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Cardiopulmonary Effects of Sevoflurane in Garnett's Greater Bush Baby (*Otolemur garnettii*)

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Purpose: **A study was conducted to assess the cardiopulmonary and anesthetic effects of sevoflurane anesthesia on Garnett's Greater Bush Baby (*Otolemur garnettii*).**

Methods: **Anesthesia was induced in ten animals with 8% sevoflurane and was maintained by use of 2.5% sevoflurane for 30 minutes. Induction and recovery times were recorded. Heart and respiratory rates (RR), end-tidal carbon dioxide concentration (ET CO_2), arterial blood pressures, relative arterial blood oxygen saturation (SpO_2), arterial partial pressure of oxygen (P_aO_2), arterial partial pressure of carbon dioxide (P_aCO_2), and pH were monitored. Pre- and poststudy CBC and serum biochemical values were compared.**

Results: **Anesthesia induction was rapid (75 ± 8.7 seconds [mean ± SEM]) and smooth. Heart rate significantly increased initially, then decreased significantly over the remaining 30 minutes. There were no significant changes in RR, SpO_2, $ETCO_2$, or arterial blood pressure. The P_aO_2 values significantly increased in the 10- to 30-minute samples. The P_aCO_2 values remained steady in the 10- to 30-minute samples. A significant decrease was seen in white blood count, calcium, and total protein (TP) values, compared with values in pre-anesthesia samples. Recovery from anesthesia was smooth and rapid, with extubation at 24 ± 5.8 seconds.**

Conclusions: **At the concentrations used in this study, sevoflurane appears to be a safe and effective agent for induction and maintenance of anesthesia in *O. garnettii*.**

Otolemur garnettii is a nocturnal and arboreal prosimian (order Galagonidae) primate from sub-Saharan Africa. In captivity, they can be found in zoological collections and research facilities. They are most commonly used for behavioral and neurobiological studies, and serve as an important species for comparative studies (1–3). In addition to breeding readily in captivity (1), they are small in size, have low maintenance costs, and pose fewer health risks to handlers and caretakers, compared with many Cercopithecine primates.

Anesthetic restraint of non-human primates typically involves use of injectable agents, many of which can be associated with prolonged induction and recovery. Sevoflurane is a new inhalant anesthetic. It is currently being used in human and veterinary medicine for rapid inhalation induction and maintenance of anesthesia. The appeal of sevoflurane is its low blood-gas partition coefficient (0.69 at 37°C) (blood-gas solubility) that allows for rapid induction and recovery from anesthesia (4). Additionally, the low blood-gas solubility allows for more rapid control of anesthesia depth. Compared with the inhalant agents most commonly used in veterinary medicine (halothane, isoflurane), sevoflurane has been documented to be associated with the fastest and smoothest anesthesia induction in a variety of species (5–8). Sevoflurane is also less irritating to the respiratory tract, compared with other inhalant anesthetics (9, 10), and therefore, may allow easier inhalant induction. The purpose of the study reported here was to evaluate the cardiopulmonary effects of sevoflurane and the practicality of its use for inhalation induction and maintenance of anesthesia in *O. garnettii*.

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Materials and Methods

Ten healthy *O. garnettii* (six male and four female) were anesthetized for this study. Mean body weight was 1,022.5 (range, 800 to 1,345) g, and age ranged from 2 to 8 years. The animals were housed in a temperature-controlled environment (25 to 27°C) and were maintained on a 12/12-hour light/dark cycle. The animal care and use program of the University of Tennessee is accredited by AAALAC, International. This study was approved by the University of Tennessee Animal Care and Use Committee.

One week prior to study, all animals were sedated with ketamine hydrochloride (10 mg/kg of body weight) (Ketaset, Fort Dodge Animal Health, Fort Dodge, IA) given intramuscularly. Each animal was given a physical examination, and blood was drawn from the femoral vein for complete blood count (CBC) and serum biochemical analysis.

Food was withheld from the animals for 12 hours prior to the start of the study. Each animal was removed from its cage and manually restrained for mask induction, using heavy leather gloves. A face mask attached to a non-rebreathing circuit was placed around the nose and mouth, and the animal was allowed to breathe O_2 at a flow rate of 2 L/min. Pre-oxygenation times varied, but were < 1 minute. Anesthesia was then induced with sevoflurane (Ultane, Abbott Laboratories, North Chicago, IL) at a concentration of 8% delivered through an agent-specific vaporizer (North American Drager, Medizintechnik GmbH, Lubeck, Germany) in O_2 at a flow rate of 2 L/min. A 20-gauge, 2-in. over-the-needle intravenous catheter (Angiocath, Becton Dickinson Vascular Access, Sandy, UT) was placed in the mask to determine sevoflurane concentration within the mask during induction. The time from the start of sevoflurane administration to recumbency was recorded as induction time. Recumbency was defined as the time at which restraint of the animal was not necessary and voluntary movement was absent. After induction, animals were intu-

bated, using a cuffed 3.0-mm (O.D.) endotracheal tube. The time from start of sevoflurane administration to intubation was recorded as the intubation time. Intubation time was considered time zero for recording of cardiopulmonary parameters.

After intubation, animals were positioned in dorsal recumbency on a circulating hot water pad (T/Pump, Gaymar Industries Inc., Orchard Park, NY). A lead-II ECG, rectal pulse oximetry probe, and esophageal temperature (T) probe were connected to a multi-function monitor (SDI Vet/Ox Plus 4700, Heska, Ft. Collins, CO). A 22-gauge, 8-in. catheter was placed inside of the endotracheal tube prior to intubation and positioned at the distal end of the tube for continuous sampling of end-tidal CO_2 concentration ($ETCO_2$), end-tidal sevoflurane concentration (ET_{sevo}), and respiratory rate (RR). The aforementioned parameters were continuously monitored by use of a multi-function monitor (Datex Capnomac Ultima, Datex Instrumentation Corporation, Helsinki, Finland). Vaporizer settings were maintained at an ET_{sevo} concentration of 2.5%. Systolic (SAP), mean (MAP), and diastolic (DAP) indirect blood pressures were monitored by use of a cuff placed over the brachial artery (Dinamap veterinary blood pressure monitor model 8300, Critikon Inc., Tampa, FL). The width of the cuff was approximately 40% of the limb circumference.

Measurements of heart rate (HR), RR, $ETCO_2$, relative arterial blood oxygen saturation (SpO_2), T, and ET_{sevo} were recorded at 1, 2, 3, 4, and 5 minutes and every 5 minutes thereafter for 30 minutes. The SAP, MAP, and DAP values were recorded at 4 and 5 minutes and every 5 minutes thereafter for 30 minutes. Samples for analysis of blood gas tensions were collected at 10 and 30 minutes from the femoral and/or ventral tail artery. Arterial blood gas samples were collected anaerobically into heparinized syringes and were stored on ice until analyzed. These samples were analyzed within one hour of collection. A second CBC and serum biochemical analysis were performed at 30 minutes for comparison with values in pre-study samples. At the end of 30 minutes, the vaporizer was turned off and the animals were allowed to recover by breathing 100% oxygen via face mask at a flow rate of 2 L/min.

Animals were positioned in lateral recumbency at discontinuation of anesthesia. The time from discontinuation of sevoflurane to extubation, and the time of the first noticeable movement was recorded. The criteria for extubation were based on the animals regaining their laryngeal reflex or exhibiting voluntary movement. After extubation, animals were given 100% oxygen via face mask until being returned to their recovery cages.

Statistical analysis was determined by use of ANOVA. Results are reported as mean ± SEM. Each time point was compared to determine whether there was significant difference between the initial reading and each additional reading. A comparison of differences between sexes also was investigated. Results were considered significant at $P \leq 0.05$.

Results

All animals were healthy on the basis of results of CBC, serum biochemical analysis, and physical examination. Use of 8% sevoflurane resulted in rapid and smooth anesthesia induction within 75 ± 8.7 (range, 45 to 125) seconds. Sevoflurane gas concentration within the face mask at induction was 7.5 ± 0.2 (range, 6.1 to 8.6) % (N = 9). Time to intubation was 179 ± 25.1 (range, 105 to 315) seconds.

Heart rate under sevoflurane anesthesia was significantly increased at two and three minutes, compared with the one-minute reading. The HR then began to decrease at four minutes. At 25 and 30 minutes, HR was significantly decreased, compared with the initial 1-minute reading (Figure 1). However, HR stayed within clinically acceptable limits during the entire procedure; RR (Figure 1) and SpO_2 and $ETCO_2$ (Figure 2) did not change significantly during the study. Values of SAP, MAP, and DAP decreased at 5 minutes; however, this change was not significant (N = 8) (Figure 3). The 30-minute P_aO_2 value (431 ± 48.8 mm Hg) was significantly increased over the initial P_aO_2 value (326 ± 50.7 mm Hg) at 10 minutes. There was also a significant increase in pH between the 10 (7.38 ± 0.03)- and 30 (7.45 ± 0.02)-minute samples. The P_aCO_2 values remained steady between the 10 (36 ± 2.3 mm Hg)- and 30 (33 ± 2.2 mm Hg)- minute samples.

There was a significant decrease in T at 10, 15, 20, 25, and 30 minutes of anesthesia, compared with the 3-, 4-, and 5-minute readings. Readings for T were not available for the 1- and 2-minute examinations. Starting temperature was 36.4 ± 0.3°C at 3 minutes, and decreased to 35.7 ± 0.3°C by 30 minutes of anesthesia.

There was no significant difference between pre- and postsevoflurane packed cell volume (PCV), hemoglobin (Hb), and phosphorus (PO_4) values. However, the PCV and Hb values were significantly lower in females, compared with males, regardless of sample collection time. The PCV for males and females was 51.3 ± 1.5 and 44.1 ± 1.5%, respectively. The Hb values were 17.8 ± 0.51 g/dl for males and 15.3 ± 0.54 g/dl for females. The plasma total protein (TP), calcium (Ca) and white blood cell (WBC) values decreased significantly in the poststudy samples. The WBC count prior to the study was 10.5 ± 0.9 x 10^3 cells/μl, and had decreased to 6.4 ± 1.0 x 10^3 cells/μl at the end of the study. The TP value decreased from 7.9 ± 0.1 g/dl to 6.9 ± 0.1 g/dl, and Ca concentration decreased from 11.7 ± 0.4 mg/dl to 10.3 ± 0.4 mg/dl.

Muscular relaxation was considered excellent throughout the anesthetic event. Recovery was rapid, with extubation at 23.9 ± 5.82 (range, 0 to 50) seconds and initial movement noted at 25.5 ± 8.2 (range, 0 to 70) seconds.

Discussion

In our study, use of sevoflurane in *O. garnettii* resulted in fast and smooth anesthesia induction. There was mild resistance to initial placement of the face mask; however, increase in strug-

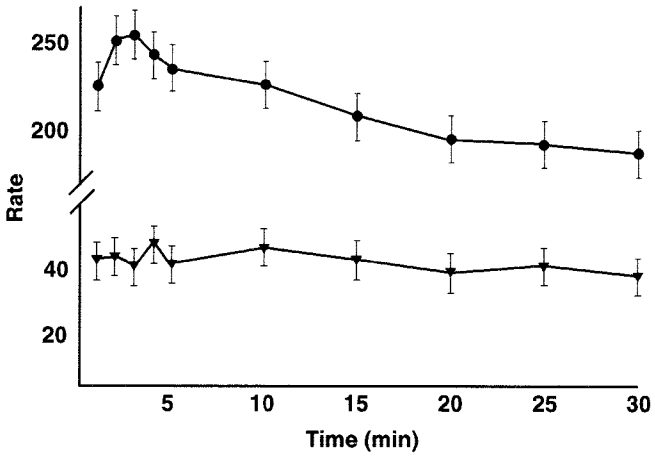

Figure 1. Heart rate (beats/min; filled circles ●) and respiratory rate (breaths/min; down arrows ▼) during 30 minutes of sevoflurane anesthesia in *Otolemur garnettii*. Values are reported as mean ± SEM.

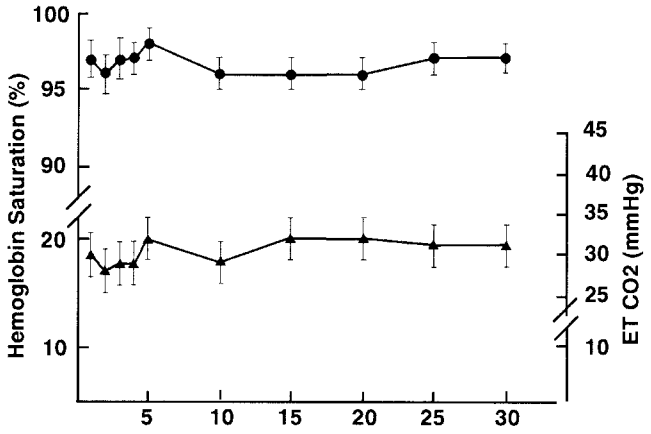

Figure 2. Relative arterial blood oxygen concentration (SpO_2) (filled circles ●) and end tidal carbon dioxide concentration ($ETCO_2$) (up arrow ▲) concentrations during 30 minutes of sevoflurane anesthesia in *O. garnettii*.

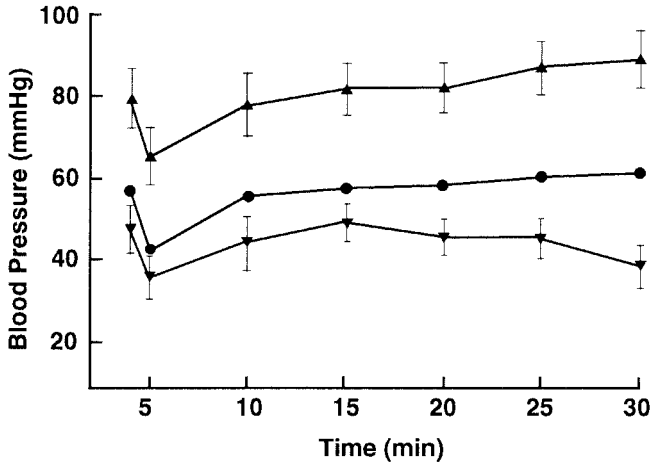

Figure 3. Systolic arterial pressure (up arrow ▲), mean arterial pressure (filled circle ●), and diastolic arterial pressure (down arrow ▼) during 30 minutes of sevoflurane anesthesia in *O. garnettii*.

gling was not evident at initiation of sevoflurane gas delivery. The initial struggle was likely due to the physical placement of the mask onto the animal's face. The lack of struggling at initiation of the anesthetic gas was likely due to the rapid induction experienced with this agent and the fact that there is little to no pungency associated with sevoflurane. Sevoflurane has been observed to be less irritating to the respiratory tract, compared with other inhalation agents (isoflurane) in humans (9, 10). In a study of children in which anesthesia was rapidly induced with either sevoflurane (8%) or halothane (5%) (another minimally irritating inhalant), sevoflurane caused less struggling and was preferred by the child's parents (11). Sevoflurane use in other species supports our findings of rapid, smooth induction (5–8).

Minimum alveolar concentration (MAC) determinations for *O. garnettii* have not yet been determined. We maintained ET_{sevo} concentrations at 2.5%. Sevoflurane MAC values in other species are as follows: dog, 2.36% (12); human, 2.07% (13); and pig, 2.66% (14). On the basis of the MAC values for sevoflurane in other species, anesthesia was thought to be maintained near 1 MAC in this study. Anesthesia depth was sufficient for intubation in all animals, and they remained unresponsive to manipulations, such as venipuncture and arterial puncture, and muscular relaxation was excellent during the entire 30 minutes of anesthesia. Anesthesia at 1 MAC is, however, generally not sufficient for major surgical procedures.

In this study, there was an initial increase in HR during the first 3 minutes, followed by a decrease over the remaining 30 minutes. The initial increase in HR may have been due to the anesthesia depth becoming light after the face mask was removed for intubation. Mean time for intubation of animals was 104 seconds. This may represent sufficient time for the animals to awaken and cause the associated increase in HR. We are unable to determine whether this was the cause because there was no clinical change in depth of anesthesia during intubation. It is also possible that the increase in HR was due to a reflex response to decreased blood pressure during induction. In studies involving other species, HR has been found to remain unchanged or decrease slightly as sevoflurane concentration increased (14, 15). This is similar to the finding reported here after the initial three minutes of anesthesia. Others studies have reported increased HR during sevoflurane anesthesia (5, 16, 17). The HR experienced during this study remained within clinically acceptable limits.

The SAP, MAP, and DAP decreased at the five-minute time point. This decrease, however, was not significant. Arterial pressures were low (Figure 3) throughout the study, but remained stable. This may be due to the insensitivity of using non-invasive cuff measurements for determining arterial blood pressure; however, dose-dependent decreases in arterial pressures in other species under sevoflurane anesthesia have been reported (16–18). The low arterial pressures experienced by animals during this study also may have been due to the high concentration of sevoflurane used at induction. Due to this possibility, a lower concentration of sevoflurane for induction should be considered if decreased blood pressure is a concern.

Respiratory rate remained stable during the entire 30 minutes of anesthesia. Studies involving other species, however, have indicated dose-dependent decreases in RR associated with sevoflurane (16, 19). Blood gas analysis indicated significant increase in the P_aO_2 value from the 10- to the 30-minute sample. This was the result of breathing 100% O_2 during the anesthesia period. In addition, the P_aCO_2 values remained steady between the 10- and 30-minute samples and corresponded to $ETCO_2$ values that remained steady and within clinically acceptable values. These findings support the lack of respiratory depression experienced by the animals of this study, whereas other studies have indicated respiratory depression associated with sevoflurane as similar to that induced by isoflurane (15, 17). A dose-response analysis of respiratory depression was not preformed in this study, but would be needed to confirm the degree of respiratory depression associated with this agent in this species.

The SpO_2 values remained steady and within clinically acceptable limits (> 95%) during anesthesia. These findings corresponded to the P_aO_2 values reported for blood gas analysis.

There was a significant decrease in body temperature during the 30 minutes of anesthesia despite the use of a recirculating water blanket. The body surface area-to-mass ratio of these animals most likely contributed substantially to the decrease in body temperature experienced during anesthesia. The decrease in body temperature, however, did not seem to impact recovery times in these animals.

The CBC and serum biochemical data were compared with published values for *O. garnetti* (20). Pre- and postanesthesia results also were compared. We found a statistically significant difference between PCV and Hb values for males and females. These findings are similar to those reported by Izard et al. (20) for this species. There was also a significant decrease in Ca, TP, and WBC values after sevoflurane anesthesia. The values remained within clinically acceptable limits. There have been reports of similar findings of decreased WBC count and TP values in *Macaca mulatta* given ketamine hydrochloride (21). This has been associated with reversal of the stress response in *Macaca mulatta* brought about by capture and relieved by anesthesia (22). This may have contributed to the results reported here; however, the response we noticed in *O. garnettii* may be associated with other mechanisms. It is also possible that the differences noted in Ca, TP, and WBC values are coincidental findings unrelated to anesthesia. Further investigation is required to determine the cause of the changes in the CBC and serum biochemical data reported in our study.

There has been no systemic toxicity associated with the clinical use of sevoflurane in human or veterinary patients (23, 24). Evaluation of serum biochemical data after anesthesia did not reveal any substantial changes in hepatic or renal parameters. A study of human patients indicated no additional risk of increased hepatic and renal values after repeated exposure to sevoflurane (25). However, a study in cynomolgus macaques repeatedly exposed to sevoflurane revealed a dose-dependent transient increase in liver enzyme activities after anesthetic exposure (26). Histologic changes, however, were not apparent in these macaques (26). The results obtained in our study do not support changes in serum biochemical analytes, or toxicity associated with use of sevoflurane anesthesia.

Recovery was rapid, and most animals were extubated in less than a minute, with presence of voluntary movement at or near the same time. The extremely rapid recovery might have been due to the animals only being anesthetized for a little over 30 minutes and anesthesia being maintained at a light plane. Other studies support the rapid and smooth recoveries experienced here with sevoflurane, compared with other inhalant anesthetics (24, 27, 28). Recovery may be prolonged in obese animals due to sevofluranes high lipid solubility. The animals used in this study were lean and were anesthetized for only 30 minutes; therefore, this probably did not have an effect on recovery time for this study. Consideration should be given to the importance of intra- and postoperative analgesics when using inhalant anesthetics alone during painful procedures.

Isoflurane is the inhalant anesthetic most commonly used in veterinary medicine for traditional and exotic animal patients. Sevoflurane's cardiopulmonary effects are similar to those of isoflurane in other species (dog, cat, pig, human) (14–16, 29). However, sevoflurane's inductions appear to be faster and smoother than those of isoflurane (5–7). Deleterious cardiopulmonary or anesthetic effects were not found in *O. garnettii* during this study. Heart rate and RR remained stable, and arterial pressures although low also remained steady during the 30 minutes of anesthesia. Due to *O. garnettii*'s small size, they are relatively easily hand caught and anesthesia can be quickly induced by use of gas anesthesics. In addition, on the basis of results from other studies, sevoflurane is thought to provide less airway irritation during inhalation, compared with isoflurane (9, 10). We found sevoflurane to be a safe and effective agent to induce and maintain anesthesia in this species.

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