

## **Clinical and haematological responses of feline blood donors anaesthetised with a tiletamine and zolazepam combination**

**Eva Spada, Daniela Proverbio, Giada Bagnagatti De Giorgi, Roberta Perego, Emanuela Valena, Alessandra Della Pepa and Luciana Baggiani**

Veterinary Transfusion Unit (REV), Department of Health, Animal Science and Food Safety (VESPA), University of Milan, Milan, Italy

### **Corresponding author:**

Eva Spada DVM, PhD, Researcher, Veterinary Transfusion Unit (REV), Department of Health, Animal Science and Food Safety (VESPA), University of Milan, via G Celoria, 10, 20133 Milan, Italy Email: eva.spada@unimi.it

### **Abstract**

This prospective study investigated the effect on clinical and haematological variables of the anaesthetic combination of tiletamine and zolazepam in feline blood donors. Blood (10 ml/kg bodyweight to a maximum volume of 60 ml) was collected from the jugular vein of 31 owned healthy cats anaesthetised with 2.5 mg/kg of tiletamine and 2.5 mg/kg of zolazepam intramuscularly. Rectal temperature (RT), systolic arterial pressure (SAP), mean arterial pressure (MAP), diastolic arterial pressure (DAP), heart rate (HR) and complete blood count (including red blood cells [RBC], haemoglobin [HB], haematocrit [HT], platelet [PLT] count, white blood cells [WBC], lymphocytes, neutrophils, eosinophils, monocytes and basophils) were evaluated pre- and postdonation. RT decreased significantly ( $P < 0.01$ ) after blood donation (mean change in RT  $-0.7^{\circ}\text{C}$ ). Significant increases in SAP ( $P = 0.03$ ), MAP ( $P < 0.01$ ) and DAP ( $P < 0.01$ ) occurred after blood donation (mean increase 13 mmHg, 12 mmHg and 11 mmHg, respectively). Although RBC, HT, HB, WBC, PLT, neutrophil and monocyte counts decreased, and HR, and lymphocyte, eosinophil and basophil counts increased after blood donation this change was not statistically significant. Mean time from pre- to postdonation evaluation was  $39 \pm 11$  mins (range 24–76 mins). None of the cats had evidence of pallor or collapse after recovery from anaesthesia. The collection of blood at 10 ml/kg bodyweight to a maximum volume of 60 ml in healthy cats using a low dose tiletamine and zolazepam anaesthetic appears to be well tolerated by feline blood donors.

**Accepted:** 16 June 2014

### **Introduction**

Owing to the problems associated with manual restraint, and the importance of sterility and minimisation of trauma to donor's veins, cats typically require sedation for blood collection, and blood donors are anaesthetised in many feline blood donor programmes.<sup>1–5</sup>

Clinical blood donation involves controlled loss of approximately 15–20% of the donor's blood volume over 5–10 mins.<sup>6</sup> It is therefore desirable to use anaesthetic agents that cause minimal cardiovascular alterations.

In feline medicine, combination anaesthesia with tiletamine and zolazepam has been used in a variety of short procedures requiring sedation (eg, examinations) or anaesthesia (eg, microsurgery), and also for some major surgeries.<sup>7</sup> Tiletamine, a dissociative anaesthetic agent, increases heart rate (HR) and blood pressure, and causes

minimal vasoconstriction. Zolazepam, a benzodiazepine tranquilliser, was combined with tiletamine because of its effectiveness as an anticonvulsant and muscle relaxant.<sup>7,8</sup> The cardiovascular and muscular effects of this anaesthetic combination should be appropriate for use in blood collection.

The aim of this study was to investigate the effect on selected clinical and haematological variables of this anaesthetic combination in feline blood donors. Our hypothesis was that this anaesthetic combination would provide adequate anaesthesia for blood collection with minimal effects on blood pressure, HR and haematological parameters.

## Materials and methods

In this prospective study, data from 31 owned healthy cats (18 castrated males and 13 spayed females), enrolled as blood donors at the Veterinary Transfusion Unit of the University of Milan, Milan, Italy, were studied. Data used in this study came from routine monitoring of the blood donor procedure.

Written owner consent for blood collection and for the use of blood samples and all data for scientific purposes is routinely given at the admission examination each time a patient visits the clinic during routine visits prior to blood donation. Therefore, based on the regulations, formal ethical approval for this study was not needed.

The mean weight of the feline donors was 5.2 kg (range 4.7–8.4 kg), mean age was 5 years (range 1–8 years) and all were European domestic cats. All cats had a current vaccination status and tested negative for feline immunodeficiency virus, feline leukaemia virus, haemotropic *Mycoplasma* species and heartworm.<sup>9</sup>

Cats were anaesthetised with 2.5 mg/kg of tiletamine and 2.5 mg/kg of zolazepam (Zoletil 100; Virbac) IM. Time at injection and at the induction of anaesthesia was recorded, as well as the response to injection. After induction, the cat was placed in lateral recumbency on a heated electric blanket, and ophthalmic lubricant was applied. Rectal temperature (RT) was measured with a digital thermometer (Vedo Digit II; Artsana). A 20–22 G intravenous catheter was placed in the cephalic vein, a predonation blood sample was collected via the cephalic catheter and 90 ml of lactate Ringer solution was administered subcutaneously. Using a Cell-Dyn 3500 haematology analyser (Abbott Diagnostic Laboratories), the predonation blood sample was used to determine complete blood count (CBC), including white blood cells (WBC), red blood cells

(RBC), haemoglobin (HB), haematocrit (HT) and platelet (PLT) count. The percentage of lymphocytes, neutrophils, eosinophils, monocytes and basophils were assessed manually on a blood smear.

High-definition oscillometry (Memo Diagnostic; S+B medVET) was used to measure systolic arterial pressure (SAP), mean arterial pressure (MAP), diastolic arterial pressure (DAP) and HR, applying the

C1 cuff, as recommended by the manufacturer's instructions, to the tail- base of each cat. Three consecutive readings were taken.

A small area on the ventral neck was clipped to expose the left jugular vein, and disinfected with three scrubs of isopropyl alcohol. Blood (10 ml/kg to a maximum volume of 60 ml) was collected, via a 19 G butterfly needle, into 20-ml syringes containing citrate-phosphate-dextrose-adenine1 anticoagulant (CPDA-1) in a ratio CPDA1: blood of 1:7. Lactate Ringer solution (60 ml/kg) was administered intravenously by rapid infusion starting halfway through the donation. Blood collection was completed within 3–5 mins. Immediately following blood collection, RT was measured and three consecutive blood pressure readings were again obtained. After the final reading, a blood sample was collected from the cephalic vein by direct venipuncture to measure postdonation CBC. Cats were allowed to recover on a heated blanket.

The Gaussian distribution of the data was assessed using the Kolmogorov–Smirnov test. ANOVA for repeated measures was used to assess differences between males and females, and to compare differences in all the variables between the time points before and after blood collection. All statistical calculations were performed with MedCalc version 12.7.0. Results were considered significant when  $P < 0.05$ .

## Results

All the variables studied were normally distributed at the timepoints before and after blood collection. No significant differences were found between males and females for any of the variables; therefore, the data were analysed as a single group of 31 cats. The clinical and haematological variables are reported in Tables 1 and 2, respectively.

**Table 1** Selected clinical variables evaluated before and after blood donation in 31 healthy blood donor cats anaesthetised with tiletamine and zolazepam

	RT (°C)		SAP (mmHg)		MAP (mmHg)		DAP (mmHg)		HR (bpm)	
	Before	After	Before	After	Before	After	Before	After	Before	After
Mean	38.3	37.4*	141	153*	98	109*	75	86*	216	224
± SD	0.5	0.6	17	23	13	15	12	12	40	43
Range	37.5– 39.4	36.5– 38.6	105– 169	106– 199	72– 117	86– 136	53– 95	64– 108	108– 283	102– 287

\* Statistically significant ( $P < 0.05$ )

RT = rectal temperature; SAP = systolic arterial pressure; MAP = mean arterial pressure; DAP = diastolic arterial pressure; HR = heart rate; bpm = beats per min

**Table 2** Selected haematological variables evaluated before and after blood donation in 31 healthy blood donor cats anaesthetised with tiletamine and zolazepam RBC HT HB WBC Lymphocytes Neutrophils Eosinophils Monocytes Basophils Platelets

**Table 2** Selected haematological variables evaluated before and after blood donation in 31 healthy blood donor cats anaesthetised with tiletamine and zolazepam

	RBC ( $\times 10^6/\mu\text{l}$ )		HT (%)		HB (g/dl)		WBC ( $\times 10^3/\mu\text{l}$ )		Lymphocytes (%)		Neutrophils (%)		Eosinophils (%)		Monocytes (%)		Basophils (%)		Platelets ( $\times 10^3/\mu\text{l}$ )	
	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After
Mean	7.4	7.0	29.8	28.5	10.9	10.4	7.8	7.5	34.6	31.4	56.9	59.3	6.7	7.3	2.1	1.9	0.2	0.1	319.0	318.0
$\pm$ SD	0.9	1.2	4.3	4.9	1.7	1.8	2.3	2.4	20.2	18.0	20.1	18	4.7	4.7	2.3	2.1	0.4	0.3	165.0	148.0
Range	5.6– 9.5	5.1– 9.0	24.3– 38.2	21.9– 42.8	8.5– 14.5	7.2– 14.4	3.7– 12.9	3.4– 15.2	7.0– 62.0	6.0– 60.0	10.0– 90.0	30.0– 92.0	0.0– 22.0	1.0– 17.0	0.0– 9.0	0.0– 9.0	0.0– 1.0	0.0– 1.0	50.0– 705.0	35.0– 675.0

RBC = red blood cells; HT = haematocrit; HB = haemoglobin; WBC = white blood cells

Induction of anaesthesia occurred in a mean time of  $5 \pm 2$  mins (range 3–8 mins). A significant decrease in RT ( $P < 0.01$ ) occurred after blood donation. The change in RT ranged from 0 to  $-2.1^\circ\text{C}$ , with the mean change being  $-0.7 \pm 0.5^\circ\text{C}$ . Significant increases in SAP ( $P = 0.03$ ), MAP ( $P < 0.01$ ) and DAP ( $P < 0.01$ ) occurred after blood donation. The mean increases in SAP, MAP and DAP were 13 mmHg, 12 mmHg and 11 mmHg, respectively.

RBC, HT, HB, WBC, PLT, neutrophil and monocyte counts decreased, and HR, lymphocytes, eosinophils and basophils counts increased after blood collection, but these changes were not statistically significant. The mean time for the full blood donation procedure, including time for pre- and postdonation evaluation, was  $< 40$  mins, with a mean duration of  $39 \pm 11$  mins (range 24–76 mins). None of the cats had any evidence of pallor or collapse after recovery from anaesthesia.

## Discussion

Regardless of temperament, most cats require some form of sedation or anaesthesia to facilitate blood donation. Sedation is advisable even in tolerant cats because sudden movement during collection can render the product useless, lead to aborted donation and damage the donor's blood vessels. Use of a combination of tiletamine and zolazepam (at the lowest dose required for restraint) has previously been reported,<sup>10</sup> but no data were reported on the effect on clinical or haematological parameters in donors. In this study, we evaluated the effect on selected clinical and haematological parameters.

Many cats in this study were hypothermic immediately after donation (minimum temperature  $36.5^\circ\text{C}$ ), with a statistically significant decreased body temperature with respect to predonation temperature. It is well known that a combination of tiletamine and zolazepam can cause hypothermia, and it is thought that this occurs as a consequence of muscle relaxation.<sup>8</sup> Therefore, body temperature should be monitored and supplementary heat provided to cats during blood donation.

Hypotension is common during donation owing to the combination of blood loss and anaesthesia. A variety of anaesthetic protocols are documented to be safe for blood collection in cats, but donor cats always show significant hypotension,<sup>2,3</sup> and this sometimes requires intervention.<sup>4</sup> In this study, there was a statistically significant increase in blood pressure after blood donation. Postdonation mean values for SAP and DAP were in the range for minimal risk of target organ disease (TOD) for DAP ( $< 95$  mmHg) and mild risk of TOD for SAP (150–159 mmHg);<sup>11</sup> however, no cat required intervention. The increase in HR and blood pressure after the injection of tiletamine and zolazepam is due to direct central nervous system stimulation accompanied by an increased sympathetic tone.<sup>8</sup> Other anaesthetic protocols, such as dexmedetomidine in isoflurane-anaesthetised cats, have been shown to lead to an increase in systemic arterial blood pressure.<sup>12</sup> The cardiovascular changes in this study may also reflect the activation of a variety of

compensatory neuroendocrine responses. In humans and small animals, reduced arterial and capillary pressure and rapid decreases in blood volume (as happens during blood donation) causes an intense sympathetic discharge within seconds; this increase in sympathetic activity results in an increased HR and contractility, and generalised arteriolar and venous constriction, and thus preservation of arterial pressure.<sup>13</sup>

Advantages of tiletamine/zolazepam anaesthesia are that this combination is fairly inexpensive, accessible and easy to administer. Cats showed minimal reaction to intramuscular injection of the anaesthetic combination. On average, it took <5 mins to induce an appropriate level of sedation when given intramuscularly at very low doses, and the cats were adequately sedated for the entire procedure.

The limitation of the study is that we used an oscillometric instrument and did not measure pressure directly by means of an intra-arterial catheter connected to a pressure sensor, which is considered to be the gold standard method in cats. Oscillometry has been shown to overestimate low pressure and underestimate high pressure values compared with the Doppler method.<sup>14</sup> However, if the operator is able to work in a quiet environment and repeat the measurements, then accurate blood pressure measurements can be obtained in small animals with this kind of oscillometric instrument.<sup>11,15</sup>

In addition, pressure readings were taken from the tail, and one study showed significant differences between readings from tail and forelimb when the cuff was positioned on the tail in anaesthetised cats.<sup>11</sup> However, as our aim was to document the trend of the pressure after blood donation using a tiletamine and zolazepam anaesthetic combination, the bias from measuring blood pressure at the level of the tail was probably not important.

## Conclusions

Animal welfare is a major concern in any blood donor programme. The collection of 10 ml/kg blood to a maximum volume of 60 ml using a low-dose tiletamine and zolazepam combination anaesthetic appears to be safe and well tolerated by feline donors.

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

**Funding** This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

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