Original Article

jfms Journal of Feline Medicine and Surgery

Journal of Feline Medicine and Surgery
14(10) 701–705

DOI: 10.1177/1098612X12448588
jfms.com
SAGE

Effects of a standardized anesthetic protocol on hematologic variables in healthy cats

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Abstract

This study evaluated the effects of an anesthetic protocol using intravenous ketamine and midazolam, and intramuscular buprenorphine on hematologic variables in cats. Twelve healthy adult cats had blood collected for a complete blood count before and after the induction of anesthesia. There were significant decreases in red blood cell counts, hemoglobin concentrations and hematocrits after the induction of anesthesia. On average, red blood cell counts and hematocrits decreased by 25%, and hemoglobin concentrations decreased by 24%. Based on hematocrit, 3/12 samples (25%) taken while the cats were anesthetized would have been interpreted as belonging to anemic patients while none of the cats would have been considered anemic before anesthesia. This study suggests that a complete blood count performed on blood taken under anesthesia with this anesthetic protocol should be interpreted cautiously in order to not make a false diagnosis of anemia.

Accepted: 23 April 2012

Introduction

The fractious nature of some cats can occasionally prevent clinicians from performing routine procedures, such as a thorough physical examination or blood collection in an awake cat. In such cases, sedation or short general anesthesia may be performed. The effects of heavy sedation or general anesthesia on hematologic variables in cats can vary depending on the protocol used.[1–5] Different sedative drugs can affect vascular tone, splenic size, and intracellular and extracellular fluid volumes, resulting in altered blood cell counts. If hematologic variables are to be interpreted accurately for a sample collected from a sedated or anesthetized cat, it is important for the clinician to anticipate any potential reactive changes induced by the specific combination of sedative or anesthetic drugs used. If induced changes are pronounced enough to result in values outside of the reference interval, one or more misdiagnoses may result.

The purpose of this study was to assess the effects of a standardized injectable anesthetic protocol using intravenous ketamine hydrochloride and midazolam, and intramuscular buprenorphine, on the hematologic variables of cats. We hypothesized that this ketamine-based anesthetic protocol would induce a significant decrease in the circulating erythrocyte concentration.

Materials and methods

Animals

Twelve healthy adult research cats (five castrated males and seven intact females) ranging in age from 2 to 5 years (mean 3.42 ± 1.16 years) and ranging in body weight from 3.0 to 5.9 kg (mean 4.09 ± 0.89 kg) were included in this study. All of the cats were negative for feline immunodeficiency virus antibody and feline leukemia virus antigen. Nine of the cats were domestic shorthair and three were domestic longhair. The cats were determined to be healthy at the time of the study on the basis of normal physical examination findings and a two-day observation period of their appetite and activity level. During the study, cats were housed individually in cages in the Animal Care Unit of the Western College of Veterinary Medicine, University of Saskatchewan, where food and water were provided ad

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libitum, except for the 12-h period preceding each anesthetic episode when cats were fasted.

Anesthetic protocol

All 12 cats were anesthetized using a standardized protocol. Prior to collection of blood samples and induction of general anesthesia, all cats were fasted for 12 h and water was withheld for 3–6 h. The anesthetic protocol used consisted of 10 mg/kg of ketamine hydrochloride (Vetalar; Bioniche Animal Health) and 0.5 mg/kg of midazolam (Midazolam Sandoz Standard; Sandoz Canada), given intravenously (IV) through a 22-gauge catheter placed in the cephalic vein, immediately followed by 10 µg/kg of buprenorphine (Vetergesic; Reckitt Benckiser Healthcare UK) given intramuscularly (IM). Immediately after induction of general anesthesia, cats were intubated with an appropriately sized endotracheal tube and oxygen was provided at 1 l/min. No intravenous fluids were provided during general anesthesia.

Collection of blood samples

For each cat, a blood sample was collected immediately prior to the administration of injectable anesthetic drugs (pre-induction sample) and a second blood sample was collected while the cat was under general anesthesia (post-induction sample). The mean time between induction of general anesthesia and collection of the second blood sample was 20.5 ± 9.0 min. Each blood sample was collected from either the left or right jugular vein using a 22-gauge needle attached to a plastic syringe. Blood was immediately transferred into an ethylenediaminetetraacetic acid (EDTA) micro-collection tube (BD Microtainer tube with K2EDTA; Becton Dickinson), according to the manufacturer recommendations. All 12 cats had paired pre-induction and post-induction samples collected.

Hematological analysis

A complete blood count (CBC) was performed on each blood sample the day of blood collection at the Prairie Diagnostic Services Laboratory (Saskatoon, SK, Canada) using an automated hematology analyzer (Cell-Dyn 3500; Abbott Laboratories). Blood smears were performed at the time of sample submission by laboratory technicians and stained using a modified Wright's stain (Hema-Tek; Bayer Health Care). Hematological values provided by the hematology analyzer included: red blood cell (RBC) count; hemoglobin (Hb) concentration; hematocrit (HCT); mean red blood cell volume (MCV); mean corpuscular hemoglobin (MCH); mean corpuscular hemoglobin concentration (MCHC); red blood cell distribution width (RDW); total white blood cell (WBC) count; segmented neutrophil (SEG) count; eosinophil (EOS) count; basophil (BASO) count; lymphocyte (LYMPHO) count; monocyte (MONO) count; and platelet (PLT) count. A clinical pathology technician, who was blinded to whether the sample was from an awake or anesthetized cat, reviewed all blood smears, performed a differential cell count of the leukocyte population (total of 100 WBCs counted under 500× magnification) and subjectively assessed leukocyte toxic change, RBC morphology and the degree of platelet clumping. Plasma total protein concentration (TP) was determined for each sample using a refractometer on plasma separated from a whole blood sample spun down in a microhematocrit tube. Evaluation for the presence of gross hemolysis, as assessed by red discoloration of the plasma after centrifugation, was performed. Hematologic results were interpreted using reference intervals previously established by the laboratory based on samples from 60 non-sedated, healthy cats between the age of 1 to 9 years, which had been fasted for a minimum of 12 h prior to blood collection.

Statistical analysis

The Wilcoxon signed-rank test was used to compare pre-induction variables to post-induction variables. A total of 15 variables were evaluated for possible variation and a Bonferroni-adjusted P value of 0.05/15 = 0.0033 was used to determine statistical significance. A statistical software program (Statistix 9; Analytical Software) was used for statistical analyses.

This study protocol was approved by the University Committee on Animal Care and Supply (UCACS) Animal Research Ethics Board (AREB) of the University of Saskatchewan.

Results

There were statistically significant decreases in the median RBC count, Hb concentration and HCT in the post-induction samples compared with the pre-induction samples. Results are presented in Table 1.

Erythrocytes

On average, the RBC count post-induction was 24.7% lower than the RBC count pre-induction (P = 0.0025). The Hb concentration post-induction was 23.8% lower than the Hb concentration pre-induction (P = 0.0025). The HCT post-induction was 24.9% lower than the HCT pre-induction (P = 0.0025). All pre-induction blood samples had a RBC count, Hb concentration and HCT within the reference interval. However, 5/12 (41.7%) post-induction samples had a RBC count lower than the reference interval, 4/12 (33.3%) had a Hb concentration lower than the reference interval, and 3/12 (25%) had a HCT lower than the reference interval. All the RBC counts, Hb concentrations and HCT values measured in the post-induction samples were lower than in the corresponding pre-induction samples.

Table 1 Hematologic variables pre- and post-induction of general anesthesia in 12 healthy cats. Variables for which statistically significant difference was found between pre- and post-induction samples are in bold. A Bonferroni-adjusted *P* value of 0.05/15 = 0.0033 was used to determine statistical significance

	Pre-induction					Post-induction						
	Mean	Standard deviation	Median	Minimum	Maximum	Mean	Standard deviation	Median	Minimum	Maximum	Reference interval	*P* value
RBC count ($x10^{12}$/l)	**9.44**	**0.93**	**9.42**	**7.11**	**11.1**	**7.11**	**0.75**	**7.14**	**5.58**	**8.02**	**6.89–10.8**	***P* = 0.0025**
Hg (g/l)	**138.75**	**11.78**	**140**	**113**	**152**	**105.75**	**12.21**	**108**	**88**	**130**	**99–159**	***P* = 0.0025**
HCT (l/l)	**0.43**	**0.03**	**0.44**	**0.35**	**0.47**	**0.32**	**0.03**	**0.32**	**0.27**	**0.39**	**0.285–0.477**	***P* = 0.0025**
MCV (fl)	45.22	2.21	45.2	41.9	48.7	44.91	2.25	45	41.7	48.5	36.4–50	*P* = 0.031
MCH (pg)	14.78	0.9	14.95	13.1	16	14.88	0.86	15	13.3	16.2	12.4–16.8	*P* = 0.033
MCHC (g/l)	326	7.17	327.5	314	336	331.3	5.47	332	320	339	319–357	*P* = 0.0076
RDW (%)	19.71	1.19	19.55	17.6	21.9	18.95	1.57	19.15	15.8	21.5	17.2–22.8	*P* = 0.0776
TP (g/l)	86.1	7.09	87	68	98	74.3	6.4	72	65	87	58–82	*P* = 0.0135
WBC count ($\times10^9$/l)	12.47	5.81	10.75	4.8	25.9	10.42	3.81	10.35	3.7	17	3.9–18.1	*P* = 0.0546
SEG count ($\times10^9$/)	7.68	3.67	7.57	2.74	16.06	6.93	3.23	6.16	2.44	12.24	2.1–15	*P* = 0.2553
EOS count ($\times10^9$/l)	0.54	0.42	0.41	0.2	1.50	0.28	0.22	0.16	0	0.66	0.1–1.5	*P* = 0.0917
BASO count ($\times10^9$/l)	0.06	0.09	0	0	0.22	0.02	0.04	0	0	0.12	0–0.2	*P* = 0.0591
LYMPHO count ($\times10^9$/l)	3.73	1.84	4.13	1.11	7.51	2.75	1.15	3.25	0.81	4.45	1.0–6.9	*P* = 0.0068
MONO count ($\times10^9$/l)	0.41	0.25	0.24	0	1.06	0.06	0.26	0.24	0	1.06	0–0.6	*P* = 0.1698
PLT count ($\times10^9$/l)	212.18	169.16	167.5	58.1	647	246.17	84.48	227	126	455	300–700	*P* = 0.4101

RBC = red blood cell, Hg = hemoglobin concentration, HCT = hematocrit, MCV = mean cell volume, MCH = mean corpuscular hemoglobin, MCHC = mean corpuscular hemoglobin concentration, RDW = red blood cell distribution width, TP = plasma total protein concentration, WBC = total white blood cell, SEG = segmented neutrophil, EOS = eosinophil, BASO = basophil, LYMPHO = lymphocyte, MONO = monocyte, PLT = platelet

There were no significant differences between the median pre-induction and the median post-induction MCV, MCH, MCHC and RDW.

Gross hemolysis was present in 2/12 blood samples after centrifugation, in one pre-induction sample and in one post-induction sample.

Total protein

There was no significant difference between the median pre-induction TP and the median post-induction TP.

Leukocytes

There were no significant differences between the median pre-induction and the median post-induction WBC, SEG, EOS, BASO, LYMPHO and MONO counts.

Platelets

There was no significant difference between the median pre-induction automated PLT count and the median post-induction automated PLT count. The median (minimum–maximum) pre-induction PLT count was 167.5 × 10^9/l (58.1 × 10^9–647 × 10^9) and the median post-induction PLT count was 227 × 10^9/l (126 × 10^9–455 × 10^9). Both of these values were lower than the feline reference interval (300 × 10^9–700 × 10^9/l). Evaluation of blood smears revealed the presence of PLT clumps in all samples. The PLT count was estimated as normal in all samples.

Discussion

This study showed a major variation in the circulating erythrocyte concentration in cats following induction of general anesthesia with this particular anesthetic protocol. This was indicated by decreases in the RBC count, Hb concentration and HCT.

Sequestration of erythrocytes outside of the circulation during anesthesia could explain the variation in the circulating erythrocyte concentration seen between pre- and post-induction samples. The organ most commonly considered to have the ability to sequester erythrocytes, through variation of its volume, is the spleen.[6–10] Splenic vascular relaxation, as induced by many sedative and anesthetic drugs, would lead to a decrease in the concentration of circulating erythrocytes in the peripheral blood or an increase in the splenic reserve pool of erythrocytes.

Splenic contraction owing to stress could have increased the circulatory pool of erythrocytes in the awake cats pre-induction. It has been established that catecholamines, such as epinephrine and norepinephrine, are responsible for splenic contraction in many species, including cats.[6–11] With the acute stress of handling and restraint for blood collection, serum concentrations of catecholamines may increase in conscious healthy cats well above concentrations seen in healthy anesthetized cats. This could explain the higher concentration of circulating erythrocytes in the pre-induction blood samples compared with the decreased numbers seen post-induction of anesthesia in the cats used in this study.

In our study, ketamine hydrochloride (a dissociative anesthetic agent) and midazolam (a benzodiazepine) were given IV at a dose of 10 mg/kg and 0.5 mg/kg, respectively. These doses are commonly used for short procedures. Buprenorphine, an opioid, was given IM at a dose of 10 µg/kg. Because buprenorphine was given IM, its peak effect at the time of post-induction sampling may not have been reached. Two previous studies in cats showed a significant, and repeatable, decrease in HCT following sedation with ketamine hydrochloride as a sole agent given either IV or IM.[3,4] However, in another study in cats ketamine administered subcutaneously as a sole agent did not lead to a significant decrease in HCT.[5] It has been shown that ketamine can directly induce vasodilation of vascular smooth muscles.[12,13] The effect of this drug on splenic vascular smooth muscles could explain the decrease in circulating erythrocyte concentration through splenic sequestration of erythrocytes.

A recent study in dogs showed a significant increase in splenic volume following administration of various anesthetic drugs. In that study, it was noticed that the most significant increase in splenic volume was obtained with an anesthetic protocol using ketamine hydrochloride and diazepam, but there was no clear correlation between the variation in splenic volume and the variation in HCT, suggesting that other sites of RBC sequestration must exist, such as the liver, the skin or the skeletal muscles.[14]

Two other studies evaluating the effects of general anesthesia using propofol on various clinical parameters in cats also showed a decrease in HCT following the induction of general anesthesia.[1,2] This is in agreement with our findings that general anesthesia, either by suppression of release of catecholamines, or by direct effects of the anesthetic drugs on organs (possibly inducing smooth muscle relaxation), is responsible for RBC sequestration within organs.

Post-induction samples showed results below the reference interval for RBC count in 41.7% of the samples, for Hb concentration in 33.3% of the samples and for HCT in 25% of the samples. Therefore, if only the HCT was measured, as is often performed for monitoring or in emergency situations, then a quarter of the samples taken from cats under general anesthesia in this study would have been inappropriately interpreted as belonging to anemic cats.

The automated analyzer used in this study had a tendency to provide PLT counts lower than what was estimated by a laboratory technician after evaluation of blood smears for PLT clumps, which were detected in all cases. Automated hematology analyzers cannot appropriately interpret PLT clumps owing to their larger size in comparison with a normal PLT.[15,16] If clumping is severe, this can lead to an artifactual measured thrombocytopenia. This finding is consistent with a common belief that feline platelets tend to aggregate quickly during, or immediately after, blood collection, prior to transfer to an EDTA blood collection tube.[15,16]

This study showed a significant decrease in circulating erythrocyte concentration in association with this commonly used anesthetic protocol in healthy cats. Clinicians should be aware of these changes to avoid inappropriately classifying cats as anemic based on decreased RBC count, Hb concentration or HCT values on samples collected while cats are anesthetized with this combination of drugs.

Acknowledgements The authors would like to thank the technicians Kim Appelt, Kim Christiansen, Lorena Cruz, Shelley Eggum, Gloria Patry and Lori Schappert from the clinical pathology laboratory of Prairie Diagnostic Services for their contribution to this work.

Funding This study was supported by a grant from the Western College of Veterinary Medicine Companion Animal Health Fund.

Conflict of interest The authors do not have any potential conflicts of interest to declare.

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