

Comparison of Sevoflurane and Isoflurane in Domestic Ferrets (*Mustela putorius furo*)

A. K. Lawson, DVM^a

M. Lichtenberger, DVM, DACVECC^b

T. Day, DVM, MS, DACVA, DACVECC^c

J. Ko, DVM, MS, DACVA^d

R. Kirby, DVM, DACVIM, DACVECC^e

^a*Puget Sound Veterinary Referral Center
5608 South Durango
Tacoma, WA 98409*

^b*11015 North Mequon Square Drive
Mequon, WI 53092*

^c*Louisville Veterinary Specialty and Emergency Services
12905 Shelbyville Road, Suite 3
Louisville, KY 40243*

^d*Department of Veterinary Clinical Sciences
Veterinary Teaching Hospital
School of Veterinary Medicine
Purdue University
West Lafayette, IN 47907*

^e*Animal Emergency Center
2100 Silver Spring Drive
Glendale, WI 53223*

CLINICAL RELEVANCE

Isoflurane anesthesia is commonly used in ferrets for routine examinations and diagnostics. Sevoflurane is now being used as well, but there have been no studies to date directly comparing these agents in domestic ferrets. A prospective study was designed to evaluate the quality and speed of anesthetic induction and recovery using isoflurane and sevoflurane in ferrets. In addition, effects on heart rate, blood pressure, and packed cell volume were also recorded. No significant differences were noted between anesthetic agents.

■ INTRODUCTION

Isoflurane is a primary component in most anesthetic regimens for ferrets. Being a vapor anesthetic, it can be delivered via facemask or endotracheal tube rather than injection. Controlling the depth of anesthesia is easier with a vapor anesthetic than an injectable agent. Isoflurane is the most popular vapor anesthetic because of its safety and rapid induction and recovery. Recently, sevoflurane has become available. Sevoflurane is less soluble in the

blood than is isoflurane, leading to a more rapid equilibration within the blood and central nervous system and resulting in a more rapid induction and, theoretically, a more rapid recovery.¹ Because of the quick onset and recovery with sevoflurane, the excitement phase should be shorter, which entails less risk to both the handler and the ferret. Sevoflurane anesthesia has been shown to have a more rapid induction than isoflurane in some animals, including polecats.²

Isoflurane and sevoflurane appear to have many of the same dose-dependent cardiovascular effects, such as decreased heart rate and blood pressure.³⁻⁵ A recent study on hemodynamic parameters in ferrets under sevoflurane anesthesia showed minimal cardiovascular effects.⁶

Critically ill ferrets may require blood transfusions to alleviate anemia. Ill ferrets may have decreased erythrocyte production with estrogen toxicity as well as chronic disease, and blood loss can occur secondary to gastrointestinal ulcers, parasites, and tumors. Most blood collections are done with the donor under isoflurane anesthesia because of the fractious

included in the study. The age range was 1 to 4 years (mean age, 2.7 years), and the weight range was 625 to 1,260 g (mean weight, 881 g). Before the study, health status was evaluated on the basis of physical examinations (including body weight, pulse, rectal temperature, and respirations) and electrocardiography (ECG). ECG was performed on each ferret before and during anesthesia. PCV and total protein values were recorded for each ferret at the beginning of each study period before anesthesia was administered. The ferrets were housed individually in stainless-steel cages; they were fed commercial cat food and had ad libitum

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nature of ferrets. However, isoflurane anesthesia in ferrets has been associated with a significant drop in packed cell volume (PCV), likely due to sequestration in the spleen,^{7,8} which is an important consideration when blood transfusions are required in this species. An anesthetic with similar safety margins that does not cause a drop in PCV would be beneficial.

The purpose of this study was to compare the time and quality of induction and recovery when using sevoflurane versus isoflurane anesthesia in ferrets. The effects of each anesthetic agent on heart rate, blood pressure, and PCV were also compared.

■ MATERIALS AND METHODS

Animals

All animals were privately owned, and informed consent was given by the owners. Eight adult ferrets (four males and four females) were

access to water (food was withheld for at least 3 hours before anesthesia). Each ferret was provided with a litter pan and a blanket. Ferrets were not medicated before anesthesia.

Study Design

The research design was a random, cross-over study in which each ferret was anesthetized with each vapor anesthetic in two separate study periods. Four ferrets received isoflurane in the first study period and sevoflurane in the second; the other four ferrets received sevoflurane in the first study period and isoflurane in the second. Consequently, each ferret was anesthetized with sevoflurane and isoflurane in study periods separated by 14 days.

Induction

Agent-specific, out-of-circuit vaporizers (Sevotec 3, Datex-Ohmeda, Madison, WI) were used

Stages of Anesthesia

Stage I—Excitement phase marked by struggling, increased heart and respiratory rate, and dilated pupils.

Stage II—Loss of consciousness; ventilation is irregular and involuntary excitement may occur.

Stage III—Surgical anesthesia:

- **Plane One**—Still responsive to painful stimuli; palpebral reflex is present, and the eyeball is centrally positioned.
- **Plane Two**—Laryngeal reflexes are lost, and the eyeball rotates down; palpebral and pedal reflexes are lost; no response to painful stimuli.
- **Plane Three**—Drop in heart rate, blood pressure, and respiratory rate; the eyeball is centrally positioned with no palpebral reflex.

Stage IV (overdose)—Paralysis of the intercostal respiratory muscles occurs; pulse becomes weaker; pupils start to dilate and the cornea looks very dry. If these warning signs go unheeded, complete paralysis of the medulla of the brain and cardiopulmonary collapse occur.

Subjective Induction and Recovery Quality Scores

One—No struggling, ataxia, or excitement

Two—Minimal struggling

Three—Extended or more persistent struggling and excitement

Four—Violent struggling requiring physical restraint to prevent injury to ferrets or their handlers

anesthesia was established, the vaporizer was reduced to a setting to maintain stage III, plane 2 anesthesia (between 1 and 1.5 MAC). MAC was defined as 1.52% for isoflurane and 2.58% for sevoflurane. Each ferret was given a subjective score on ease of induction (see Subjective Induction and Recovery Quality Scores, above).

Maintenance

After anesthesia was induced, the ferrets were placed in right lateral recumbency and two ECG measurements were taken, one using a handheld device placed on the chest of each ferret and the other using a standard ECG setup with three clip attachments. Blood pressure was measured using an ultrasonic Doppler crystal (Ultrasonic Doppler Flow Detection Model III, Park's Medical Electronics, Aloha, OR) with a #1 blood pressure cuff (Classi-cuf, Criticare, Waukesha, WI) placed proximal to the crystal on the left rear foot. Heart rate and respiratory rate were recorded. Blood was drawn for determination of PCV and total protein between 12 and 15 minutes after induction.

Recovery

At a time between 15 and 17 minutes after induction, when the ferrets were judged to be stable at stage III, plane 2 anesthesia, the vaporizer was turned off and the ferret was disconnected from the circuit. The time needed

for each of the anesthetic agents. Anesthesia was induced rapidly with $2.5 \times$ minimum alveolar concentration (MAC) (3.8% isoflurane [Aerrane, Baxter Healthcare, Deerfield, IL] or 6.5% sevoflurane [Sevoflo, Abbott Laboratories, Abbott Park, IL]) delivered in 2 L/minute of oxygen through a non-rebreathing circuit and a tight-fitting mask.^{9,10} Once they reached stage II anesthesia (see Stages of Anesthesia, above), the ferrets were intubated with a noncuffed 2-mm endotracheal tube (Sheridan, Hudson RCI, Research Triangle Park, NC). This time to induction was recorded for each ferret. Once a specified plane of

TABLE 1. Comparisons of Isoflurane and Sevoflurane

<i>Variable</i>	<i>Isoflurane</i>	<i>Sevoflurane</i>	<i>P Value</i>
Induction time (min)	3.8 ± 2.5	2.7 ± 1.2	.15
Induction quality	2 ± 0.8	1.9 ± 0.6	.36
Recovery time (min)	5.7 ± 1.6	6.4 ± 2.8	.26
Recovery quality	1.9 ± 0.8	1.5 ± 0.8	.18
Decrease in PCV (%)	38 ± 9	43 ± 12	.12
Systolic blood pressure (mm Hg)	103 ± 52	94 ± 31	.33
Percent change in heart rate	7.8%	1.2%	.26

to achieve righting reflex was recorded, and the ease of recovery was measured subjectively using the same scale used for induction. Blood was obtained from the ferrets at 1 and 2 hours after anesthesia.

The same investigator recorded the times and assigned the subjective quality scores for induction and recovery for all ferrets. This investigator also monitored and maintained the depth of anesthesia.

Statistical Analysis

Single-tailed Student's *t*-test was used to compare sets of variables in each case. For each case, *P* values < .05 were considered statistically significant.

RESULTS

Ferrets in this project were used as their own controls, so there were no prestudy comparisons to be made. Induction and recovery values summarized in Table 1 are a combination of data from both study periods. Significant differences in recovery and induction time and quality with sevoflurane versus isoflurane were not noted. No significant differences were seen in blood pressure or heart rate while ferrets were under anesthesia with the two agents. ECGs showed no arrhythmias in either group.

Both anesthetic agents caused a significant decrease in PCV: Isoflurane decreased PCV

from an average of 59% to an average of 37%, a change of 38% (*P* < .05), and sevoflurane caused a 46% decrease in PCV, from an average of 57% to an average of 31% (*P* < .05). There was no significant difference in the amount of the decrease between isoflurane and sevoflurane. Regardless of agent used, PCV returned to normal levels by 2 hours after anesthesia.

DISCUSSION

Our study revealed that sevoflurane and isoflurane, when administered to ferrets with no premedication, have similar induction and recovery times and similar anesthetic qualities. Blood pressure, heart rate, and the decrease in PCV under anesthesia were not statistically different. These results suggest that sevoflurane is a safe and effective anesthetic for mask induction in adult ferrets, comparable to isoflurane. It has been reported that sevoflurane has a lower pungency and is less irritating to the airway than isoflurane.¹¹ This should make induction quality easier with sevoflurane, although this was not seen in our study. Recovery and induction quality are likely also related to the speed of induction and recovery, minimizing the time in phase 2 (excitement phase) of anesthesia.

The speed of induction of and recovery from gas anesthetic are determined by the blood:gas solubility of the anesthetic. Other factors include inspired anesthetic concentration, oxygen

flow rate, alveolar ventilation, and cardiac output. Gas anesthetics with lower solubilities equilibrate more quickly, causing a more rapid onset and recovery. In comparing these two anesthetics, an attempt was made to use the same relative dose of anesthesia. To do this, we used settings of anesthesia corresponding to multiples of the MAC. Because the MAC is a measurement of an anesthetic's potency, using the same multiples of MAC allowed the ferrets to be exposed to equipotent doses of anesthetic.

MAC is a calculated value, defined as the concentration of anesthetic required to prevent purposeful movement to a painful stimuli in 50% of those exposed.¹² The isoflurane MAC in ferrets has been determined, but no study

sevoflurane as compared with isoflurane. In one study using dogs in which there was no significant difference in recovery times, the authors suggested that this finding may be related to isoflurane not equilibrating within the study period.³ This would leave less isoflurane in the tissue and lead to a more rapid recovery than if the isoflurane had equilibrated. This hypothesis may be true because isoflurane does have a higher solubility. Maintenance anesthesia periods for these studies ranged from 15 to 30 minutes. Ferrets in our study ventilated on their own, and individual differences in ventilation and cardiac output may have contributed to the wide variation seen in induction and recovery times.

Significant differences in recovery and induction time and quality with sevoflurane versus isoflurane were not noted.

has been conducted to determine the MAC for sevoflurane in ferrets.⁹ Given the similarity in MACs between ferrets and cats for other anesthetic gases, including isoflurane, the MAC for sevoflurane in ferrets was estimated to be the same as that calculated for sevoflurane in cats.

The blood:gas solubility is lower for sevoflurane than for isoflurane; therefore, quicker induction and recovery as well as more rapid changes in anesthetic depth are expected. Studies performed in other species have had differing results. More rapid induction times were seen in polecats, psittacines, and dogs,^{2,3,13,14} but none of these studies showed a statistically significant difference in recovery time; however, recovery appeared smoother with sevoflurane in the psittacine study.¹⁴ Studies in cats, rats, and horses show shortened recovery times, with no differences noted in induction times.^{10,15,16} No study showed both a shortened induction and a shortened recovery time with

Studies in polecats and goats showed a statistically significant difference in blood pressure between the two anesthetic agents, with those under sevoflurane having higher blood pressure.^{2,17} No significant difference in heart rate was observed in these studies. In our study, there was no statistically significant difference in either blood pressure or heart rate between sevoflurane and isoflurane.

Anesthesia is often used when collecting blood from ferrets. As stated previously, isoflurane has proven to be safe for use in ferrets^{2,18} but causes a significant drop in PCV.⁷ Isoflurane has also been shown to cause splenic sequestration of erythrocytes, likely leading to the drop in PCV.⁸ The significant drop in PCV prevents accurate knowledge of an anesthetized ferret's erythrocyte count and prevents the collection of adequate numbers of erythrocytes for transfusions. Sevoflurane appears to have the same effect on PCV in ferrets, likely by the

same mechanism, although this could not be proven from our study.

CONCLUSION

Isoflurane and sevoflurane provide similar safety, cardiopulmonary, and hematologic effects in ferrets. This study shows no significant differences in ferrets that would make the use of sevoflurane more advantageous than isoflurane with regards to induction and recovery, cardiopulmonary effects, or maintenance of PCV.

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