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RESEARCH PAPER

Comparison of two anesthetic protocols for feline blood donation

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Abstract

Objective To compare hemodynamic variables during, and recovery quality following, anesthesia for feline blood donation using intramuscular ketamine–midazolam–butorphanol (KMB) *versus* inhaled sevoflurane in oxygen (SEV).

Study design Prospective blinded, randomized, crossover study.

Animals Twenty healthy, client-owned, mixed breed cats, aged 4–8 years, weighing 5.2–6.4 kg.

Methods Cats were anesthetized with KMB for one donation and SEV for another. Heart rate (HR), respiratory rate (f_R), pulse quality, mucous membrane color, capillary refill time, arterial hemoglobin saturation with oxygen (SpO_2), and noninvasive arterial blood pressure (Doppler) were assessed by a blinded observer every 1 minute during collection. A nonblinded anesthesiologist delivered drugs and responded to hemodynamic changes. Each donation consisted of 55 mL of whole blood drawn via jugular puncture over 5–22 minutes. Donors received 60 mL subcutaneous lactated Ringer's solution before recovery. Donors were monitored for a minimum of 4 hours post-donation, before returning home. Owners, unaware of anesthetic protocol, completed a questionnaire regarding their cat's behavior during the 24 hours following donation.

Results Both protocols provided adequate restraint but were complicated by significant hypotension, requiring intervention in 16 (84%) SEV cats, and eight (42%) KMB cats. KMB cats experienced post-procedure hyperthermia, with body temperatures >103.5°F. All animals responded to symptomatic therapy within 2 hours. Owners noted a significantly faster return to normal behavior at home following SEV.

Conclusion All cats experienced hypotension, with many animals requiring intervention. There was no significant difference between protocols in incidence and severity of hypotension. The primary post-procedure complication was hyperthermia with KMB.

Clinical relevance As a result of the potential for hypotension during blood donation, intravenous (IV) access and blood pressure monitoring are recommended for all anesthetized donor cats, regardless of the anesthetic protocol. Post-procedure hyperthermia is a risk with KMB, so temperature monitoring is recommended. Return to normal behavior is faster with SEV.

Keywords feline, hyperthermia, hypotension, inhalation, injectable anesthesia.

Introduction

Blood products for transfusion, such as plasma and red cells, are necessary items for appropriate care of client-owned veterinary patients in referral and emergency hospitals. As a result of the agile nature of most cats, as well as the need to maintain sterility

and minimize vascular trauma to donor's veins, most donor programs routinely sedate and/or anesthetize cats for blood donation (Bucheler & Cotter 1992; Lucas et al. 2004; Troyer et al. 2005). Sedation may be a sufficient restraint method in some donor programs, but it requires skilled phlebotomists and easily-managed cats. In a program using client-owned donors, the trend has been to fully anesthetize donors in order to accommodate phlebotomists of less experience and cats that have in many cases become progressively resistant to handling (L Graham, personal observation, Troyer et al. 2005). Currently no published prospective studies exist evaluating the use of anesthetic agents for feline blood donation. Available information is most often authors' opinions in literature reviews (Henness 1989; Bucheler & Cotter 1992; Kaufman 1992; Lanevschi & Wardrop 2001; Lucas et al. 2004; Troyer et al. 2005).

Clinical blood donation involves a controlled loss of approximately 20% of the donor's blood volume over 5–10 minutes. Therefore, anesthetics, which result in minimal cardiovascular alterations, are desired. Feline blood donation may occur as frequently as once per month. As volunteer donors are often client-owned, personal satisfaction with the donor experience can be key to a successful donor program. Therefore, effective and safe methods of sedation and/or anesthesia are necessary, allowing for the rapid return to normal function. Commonly used, rapid acting, injectable agents, such as propofol, have been anecdotally associated with an unacceptably high incidence of morbidity and mortality in feline blood donors (ACVA list discussion) and relatively high expense (Troyer et al. 2005). Other commonly used sedatives, such as alpha-2 agonists, are associated with adverse cardiovascular side effects (Hall & Taylor 1994; Granholm et al. 2006) and difficult phlebotomy as a result of vasoconstriction (Troyer et al. 2005). Many of these effects would be commonly considered unacceptable in the face of the acute, volume associated, cardiovascular changes that occur during feline blood donation.

Ketamine-based protocols have been used for feline donor sedation or anesthesia (Henness 1989; Bucheler & Cotter 1992; Kaufman 1992; Lanevschi & Wardrop 2001; Lucas et al. 2004; Troyer et al. 2005). Dissociative anesthetics are widely recognized as providing predictable results with wide safety margins, while preserving airway reflexes and sympathomimetic effects, which support cardiovascular function (Child et al. 1972; Haskins et al. 1975; Fox et al. 1985; Hall & Taylor 1994). However, clinically, some cats suffer from prolonged recoveries (Lucas et al. 2004; Troyer et al. 2005) with altered and hallucinogenic behavior for days to weeks after anesthesia with ketamine (L Graham, personal observation) and repeated use over time may lead to donor cats becoming more difficult to handle (Troyer et al. 2005). As a result of the variability in response to injectable agents, attaining and maintaining a sufficient depth of anesthesia can be difficult. Inhaled anesthetic agents may be added after administering the IM dissociative mixture, in order to attain a sufficient depth of anesthesia.

However, use of these multiple drugs can extend the duration of the anesthetic period resulting in a frustrating anesthetic experience and leading to a prolonged recovery. Sevoflurane is approved for use in veterinary patients, and use of sevoflurane in cats has been well documented for the last two decades (Doi et al. 1988; Pypendop & Ilkiw 2004). Due to the unique solubility properties of sevoflurane, it is widely recognized to provide rapid, pleasant anesthetic inductions (Hikasa et al. 1996; Johnson et al. 1998; Galloway et al. 2004). Mask induction of a cat is faster with sevoflurane than with isoflurane (Lerche et al. 2002). In addition, clinical use of sevoflurane, administered in oxygen, allows for a rapid (5–10 minutes) return to normal function for cats (Hikasa et al. 1996; Lerche et al. 2002). Sevoflurane causes less respiratory depression than isoflurane (Galloway et al. 2004). Sevoflurane can cause dose-dependent myocardial depression, but the ability to change concentrations rapidly allows one to minimize this effect with appropriate blood pressure monitoring (Pypendop & Ilkiw 2004).

Our hypothesis was that inhalant anesthesia with sevoflurane in oxygen would provide adequate anesthetic depth for blood donation, with donor blood pressures not significantly lower than in those anesthetized with an injectable protocol of ketamine–midazolam–butorphanol. We also hypothesized that the cats would return to normal behavior faster with the sevoflurane protocol and that their owners would be more likely to continue to volunteer their cats for the donor program, based on the recovery they experienced with the sevoflurane protocol.

Materials and methods

This project was approved by the University Animal Care and Use Committee (IACUC) as a separate project and as an addition to the IACUC approval for

the University Volunteer Blood Donor Program. Informed, written owner consent was obtained before enrolling in this clinical study. Twenty healthy, client-owned, mixed breed cats, aged 4–8 years and weighing 5.2–6.4 kg were enrolled in the study. Preceding initial enrollment in the University volunteer blood donor program, each cat received a thorough physical examination, and a complete blood count/differential and full serum chemistry panel (blood urea nitrogen, creatinine, potassium, sodium, magnesium, chloride, phosphorus, alanine transferase, ALP, AST, bilirubin,) were performed. In addition, potential donors were screened for blood-borne pathogens per the ACVIM guidelines (Wardrop et al. 2005) and blood typing was performed. Prior to each donation, packed cell volume (PCV) and total plasma protein (TPP) were measured and a basic physical examination was repeated, including measuring body weight. A temporary, over-the-needle, 2.5 cm, 22-gauge catheter was aseptically placed in the right cephalic vein of each cat prior to each donation.

Each client-owned cat was anesthetized for two blood donations, once under an injectable protocol and once under an inhalant protocol. The order of anesthetic protocol was randomized by a coin flip. A minimum of 6 weeks (range 6.6–14.9 weeks) occurred between donations. The injectable anesthetic protocol (KMB) used an intramuscular injection of ketamine hydrochloride 5 mg kg^{-1} (KetaSet; IVX Animal Health, MO, USA), butorphanol tartrate 0.3 mg kg^{-1} (Torbugesic; Fort Dodge Animal Health, IA, USA), and midazolam 0.2 mg kg^{-1} (Midazolam; Hospira, IL, USA). Injections were administered into the epaxial muscles. The inhalant anesthesia protocol (SEV) consisted of induction and maintenance of anesthesia with sevoflurane (SevoFlo; Abbott Laboratories, IL, USA) in 2 L $minute^{-1}$ oxygen, delivered via a face mask and a Bain nonrebreathing circuit or, initially, a chamber induction if deemed necessary because of the temperament of the individual cat. Vaporizers were calibrated at the beginning of the study. Each cat received oxygen by face mask, delivered via an anesthesia machine and Bain nonrebreathing circuit, during every blood donation in order to minimize any risk of hypoxemia. All drugs were administered and supervised by a board certified veterinary anesthesiologist (L Graham) who was not blinded to the treatment used, allowing rapid response in the event of an emergency or unexpected complication. This nonblinded investigator also assessed anesthetic induction quality for each cat and graded it on a scale from 1–5 (Appendix 1).

During the SEV protocol, this nonblinded investigator adjusted the vaporizer setting, as deemed necessary to maintain an acceptable plane of anesthesia (as determined by withdrawal reflex, mucous membrane color and capillary refill time recorded by this investigator). In addition, pulse rate (PR), electrocardiogram (ECG), respiratory rate (f_R), noninvasive (Doppler) systolic arterial blood pressure (SAP) (plantar artery, with a size #2 cuff, with measured width approximately 40% of limb circumference, placed above the hock) and arterial hemoglobin saturation (SpO_2) (plantar digit on the contralateral pelvic limb) (Matthews et al. 2003) were being assessed by a separate, blinded investigator (M Killos) and dictated, as necessary, to the nonblinded investigator, allowing appropriate adjustments to the inhalant vaporizer setting (and further treatment of hypotension, as described later). During the KMB protocol, the nonblinded investigator was prepared to re-dose the injectable anesthetic agents once IM at one-half of the original doses, in the event that an insufficient level of anesthesia was achieved or maintained.

The blinded investigator (M Killos) entered the room after each cat was anesthetized, instrumented with noninvasive monitors, and draped off so as to maintain blinded status to the anesthetic being used. This investigator was responsible for assessing and recording PR, f_R, SAP, and SpO_2 once every minute during blood donation and every 2–5 minutes from the end of the blood draw until the patient was sternal and aware. This investigator also graded the recovery of each cat on a scale from 1–5 (Appendix 2), in addition to recording the amount of time from the end of the draw to sternal recumbency.

A third, nonblinded assistant drew the blood for processing. The patients were prepared for donation by being placed in dorsal recumbency with their heads tipped back, thus exposing the jugular veins on the ventral neck. The hair over one vein was clipped, in a 3-cm square patch, and the skin was prepared aseptically with three alternating scrubs of betadine and isopropyl alcohol. While one investigator (LG) occluded the jugular vein at the level of the thoracic inlet, a 21-gauge butterfly needle (Terumo; Japan) was inserted through the aseptically prepared skin and into the vessel. This butterfly needle was attached to a three-way stopcock with a blood collection bag and a 60 mL syringe containing 5 mL EDTA on its two remaining ports.

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The stopcock was turned to open the path between the butterfly needle and the syringe, and blood was aspirated. Based on prior experience and a pilot study, 5 minutes was chosen as the minimum target time over which the blood would be drawn. Throughout the draw, the collection syringe was gently agitated to mix the EDTA and blood. At the end of the collection, the butterfly needle was removed from the jugular vein, the stopcock was turned to open the path between the syringe and the collection bag, and the blood was aseptically transferred into the collection bag. Post-donation processing included spinning the bag to separate packed red blood cells from plasma. The feline donor was given a clean neck bandage to provide gentle pressure over the jugular vein and prevent hematoma formation. Cats experiencing hypotension during the blood draw received small intravenous (IV) fluid boluses in an effort to restore circulating blood volume, and therefore blood pressure, while minimally diluting the donated unit of blood. If the SAP decreased below 70 mmHg, each cat received 6 mL per cat of IV lactated Ringer's solution (LRS). This dose was repeated once if necessary. If hypotension persisted or worsened, the cat received 6 mL per cat of IV hetastarch (HES; hetastarch 6% in 0.9% normal saline). This dose of hetastarch was repeated, if necessary. These low volumes of IV fluids were chosen based on pilot information (LG, personal communication), and the fact that frequent blood pressure assessment allowed for rapid continuation of resuscitation if needed. In addition, if receiving sevoflurane, the vaporizer setting was decreased if the nonblinded investigator assessed the donor's anesthetic depth as sufficient to allow for a decrease in vaporizer setting.

At the conclusion of each blood donation, the SEV administration was discontinued or the KMB protocol was reversed with the administration of naloxone 0.04 mg per cat IV (naloxone hydrochloride 0.04%, Hospira, IL, USA) and flumazenil 0.1 mg per cat IV (flumazenil 0.01%, Bedford Labs, OH, USA). These reversal agents were in use by the blood donor program, at these doses, prior to this study. This naloxone dose is lower than the 0.02 mg kg^{-1} recommended in the Dolorex (butorphanol tartrate) package insert for reversal of butorphanol; however, it falls in the published dose range for naloxone of 0.002–0.02 mg kg^{-1} (Tranquilli et al. 2007) and has been noted to be clinically effective in reversing butorphanol sedation at this dose (L Graham, personal observation). Each cat received 60 mL LRS subcutaneously. Mask oxygen was maintained until each cat would either no longer tolerate mask placement or had achieved sternal recumbency. Each cat was housed in the University Veterinary Intensive Care Unit (ICU) for 4 hours, or until the cat was deemed ready to return to the owner. During that time, the blinded investigator (M Killos) monitored heart rate (HR), respiratory rate, rectal temperature and assigned a subjective recovery score (Appendix 2). These parameters were collected at 0, 1, 2, and 4 hours after donation.

Normothermia was defined as a body temperature between 99 and 102.5°F (Reece 2004; Posner et al. 2007). Cats developing a rectal temperature ≥103.5°F (39.7 C) were treated for hyperthermia. Treatment included the removal of all barriers between the cat and the cool metal cage floor, acepromazine 0.01–0.02 mg kg^{-1}, IV, and when possible, isopropyl alcohol on the foot pads or ear pinnae. Owners were unaware of which anesthetic protocol had been used. Owners were given a brief questionnaire regarding the cat's behavior, at home, during the 24 hours following blood donation (Appendix 3). Owners were asked to assess behaviors, such as eating, attention-seeking, and aggressive interactions with other household pets or humans. The owners were also asked to record the number of hours until the cat's behavior was 'normal' based on their daily experience with their cat, and whether, based on this particular donation experience, the owner would be willing to have the cat donate again.

Statistical analysis

Physiologic parameters were measured after the cats were induced (initial values), and at the completion of the draw (final values). Then for comparisons over the duration of the blood draw, each parameter was averaged over the time points associated with the draw. Once the blood draw was complete, the parameters were considered to occur in the recovery period. In order to evaluate the severity of hypotension, the number of interventions was totaled for each cat during each draw, and those totals were compared between groups. Comparisons between treatment groups were made using *t* tests for numerical measures.

Results

Twenty cats were enrolled in this clinical study, and 19 cats completed the study. One cat experienced

increased heart rate (>240 beats minute^{-1}) and blood pressure (>250 mmHg) after anesthetic induction with KMB, while the cervical area was being palpated for the jugular vein. Extra pulses were audible on the Doppler, and on ECG, these appeared to be premature complexes that were unifocal and ventricular in origin. Based on these cardiovascular abnormalities, the blood draw was abandoned and the patient was recovered. The abnormalities resolved within 2–3 minutes, without therapy. On further examination, palpation of the cervical area again caused dramatic increases in heart rate and blood pressure. This cat was removed from the donor program, and referred for a full medical workup.

As a result of the crossover design of the study, with each cat serving as its own control, no difference was seen between groups for body weight, age, or pre-anesthetic physical examination results. The mean age was 4.4 years (range 4–8 years), and mean weight was 5.6 kg (range 5.2–6.4 kg). The mean duration of the blood draw was 8.6 minutes (range 5–22 minutes). The mean duration of anesthesia was 25 minutes (range 14–38 minutes), with the majority of the extra time devoted to instrumenting the cats. Most cats allowed intravenous catheter placement prior to anesthetic induction, but in five animals, induction was necessary first, as a result of aggression and agitation associated with restraint.

No significant difference in induction score was observed between the two protocols. The median score for both groups was 2, with a range of 1 to 5 (Table 1). Two cats (10.5%) required chamber inductions during the SEV protocol. Anesthesia in the remaining 17 cats (89.5%) was easily induced by wrapping each cat in a towel, providing gentle restraint and holding a snug-fitting mask to the face. Anesthesia in all SEV cats was induced with sevoflurane in 2 L minute^{-1} oxygen. The inhalant percentage was decreased to the lowest amount that still permitted an adequate anesthetic plane in the cats (as determined by withdrawal reflex), which required a mean sevoflurane vaporizer setting of 2.5% (range 1–4%) in all cases.

On the KMB protocol, two cats required re-dosing (intramuscular injection at one-half of the original doses; 2.5 mg kg^{-1} ketamine, 0.1 mg kg^{-1} midazolam, 0.15 mg kg^{-1} butorphanol) in order to achieve sufficient anesthetic depth that the cats could be instrumented and proceed with the blood donation. No cats required redosing during the blood draw in order to maintain sufficient anesthetic depth.

Table 1 Anesthetic induction and recovery scores

	Anesthetic protocol	
Score	**SEV**	**KMB**
Induction score	2 (1–5)	2 (1–5)
Recovery score		
Immediate	2 (1–5)	1 (1–2)
1 hour	2 (1–4)	3 (1–4)
2 hours	1 (1–4)	3 (1–5)
4 hours	1 (1–4)	2 (1–4)

All were graded on a 1–5 ordinal scale where 1 is the smoothest and 5 the roughest/most difficult to manage score. Reported as median score (range).

Anesthetic depth was judged, in part, by assessing the cat's withdrawal response to a toe pinch. The response was rated on a scale from 1–5 (1 = deep, 5 = awake), and on the SEV protocol, the vaporizer setting was adjusted to achieve a withdrawal of 2–3. Nearly all patients remained in this target range for the duration of the blood draw, and there were no statistically significant differences between groups.

Pulse oximetry was not possible in three patients, most likely due to pigmentation because all occurrences of difficulties in SpO_2 measurement occurred in cats with black toes. Toes have been shown to give the most accurate SpO_2 measurement, although pulse oximetry is not accurate in the cat (Matthews et al. 2003). In the remaining cats, SpO_2 remained within normal limits (≥95%) at all times for both protocols.

Heart rate remained within an acceptable range of 110–250 beats minute^{-1} (Moore & Cannon 1930) during anesthesia for all cats that completed the study. No significant differences were observed in heart rate between the two anesthesia protocols. All cats that completed the study maintained normal sinus rhythm throughout all donations.

Blood pressure decreased in all participants. The average SAP immediately after anesthetic induction was 117 mmHg in the SEV group and 106 mmHg in the KMB group. Over the course of the blood draws, the average SAP in the KMB group was 92 mmHg and in the SEV group 100 mmHg (Fig. 1). Sixteen SEV cats (84%) and eight KMB cats (42%) required intervention for SAP < 70 mmHg. Using the number of fluid therapy interventions (individual 6 mL

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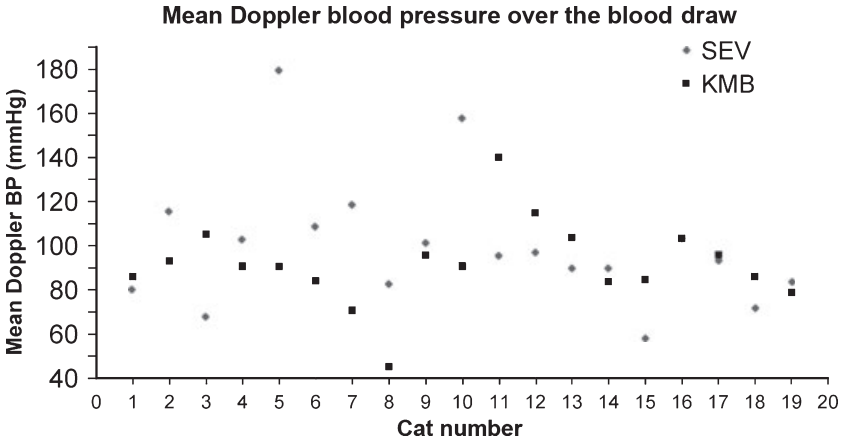

Figure 1 Mean Doppler systolic arterial blood pressures during blood removal.

boluses of LRS and/or HES) administered, as a method of measuring the severity of hypotension, no statistically significant differences were observed between the SEV and KMB protocols (Table 3).

One donor was hypotensive throughout donation with KMB, starting with an SAP of 48 mmHg, and responding only after 10 fluid boluses. In that cat, the SEV donation was without incident until the last minute when one bolus of LRS solution was required to return to normotension. Of the remaining 18 donors, hypotension tended to manifest during the third or fourth minute of donation. These patients were noted to have pale pink mucous membranes and slightly weaker pulses at approximately the same time that the SAP ≤ 70 mmHg.

Table 2 Owner survey results

	Anesthetic protocol	
Behavior	**SEV**	**KMB**
Appetite	3 (2–4)	3 (1–5)
Attention seeking from you	3 (3–4)	4 (1–5)
Attention seeking from others	3 (1–4)	3 (1–5)
Grooming	3 (3–5)	3 (1–4)
Aggressive with cats in household	3 (3–4)	3 (1–4)
Aggressive with other pets in household (not cats)	3 (1–3)	3 (1–3)
Aggressive with humans in household	3 (1–4)	3 (1–4)
Sleeping	3 (3–5)	3 (2–5)

Donor behavior during the 24 hours after donation, as reported by owners on an ordinal scale of 1–5 where 1 is much less than normal, 3 is the same as normal, and 5 is much more than normal. Reported as median (range).

Table 3 Fluid bolus interventions given due to Doppler BP < 70 mmHg – number of cats (*n*) and % of treatment group

	Treatment group			
	SEV		KMB	
Number of boluses	***n***	**%**	***n***	**%**
Zero	3	16	11	58
One	4	21	1	5
Two	4	21	3	16
Three	4	21	2	11
Four	2	11	1	5
Five	2	11	0	0
Six	0	0	0	0
Seven	0	0	0	0
Eight	0	0	0	0
Nine	0	0	0	0
Ten	0	0	1	5

The time from the end of the blood draw until sternal recumbency was shorter with SEV (mean ± SD, 9.1 ± 4.4 minutes) *versus* KMB (16.6 ± 13.3 minutes). Three cats experienced explosive emergence with the SEV protocol. In all three cases, the recovery was characterized by rapid emergence from anesthesia with profound agitation lasting 30 seconds or less. After these brief periods, all three cats returned to normal behavior without requiring further therapy. One of these cats fractured a canine tooth on recovery, requiring an

additional dental procedure the next day. The cat's anesthetic recovery from the dental procedure was unremarkable.

Recovery scores were measured at 0, 1, 2, and 4 hours after blood donation. The initial recovery scores were significantly higher with SEV (median 2) *versus* KMB (median 1). However, during the second hour, the SEV scores were significantly lower than the KMB scores (median 2 *versus* 3).

All cats had normal body temperatures (99–102.5°F) both before blood donation and at the conclusion of the blood draw. No significant difference was noted between the groups at these two time points. Six cats (31.6%) required treatment for hyperthermia during the first 2 hours after donation with the KMB protocol due to body temperatures above the predetermined maximum of 103.5°F (39.7 °C). The highest body temperature in this group was 108°F (42.2 °C). In each case, the cat appeared subjectively agitated, and demonstrated behavior, such as pacing in the kennel and crying. All of these cats received a dose of intravenous acepromazine at 0.01–0.02 mg kg^{-1}, plus removal of any blankets in their kennels and when possible, alcohol on the pinnae and foot pads. Two cats required a second dose of acepromazine when their hyperthermia and agitation were not resolving within 30 minutes. Hyperthermia resolved in these cats within 30–90 minutes of starting therapy, and did not recur in any cats. No cats experienced hyperthermia following the SEV protocol.

Owners reported that their pets returned to normal behavior faster with SEV (3.9 ± 4.3 hours) than with KMB (12.7 ± 16.9 hours). Owner reported behaviors, such as attention seeking, aggression, grooming, and sleeping, were the same with both protocols (Table 2). No significant differences were observed, between the KMB and SEV protocols, in the owners' willingness to have their cats return to the program.

Discussion

Hypotension was a significant clinical concern in many of the donor cats. In this study, hypotension was defined as an SAP ≤ 70 mmHg. The Doppler was chosen to measure blood pressure because of its usefulness over a wide range of blood pressures (Caulkett et al. 1998). Doppler measurement has, however, been shown to under-estimate systolic blood pressure when compared with direct central arterial blood pressure (Grandy et al. 1992; Caulkett et al. 1998; Pedersen et al. 2002). In one study, Doppler measurements were much more closely correlated with mean arterial pressures (Caulkett et al. 1998). In a different study, the values obtained with the Doppler were closer to the direct arterial systolic pressures (Binns et al. 1995). Thus, there is some controversy over the appropriate physiologic parameter to equate with Doppler blood pressure. In this study, 70 mmHg was the minimum tolerable arterial pressure, measured using the Doppler.

While all cats experienced some decrease in SAP during donation, 84% of SEV cats and 42% of KMB cats experienced hypotension. One of our primary concerns for cats on the SEV protocol was the combination of inhalant-induced cardiovascular depression and hemorrhage associated with blood donation. All of the modern inhalant anesthetics, including sevoflurane, caused a decrease in mean arterial pressure when administered to healthy volunteers (Souza et al. 2005). This effect is primarily because of myocardial depression in the cat (Pypendop & Ilkiw 2004). The effect was dose-dependent from 1.25 to 1.5 times MAC (Pypendop & Ilkiw 2004). In order to minimize this inhalant effect as much as possible, anesthesia was maintained at a light depth, with a moderate to strong pedal withdrawal reflex (2–3 on a scale of 1–5). Exacerbating the hypotensive effect of this negative inotropic effect is the acute volume loss experienced during blood donation. Feline blood volume is approximately 50–60 mL kg^{-1} body weight (Groom & Rowlands 1958; Hall & Taylor 1994). For our study population, the average weight was 6.0 kg, with an average calculated blood volume of 300–360 mL. Each cat donated 55 mL of blood, which is approximately 15–18% of their average blood volume. This volume was drawn over 5–22 minutes, with this range being due to the effective speed at which blood could be withdrawn. This acute blood loss during anesthesia was sufficient to cause the hypotension noted in this study.

The initially higher SEV recovery scores then decreased significantly below the KMB scores for the second hour of recovery. This may reflect the fact that cats recovered faster with SEV. The KMB protocol left them more sedate during the first hour, but they became more alert during the second and subsequent hours, and also much more difficult to manage.

As the donor cats were client-owned volunteers, the decision was made in advance to treat hyperthermia when it was noted, rather than allow the

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temperature effects to follow their natural course. For this reason, the incidence, but not the degree, of hyperthermia was measured in this study. Hyperthermia with temperatures greater than 103.5°F (39.7°C), and ranging up to 108.1°F (42.2°C) occurred in 40% of cats on the KMB protocol. Those cats experiencing hyperthermia appeared subjectively agitated, with increased pacing in their kennels compared with nonhyperthermic cats. No cats experienced post-procedure hyperthermia with the SEV protocol. There have been several recent publications exploring the possible causes of post-procedure hyperthermia in cats. Hydromorphone has been associated with increased body temperature (Niedfeldt & Robertson 2006; Posner et al. 2007) in the post-surgical period, as has morphine (Stewart & Rogoff 1922). These mu-agonist opioids have been shown to cause species-dependent changes in thermoregulation (Adams 2001). Their effect is thought to be mediated by mu receptors in the thermoregulatory center of the hypothalamus (Reece 2004). Butorphanol is a kappa opioid agonist and a mu antagonist (Stoelting & Hillier 2006). Its tendency to cause hyperthermia in cats has been mentioned in the literature (Posner et al. 2007) but not studied directly.

Ketamine is a dissociative anesthetic and an NMDA receptor antagonist, and has been associated with postoperative agitation, and increased muscle activity in cats (Wright 1982). It has not, however, been associated with increased incidence of hyperthermia when combined with a mu agonist opioid (Posner et al. 2007). Midazolam, a benzodiazepine tranquilizer, has been shown to cause restless behavior in cats at doses of 2 mg kg^{-1} IM when administered alone (Ilkiw et al. 1996a) and 0.5 mg kg^{-1} IV when administered in combination with 3 mg kg^{-1} ketamine (Ilkiw et al. 1996b). The body temperatures of the cats were not reported in either of these studies. Our cats were noted to appear agitated prior to registering increased body temperatures. Any of the aforementioned drugs may have contributed to this agitation and subsequent hyperthermia. However, all cats in this study had the butorphanol and midazolam reversed with naloxone and flumazenil, respectively. The reversal of these drugs makes their contribution to the hyperthermia less likely. There is, then, the question of whether the reversal agents may have contributed to the agitation and hyperthermia. Flumazenil has been studied extensively in the cat, with no reports of associated agitation (Ilkiw et al. 2002). Naloxone may occasionally cause excitement or anxiety after opioid reversal (Lamont & Mathews 2007). Its opioid antagonist effects last only 30–60 minutes, however, and there are no studies showing that the excitement is longer lasting. Thus, it would be possible but unlikely that naloxone was responsible for the agitation and hyperthermia noted here. Further study is warranted to better characterize the cause of the hyperthermia.

There were three cats that, after blood collection with the SEV protocol, experienced explosive recoveries. The recoveries were characterized by rapid awakening, violent thrashing, and leaping from the handler. These incidents lasted less than 30 seconds, after which the animals returned to normal behavior. Emergence agitation is a well-characterized phenomenon in human anesthesia, with screaming, crying, and the potential for self-injury. However, an underlying mechanism for this phenomenon has not been determined. Volatile anesthetics with low blood solubility have a higher incidence of emergence agitation, making rapid awakening a potential cause; however, propofol does not have the same association. A recent meta analysis looking at pediatric patients showed that patients anesthetized with sevoflurane had a significantly higher incidence of emergence agitation than those anesthetized with halothane (Kuratani & Oi 2008).

Both anesthetic protocols showed potential for severe hypotension during blood collection. Based on this information, feline blood donors should have blood pressure monitoring during collection, and intravenous fluids should be available for volume resuscitation. As the KMB protocol was associated with a risk of post-procedure hyperthermia and a more prolonged time until return of normal behavior, SEV is recommended as the preferred technique for anesthetizing cats for blood collection.

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Appendix 1

Induction score

1 = smooth, quiet

2 = mild difficulty managing

3 = required moderate restraint

4 = difficult but manageable with a towel

5 = very aggressive. Required induction box (if inhalant) or additional IM drugs (if injectable).

Appendix 2

Recovery score

1 = quiet, but rousable

2 = mild difficulty managing

3 = growling, two people for temperature, restrained with difficulty

4 = extremely difficult to restrain, two or more people required for temperature

5 = aggressive, lungeing at cage door, unable to take temperature.

Appendix 3

Owner survey

How would you describe the following behaviors in your pet during the first 24 hours after hospitalization for blood donation?

Scale from 1–5 where 1 = much less than usual, 3 = same as usual, 5 = much more than usual

Some questions also have an N/A option (not applicable)

Appetite	1	2	3	4	5	
Attention seeking from you	1	2	3	4	5	
Attention seeking from other family members	1	2	3	4	5	N/A
Grooming	1	2	3	4	5	
Interacting aggressively with other household cats	1	2	3	4	5	N/A
Interacting aggressively with other pets (not cats)	1	2	3	4	5	N/A
Interacting aggressively with humans in house	1	2	3	4	5	
Sleeping	1	2	3	4	5	

How many hours did it take for your cat to return to 'normal' behavior? _____

Are you likely to bring your cat back for blood donation based on this experience?

Very likely Likely Not likely Definitely not

Is there anything else you think we should know? Please add any additional comments below.