



Feline blood donation adverse reactions: classification and description of acute and delayed reactions in a donor population

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Abstract

Objectives This article aims to analyse the safety of feline blood donation by describing the frequency and nature of any adverse reactions and their causes, as well as propose measures to decrease the incidence of adverse reactions.

Methods In this prospective study, any blood donor adverse reactions detected by the clinical staff during and immediately after donation were recorded. The owners of the cats were also surveyed by a veterinary practitioner or veterinary nurse 5 days after donation, using a predefined questionnaire to assess for any clinical or behavioural changes. Data were collected between January 2019 and March 2020 from blood donors enrolled in an animal blood bank programme.

Results Of 3690 blood donations from 1792 feline donors assessed, post-donation reactions were reported in 1.14% (n = 42): 0.22% (n = 8) were acute reactions, which included weakness, pallor, tachypnoea and open-mouth breathing; and 0.92% (n = 34) were delayed post-donation reactions, with 0.16% involving cutaneous (haematomas and skin rashes, n = 6), 0.68% involving behavioural (n = 25) and 0.08% involving digestive (emesis and inappetence, n = 3) signs.

Conclusions and relevance The low incidence of post-donation reactions in this study is encouraging, suggesting that a well-established protocol and competent staff can help to ensure a high level of safety in a feline donor programme and, in turn, increase the confidence of cat owners.

Keywords: Blood donation; acute; delayed; adverse reaction

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Introduction

The use of blood transfusions from donors to recipients in humans has been reported since the 17th century.¹ With further advances in transfusion medicine, a need has emerged to select donors that meet the necessary criteria for blood donation, since the safety of the volunteer donors has to be guaranteed.²

The increasing demand for blood components suitable for transfusion in veterinary medicine has led to the emergence of specialised animal blood banks and thus the creation of blood donor programmes, which has resulted in a growing number of animals frequently donating blood. This requires a defined organisational structure and robust protocols, procedures, data recording and risk

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analysis, in order to ensure that the haemocomponent demand is met and that products are readily available.² Having a well-established and organised blood donor programme helps to maintain the safety of the procedure for donors and medical staff, as well as for recipients. Planned donations also allow administration of the correct treatment by providing haemocomponents instead of whole blood,² and result in a quicker response time to transfusion by reducing the need for emergency donations. To ensure best practices and a trusting relationship between owners and the veterinary team, it is vital that the donor's health status is monitored by recording all general management, preventive and clinical procedures, and ensuring that welfare is a major priority.³

According to the World Small Animal Veterinary Association (WSAVA) guidelines, animal welfare consists of good physical, emotional, psychological and environmental wellbeing of animals.³ Prolonged and severe stress may blunt homeostatic responses, leading to adverse effects on health and behaviour.³⁻⁶ As per Russo and Humm (2016), the more positive the donation experience, the more relaxed and cooperative feline donors will be on the next occasion.⁷

Although the blood donation procedure is minimally invasive, there is always the chance of post-donation adverse reactions occurring.⁸ In humans, stress-triggered vasovagal reactions lead to decreased arterial blood pressure and cerebral perfusion due to a reduction of blood flow to the brain, resulting in vasovagal syncope, characterised by feeling lightheaded or dizzy, sometimes accompanied by mild seizures and/or incontinence.^{9,10} Vasovagal reactions occur during or shortly after blood donation and include weakness, dizziness, pallor, sweating, headache, nausea, hypotension, apprehension, bradycardia and sweating.^{11,12} In veterinary medicine, although there are no reports of a direct relation with blood donation, one study reported that vasovagal reactions might have developed in two cats after cystocentesis.¹³ Concerning venepuncture-related complications, haematoma formation is the most common problem in human blood donation,¹⁴ although pain is also reported due to nerve injuries during phlebotomy.¹¹ Complication rates were previously described in 143 donations from a canine blood bank by DeLuca et al (2006).¹⁵ The study reported acute donor reactions in 2.8%, rebleeding in 2.1%, haematoma formation in 4.2% and skin irritation in 0.7% of total donations.¹⁵ Major adverse reactions are more likely to occur in animals with occult diseases, such as cardiomyopathy or chronic kidney disease.¹⁶ Therefore, physical examination and laboratory analyses should be performed prior to donation and, if abnormalities are found, animals should be withdrawn from the donor list and their owners advised to seek veterinary attention.⁷

The main objective of this study was to evaluate the safety of a feline blood donation programme, by describing the frequency and nature of any donor adverse

reactions and reviewing their causes, and to propose measures to decrease the incidence of adverse reactions.

Materials and methods

In this prospective study, feline blood donations were planned and performed according to the Portuguese Animal Blood Bank's protocol by a specialised trained team.

Owners were asked to sign an informed written consent form (see Appendix 1 in the supplementary material), which included a description of the blood donation procedure, the benefits of being a blood donor and a list of possible adverse reactions. Owners were also informed that their pet could be removed from the programme at any time upon request, without any additional obligation.

To be included in the study, the donors needed to meet the following criteria: having no clinical signs of disease; being friendly and calm; weighing >3.5 kg; being 1–10 years of age; having up-to-date vaccination, flea and worm treatments; not being on any medications; and having no heart murmurs noted on physical examination. If on physical examination heart murmurs were identified, a subsequent normal echocardiogram was mandatory to be accepted as a blood donor. Additionally, the cat needed to have never received a blood transfusion themselves.

Donations were performed at the Portuguese Animal Blood Bank or other affiliated veterinary hospital facilities in Portugal. Upon arrival, each donor was placed in the 'resting room' for a minimum of 20 mins prior to donation. This room was equipped with dedicated tables for cat carriers and cat enclosures for donors that needed to wait longer to go home, had quiet music playing and pheromone plug-ins (Feliway; Ceva), and no sight or scent of dogs. The donor was removed from the carrier according to the 'AAFP and ISFM feline-friendly nursing care guidelines'¹⁷ and a physical examination was performed. The donor was then wrapped in a blanket in sternal recumbency, leaving only the head and neck exposed. The decision of whether to sedate the donor or not was based on body language, temperament and/or data of previous donations indicating unexpected movements. In the cats that were sedated, the collection was performed after administering a mixture of diazepam (0.1–0.2 mg/kg), ketamine (0.5–1 mg/kg) and butorphanol (0.02–0.04 mg/kg) via a 24 G catheter in the cephalic vein. Then, a 2 ml blood sample was collected for analysis from all donors. A pre-donation total haemoglobin higher than 10 g/dl and a negative rapid test for feline immunodeficiency virus antibody/feline leukaemia virus antigen (IDEXX SNAP Combo Test) were required for donation to proceed. Further PCR tests (*Mycoplasma haemofelis*, '*Candidatus* Mycoplasma haemominutum' and '*Candidatus* Mycoplasma turicensis'), a complete blood count and biochemistry panel (creatinine, total protein, alanine aminotransferase and alkaline phosphatase)

were performed by external laboratories (Genevet in Carnaxide, Portugal and IDEXX in Barcelona, Spain).

Blood collections were performed by jugular puncture, alternating sides between donations. After the hair over the jugular vein was clipped, an area of skin 4 × 4 cm was cleaned and disinfected three times with alcohol and three times with chlorhexidine, alternating between one and the other, starting with the chlorhexidine. Donation was performed using a semi-closed collection system, containing a syringe with an anticoagulant of citrate, phosphate and dextrose (CPD), connected to a primary collection bag by a three-way tap. A total of 40–45 ml of blood was collected, never exceeding 12 ml/kg. Upon needle removal, digital pressure was applied for as long as required to reduce the chances of haemorrhage or haematoma formation. On average, each donation process took 10–15 mins, depending on factors such as donor temperament, the time for sedation to take effect and jugular vein quality. Each donor was placed back in their carrier and respiratory rate, heart rate, mucous membrane colour, respiratory pattern and mental state were monitored for at least 30 mins, until full awareness and motor function recovery. The intravenous catheter was removed once the cat had recovered from sedation. No volume replacement with crystalloids was provided to donors without immediate post-donation reactions.

Adverse reactions were classified as acute (less than 2 h after donation) or delayed (2 or more hours after donation) and recorded in the donor's file to be considered prior to their next donation.

Five days after each donation a telephone survey was conducted by a veterinary practitioner or veterinary nurse with each donor's owner (see Appendix 2 in the supplementary material). The owners were informed that the telephone call aimed to detect and record any clinical signs that could be attributable to the blood collection procedure. They were asked about concerns including skin irritation, bleeding or haematoma (in the cephalic or jugular vein area), inappetence, increased respiratory rate and respiratory effort, pallor, lethargy, collapse, abnormal behaviour or other abnormalities. The responses were recorded in individual post-donation reaction files. Open comments were also allowed at the end of the questionnaire.

Results

Between January 2019 and March 2020, information regarding 3690 blood donations from 1792 feline donors was recorded, making an average of 2.06 donations per donor within the 15-month period. From the 3690 donations, 104 donors donated four times in this period, 296 donated three times, 994 donated twice and 398 donated once (Table 1).

Of the 3690 donations, 19% (n = 701) were performed without the need for sedation, while 81% (n = 2989) were performed under sedation. From the 3690 donations, 42

Table 1 Number of cat donors and donations included during the 15-month study period

Number of donations per cat donor	Number of cat donors	Number of donations
1	398	398
2	994	1988
3	296	888
4	104	416
Total	1792	3690

Table 2 Description and number of acute and delayed adverse reactions seen during 3690 donations

Adverse reaction	Number of cases
Delayed reactions	34
Cutaneous	6
Haematoma (neck)	2
Haematoma (limb)	2
Skin irritation	2
Behavioural	25
Distress	7
Hissing at cohabitants	6
Attacking owners	1
Decreased activity	7
Inappropriate urination	2
Vocalisation	2
Sleepiness	2
Fear	1
Disorientated	1
Lethargy	1
Digestive	3
Inappetence	2
Emesis	1
Acute reactions* – pallor, weakness, tachypnoea, open-mouth breathing	8

*Pallor, weakness, tachypnoea and open-mouth breathing were all shown in all eight acute reactions

(1.14%) adverse post-donation reactions were reported (Table 2), with no other reactions identified in the remaining 3648 donations (98.86%). Of the 42 post-donation reactions, 88% (n = 37) were in sedated donors and 12% (n = 5) were in non-sedated donors, and 19% (n = 8) were acute reactions and 81% (n = 34) were delayed reactions. Of the 1792 donors, only two experienced more than one reaction, with both having two reactions (one cat had two acute reactions and the other cat had two delayed reactions).

Of the eight acute reactions, five (62.5%) occurred in sedated donors and three (37.5%) occurred in non-sedated donors, with all eight involving pallor, weakness, tachypnoea and open-mouth breathing. All acute reactions occurred within 10–15 mins of the donation finishing. Upon administration of a 10 ml/kg bolus over 10 mins of intravenous NaCl 0.9% and flow-by oxygen,

parameters stabilised and resolved within 10–15 mins on seven occasions; in the remaining donor it took 23 mins.

Of the five acute reactions that occurred under sedation, two were in the same donor cat, which was retired from the blood donor programme after its second acute reaction; interestingly, this cat had not had any reactions in its 12 previous donations. The remaining three acute reactions were in three different donor cats. One had given 12 donations before the acute reaction and gave two further donations after it, with no reported reactions. Another had given seven blood donations before the acute reaction and gave two further donations after it, again with no reported reactions. The last had given three donations before the acute reaction and gave four donations after it, again with no reported reactions.

Of the three acute reactions that occurred without sedation, one was in a donor that had no history of reactions during four previous donations performed under sedation; this cat continued as a blood donor but was sedated each time and had no further reactions over six subsequent donations. The second donor had given nine donations (the first five under sedation and the last four without the need for sedation) before the acute reaction but was then retired from the programme at the owner's request. The last donor had given four donations before the acute reaction, with no reported reactions, but was retired from the programme due to weight loss and increasing age.

Of the 34 delayed reactions, 32 (94%) occurred in donors that had been sedated, while two (6%) occurred in non-sedated donors. Two donors developed haematomas in the catheterised limb, one of which resulted in phlebitis and skin necrosis that required surgical debridement, while the other fully resolved within a week without treatment. Two donors developed haematomas at the cervical jugular puncture site, which both fully resolved within 5 days. Two donors developed skin irritation in the jugular area, which resolved within 5 days without treatment. Twenty-five of the delayed reactions were related to abnormal behaviour, which developed in the 24h post-donation: nine donors showed signs of distress (such as hissing and aggression towards feline cohabitants or owners), including one cat that remained very frightened throughout the donation day; seven had decreased activity until later in the donation day; two showed inappropriate urination; two were very sleepy for 24h; two showed excessive vocalisation in the evening; one was disoriented during the donation day; and one was lethargic. Behaviour returned to normal within 3 days in nearly all cases, although one donor remained lethargic for 5 days, which resolved without treatment. Two donors had inappetence on the day of the donation, fully recovering the following day, while one cat had one emetic episode at home after donation.

Of the 34 delayed reactions, 32 were in donors with single episodes of delayed reactions and two occurred in the same donor. These 32 donors had donated 3–12

times before any reaction occurred and subsequently donated 2–4 times afterwards. The donor with two separate delayed reactions had donated five times before the first reaction, and donated uneventfully a further three times before the second reaction, after which the donor successively donated a subsequent three times without any further reactions; this donor cat had one behaviour reaction (hissing at its feline cohabitants) and then one cutaneous reaction. All of these donors remained in the blood donor programme.

Discussion

From 3690 blood donations in this study, 42 reactions were reported, of which 34 (0.92%) were delayed reactions. The delayed reactions were mostly behavioural in nature, with the cats showing decreased activity and apparent distress, which could possibly be explained by the stress of an unfamiliar environment and transport in a carrier.

The low incidence of delayed reactions is, in our opinion, related to the 'cat friendly' protocols employed, which reduced anxiety via the promotion of low-stress transportation, short waiting times and minimal patient restraint. A calm environment (eg, cat-only areas), with limited noise and smells, is of utmost importance to reduce donation-associated anxiety. Selection and training of the blood bank team, which performs blood collection regularly, are also crucial to ensure high safety standards, possibly reduce donor adverse reactions, and perhaps also help to perform faster and more efficient donations. This training consists of being familiar with the cat friendly protocols used in the Animal Blood Bank, as well as training in donor restraint, feline behaviour and body language, phlebotomy and emergency treatment. It is important that a multidisciplinary team, which includes veterinarians and nurses with experience in a range of areas such as restraint, anaesthesia, feline medicine and feline welfare, is able to understand feline behaviour, to prepare an optimal donation environment and to adopt specific techniques to reduce unpleasant experiences. A careful pre-donation examination aiming to ensure that the cat is healthy and eligible for donation, and careful atraumatic venepuncture for catheter placement or blood collection that minimises the chance of haematoma, swelling or bleeding also probably decrease the occurrence of post-donation adverse reactions. These protocols and techniques facilitate the blood collection process and may reduce the need for sedation, or reduce the sedation dose required. They also have the potential to positively influence future blood donations, increasing the retention rate of the donors. As blood donations were only performed by experienced and well-trained teams, and no control group with other less experienced teams was evaluated, we cannot validate a positive correlation of cat friendly protocols with sedation dose nor the number of adverse reactions.

According to Ryan et al (2019),³ it has been demonstrated that when owners are more knowledgeable about

feline blood donations there is a stronger level of confidence in veterinary staff, thus contributing to the success and safety of the donation processes.³ We find this a crucial aspect in our programme, as it further strengthens the trusting relationship between the owner and the veterinary team.

In this study, acute reactions comprising pallor, weakness, tachypnoea and open-mouth breathing developed for eight (0.22%) of the 3690 blood donations, which represents a lower rate than in human studies. Newman et al (2003) reported that the most common reactions in human blood donors were fatigue, vasovagal symptoms, nausea and vomiting.¹⁸ In rare cases, this may progress to syncope and the donor collapsing.¹⁹ Factors that led to a vasovagal reaction were stress, tiredness and lack of sleep.¹⁸ Another study conducted in humans, by Sousa et al (2015), reported that of 1132 notifications of post-donation reactions, 64.8% comprised vasovagal symptoms and 35.2% were local signs and symptoms such as haematoma, arm soreness and post-donation bleeding.²⁰ According to Zervou et al (2005), such reactions occur because the blood donation procedure is unknown or unfamiliar to the donor, and the consequent stress may affect central neural activity, stimulating peripheral vasodilatation and, during the first donation, a vasovagal reaction.¹¹ The reaction may also be related to hypotension caused by volume depletion, the orthostatic hypotension effect related with bipedal stance, and the effect of a fear of needles, pain and sight of blood.¹⁰

In cats, vasovagal reactions may occur due to the volume depletion or stress factors associated with donation, as in humans.¹² In terms of physiological stress responses, Ryan et al (2019) explained that when an animal is exposed to long-term stress, homeostatic responses may lead to inappropriate or pathological behaviours, a consequence of the close communication and coordination between the nervous and the endocrine systems.³ Although adrenaline and cortisol levels are not usually measured in clinical practice, direct physiological responses such as increased heart rate, body temperature, respiratory rate and blood glucose, increased or decreased activity levels or sweating of the footpads allow for the assessment of animal welfare.³

In the present study, the three acute reactions in non-sedated donors could have been related to stress experienced during transportation and the procedure, as well as volume depletion and potentially hypotension. In the donors sedated in this study, lower doses were used for sedation for donation than those generally described in cats for feline procedural sedation and analgesia.²¹ Thus, despite minimal cardiorespiratory effects induced by diazepam, butorphanol^{22,23} and ketamine,²⁴ the five acute reactions seen in the sedated donors in this study could have been due to volume depletion and subsequent hypotension. Unfortunately, even though the adverse reactions reported were indicative of hypotensive crises, we cannot confirm this, as arterial blood pressures were

not measured during donation. More studies, including measurement of pre- and post-donation arterial blood pressure, are warranted.

Doolin et al (2017) studied and described a series of feline blood donations with and without sedation between 2010 and 2013.⁵ Seventy donation events occurred in unsedated cats and 45 occurred in sedated cats.⁵ They recommended general anaesthesia or heavy sedation for donation because movement and donor anxiety signs were lower in sedated donations.⁵ According to the 'AAFP and ISFM feline-friendly handling guidelines',²⁵ it is always preferable to use chemical restraint pre-emptively in order to increase safety and reduce stress for the cat.²⁶ Some authors, for example Spada et al (2014), recommend sedation in order to minimise sudden movements during the donation, which may compromise the procedure.²⁷ If the donation has to be stopped due to sudden movements, the blood unit must usually be discarded and the cat's blood vessels are sometimes damaged beyond a simple puncture, leading to haematoma and bruising.²⁷ Although the approach and restraint techniques are similar in sedated and unsedated cats, adverse reactions were more common in unsedated cats in one study.⁵ Our study found that of the sedated donors, 1.23% (n = 37) had post-donation reactions, and of the non-sedated donors, 0.71% (n = 5) had post-donation reactions. However, this study was not designed to evaluate the influence of sedation. We are aware that in several cases it would have been possible to collect blood without sedation, but the risk of sudden movement and the need for more rigorous physical restraint prompted sedation to be used. Our results suggest this was correct to do, as no adverse effects related to sudden movement during donation were reported. Moreover, our study found no harmful effects of our low sedative dose in donors, as no adverse drug reactions were reported. However, our results also suggest that a significant number of donations may be accomplished without sedation (19%, n = 701), as long as donors remain cooperative and relaxed during the procedure. This is a critical point and emphasises the need for an experienced and well-trained team, able to recognise subtle feline behaviours and assess the donor's temperament when considering if sedation is required.

According to our results, the adoption of cat friendly donation protocols that maximise animal welfare, a well-trained and experienced team, a calm environment and the appropriate use of sedation might decrease anxiety and stress during feline donations, which can reduce the number of post-donation reactions. However, the lack of a control group that was not subject to cat friendly techniques does not allow us to conclude definitively from this study that these factors decrease donor anxiety or the number of post-donation adverse reactions.

Conclusions

Blood collection in cats is not a risk-free procedure. Acute and delayed adverse post-donation reactions may occur,

but according to our study these are rare. More studies are needed to evaluate the influence of the sedation protocol on such reactions. Our results suggest that strict protocols focusing on donor safety and wellbeing should be implemented.

Author note This original study was presented as a poster in the 18th Annual European Veterinary Emergency and Critical Care Congress from 6–8 June 2019 in Tallinn, Estonia, using preliminary data collected from January to March 2019.

Supplementary material The following files are available online:

Appendix 1: Blood donor's registration form.


Appendix 2: Post-donation adverse reactions phone call protocol.

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Ethical approval This work involved the use of non-experimental animals only (including owned or unowned animals and data from prospective or retrospective studies). Established internationally recognised high standards ('best practice') of individual veterinary clinical patient care were followed. Ethical approval from a committee was therefore not necessarily required.

Informed consent Informed consent (either verbal or written) was obtained from the owner or legal custodian of all animal(s) described in this work (either experimental or non-experimental animals) for the procedure(s) undertaken (either prospective or retrospective studies). No animals or humans are identifiable within this publication, and therefore additional informed consent for publication was not required.

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