypovolemia [24] are some of the factors that influence the determination of MAC. Gestation decreases MAC by around 30% in human primates [7], therefore, 2 pregnant females in ISO_{MAC} were excluded.

In this study, MAC was determined to be $2.29 \pm 0.10\%$ in ISO_{MAC} and $3.93 \pm 0.61\%$ in $SEVO_{MAC}$ at 1 atm after exposing *C. penicillata* to electrical stimulation with hypodermic needles. MAC values were standardized at sea level to avoid overestimation of values [32]. The literature on MAC determination in New and Old-World primates shows MAC values ranging from 1.28 to 1.58% for isoflurane [22,43] and from 1.84 to

2.16% for sevoflurane [9,37]. Among primates, *Lemur catta i*s the species in which MAC values for isoflurane ($1.96 \pm 0.09\%$) and sevoflurane ($3.48 \pm 0.55\%$) most closely approximate those found in the present study for *C. penicilatta* [8,9]. Discrepancies among the findings described in the literature may be explained by the different nature of the noxious stimuli applied in the MAC determination among studies, which can be of mechanical or electrical origin. Also, the method used to determine MAC may influence the values observed, although no differences in MAC were found between the bracketing or up-and-down methods in dogs and human primates [38,40]. However, it is unlikely that the high MAC values found in the present study can be attributed only to the noxious stimulus used and the up-and-down method, since MAC was high in both groups. The low weight of marmosets compared to primates from previous studies (> 2 kg), in addition to the high metabolism of *C. penicillata* [27] are factors that might be associated with the high MAC values found. The MAC findings of the present study warrant further investigation concerning other anesthetic agents and in comparison with other marmoset species.

Several methods of applying nociceptive stimulation are described in the literature. In non-human primates, the technique of tail clamping followed by electrical stimulation is commonly used. No studies validating a specific supramaximal stimulus in non-human primates have been identified, however, the noxious electrical stimulus is considered supramaximal in *Penelope obscura* [22], domestic cats [19], domestic canines, and rabbits [47]. In this study, the method of electrical stimulation with a hypodermic needle in the subcutaneous region of the tibia was chosen because it causes greater nociceptive stimulus, minor tissue injury, and ease of standardization, according to Quasha, Eger II and Tinker [32].

In the present study, MAC values were obtained in each group by averaging 4 crossovers. Four crossovers are considered adequate for estimating MAC because it has been reported that 4 crossovers produce findings that are equivalent to those of more crossovers [29]. However, analyzing quantal data with 6 crossovers when the up-and-down method is employed would decrease the likelihood of errors. The statistical analysis applied to determine the isoflurane and sevoflurane MAC values in this research differed from that used by Dixon [10], who proposed

the up-and-down method for MAC determination. In that study, MAC was estimated as the median effective dose (DE50) by a logistic regression curve. In contrast, in the present investigation, MAC was calculated by mathematical averaging as described in previous studies [1,26], but generating identical values to those estimated by the logistic regression curve technique.

Physiological parameters RR, RT, and SpO2 of *C. penicillata* were within the reference range of the species both at pre and post-stimulation [48]. Heart rate was lower in comparison to awaken animals but in agreement with HR of anesthetized marmosets at both M0 and M1 [16,36]. The negative correlation observed between reduced SpO2 and increased isoflurane but not sevoflurane concentration, and between RR and increased sevoflurane but not isoflurane concentration, is statistically justified by the small sample size.

It has been demonstrated that as the concentration of inhaled anesthetic agents increases, there will be a reduction in cardiac contractility, vasodilation, bradypnea, or even apnea, and consequently, a reduction in SpO2 [18]. Initially, a compensatory increase in HR may occur, but in clinical practice, a dose-dependent reduction in HR is usually observed during the maintenance of anesthesia [14].

Despite the large surface area in relation to body weight, animals were successfully kept in normothermia, according to temperature values for *Macaca mulata* [39], by using a thermal mattress during the procedure and by controlling the temperature of the operating room. Hypothermia was demonstrated to reduce MAC by up to 50% in dogs, however, it also delays recovery from anesthesia, promotes metabolic acidosis, and can cause death [12].

Due to the small size of the animals and the difficulty to perform arterial vascular access, noninvasive blood pressure monitoring was chosen. The smallest cuff available (2.2 cm x 11 cm) was placed proximally in the forearm to occlude the brachial artery, following the literature [5]. Arterial blood pressure was measured with an ultrasonic Doppler equipment owing to its higher accuracy in comparison to the oscillometric method in other animal species [2,30,45]. The cuff width should be 30 to 40% of the limb circumference to avoid overestimating (small cuffs) or underestimating (larger cuff) the blood pressure [46]. A previous study on primates [3] described using the base of the tail as a site for measuring non-invasive blood pressure, however, it was not used in *C. penicillata* due to the small circumference in these animals. Besides, by the oscillometric method, there is greater variability in blood pressure read at the base of the tail (7%) in comparison to the thigh (2.1%) in *Callithrix jacchus* [25]. Studies comparing the measurement of blood pressure by oscillometric methods, ultrasonic Doppler, and invasive methods in marmosets are suggested.

Both ISO_{MAC} and $SEVO_{MAC}$ showed SBP slightly below the values described for most mammals under anesthesia, including human primates [18]. Systolic blood pressure below 90 mmHg was also observed in capuchin monkeys during MAC determination, however, a mean arterial pressure above 60 mmHg was sustained in that study [31]. It has been showed that blood pressure values above 50 mmHg do not influence the determination of MAC in halothane-anesthetized rats [50].

In the present research, animals were anesthetized under spontaneous ventilation and monitored by capnography and capnometry, following previous studies with *Lemure catta* [8,9]. End-tidal CO_2, due to the air flowing dynamics and physiological dead space, usually measures 3 to 6 mmHg lower than $PaCO_2$ as demonstrated in dogs, being a surrogate parameter for $PaCO_2$ [18]. In human primates, there is a high correlation between EtCO2 and $PaCO_2$, especially if $EtCO_2$ is below 30 mmHg [6]. In the present study, $EtCO_2$ was statistically stable over time both in ISO_{MAC} (34.4 mmHg) and $SEVO_{MAC}$ (30.3 mmHg), without significant differences between the groups. Although $EtCO_2$ values were below the reference range in this investigation, only extreme $PaCO_2$ values (below 21 mmHg and above 95 mmHg) are expected to impact the MAC determination [32].

Animals were induced to general anesthesia inside a transparent plastic box, enabling a safe and adequate evaluation of the quality of anesthetic induction throughout the process without using physical restraint, as suggested by the literature [49]. Although no difference between groups was observed regarding agitation, ISO_{MAC} showed more coughing episodes and tearing. The exposure to high concentrations of isoflurane can irritate the airway leading to coughing, laryngospasm, especially in primates, and even apnea, resulting in oxyhemoglobin desaturation [41]. Unlike the unpleasant odor and the ability of isoflurane to irritate the airways [28,40], no reports concerning ocular

mucosa irritation in patients undergoing induction of anesthesia through an induction chamber have been identified in the literature.

The over-the-needle 14-18 G catheter proved to be an adequate endotracheal catheter as it has already been demonstrated [42]. However, due to the small diameter of the lumen, the sidestream probe for capturing expired gases could not be placed intraluminal but was attached proximally to the patient instead. All animals were successfully intubated after few attempts, with the help of a laryngoscope with a Miller blade and guide wire in the endotracheal tube.

It is reported in the literature that, in other species, sevoflurane presents shorter extubation and recovery times than isoflurane as a result of its lower blood-gas partition coefficient [41,48]. However, in the present study, the mean extubation time and recovery time until regaining the sternal position were not statistically different between ISO_{MAC} and $SEVO_{MAC}$. This result may be justified by the accelerated metabolism of marmosets [27] or the small number of animals used in the study.

During recovery from anesthesia, both groups presented moderate coughing (two to three coughing events), probably stimulated by the endotracheal tube. The use of lidocaine to desensitize the laryngeal mucosa prior to endotracheal intubation is suggested to avoid this kind of stimulus [15]. No agitated animals were observed in both groups, which could also be attributable to the quiet environment and the administration of butorphanol as an analgesic. Besides promoting effective analgesia for moderate pain, butorphanol has a tranquilizing action [17]. Also, butorphanol is an excellent antitussive agent [17], which may have influenced the absence of coughing observed during recovery from anesthesia.

CONCLUSION

Based on the methodology and analysis proposed in the present study, we conclude that the MAC of isoflurane and sevoflurane in *Callithrix penicillata*, determined by electrical stimulation with hypodermic needles and spontaneous ventilation was 2.29% and 3.93%, respectively. Extrapolation of doses between primates can lead to errors in anesthetic dosage.

The physiological parameters were similar between groups, however, due to the small number of animals used in this study, further investigation to evaluate the correlation between MAC and the physiological parameters is warranted.

Few adverse effects were observed in the anesthesia induction and recovery assessments in both groups, without statistical difference between them. However, isoflurane caused irritation of the airways, more coughing events, and tearing.

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1918