Management of massive blood loss in a dog under general anaesthesia during a sternotomy

A 2-year-old male neutered American Staffordshire Terrier was presented collapsed, with tachycardia, dyspnoea and pale mucous membranes. An emergency sternotomy and lateral thoracotomy was performed. Before surgery the dog's blood was typed and found to be DEA negative. The dog lost the equivalent of its entire blood volume (estimated) during the first hour of surgery. Cardiovascular parameters initially responded to boluses of crystalloids and colloids. He also received transfusions of DEA negative packed red blood cells and fresh frozen plasma. Due to ongoing haemorrhage, the dog's clinical condition, and a lack of availability of any more DEA negative blood products, the decision was made to give a unit of DEA positive packed red blood cells. The dog recovered uneventfully, although following diagnosis of an aggressive soft tissue sarcoma the dog was later euthanased. This report discusses the management of massive blood loss in veterinary medicine and the implications, potential options for management, and treatment of these cases perioperatively. 10.12968/coan.2019.24.1.8

Delphine Le Chevallier BVSc BSc MRes MRCVS) Second year resident in Anaesthesia; **Emma Love** BVMS PhD DVA DipECVAA MRCVS SFHEA, Senior Teaching Fellow in Veterinary Anaesthesia, School of Veterinary Medicine,University of Bristol, Langford, Bristol BS40 5DU. dl8832@bristol.ac.uk

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Massive blood loss may be defined as loss of one blood volume in 24 hours, or 50% of blood volume during 3 hours of surgery (Stainsby et al, 2000; Blain and Paterson, 2016). The initial physiological response is increased sympathetic tone, which maintains arterial blood pressure and perfusion to vital organs. However, once the physiological reserve has been reached, hypoperfusion will decrease the delivery of oxygen and nutrients to the tissues. This will cause both hyperlactaemia and a cascade of inflammatory responses (Gaunt and Woolley, 2014). This leads to the development of coagulopathies, systemic inflammatory response syndrome (SIRS) and ultimately cardiac arrest (Gaunt and Woolley, 2014).

Assessment of haemorrhage during surgery can be difficult, because anaesthesia can attenuate the physiological responses to haemorrhage, and because blood loss calculations may be inaccurate and often underestimate blood loss. Careful monitoring of blood loss (volume in the suction canister and weight of swabs) is essential. Cardiovascular responses to fluid administration, such as pulse pressure variation or systolic pressure variation, can be a good indicator of blood loss (Bickell et al, 1994; Drozdzynska et al, 2018).

The aims when managing an animal during haemorrhage are to restore oxygen delivery to the tissues, improve circulating volume and achieve haemostasis. The optimal fluid to use in the initial management of haemorrhage is controversial. Both crystalloids and colloids are effective in correcting hypotension, although administration of large volumes may lead to haemodilution, hypothermia, acidosis and coagulopathies (Cullen, 2012; Gaunt and Woolley, 2014; Chodan and Davidow, 2015; Grimm, 2015). Importantly, blood products (packed red blood cells (pRBC) and whole blood) are the only fluids to provide oxygen carrying capacity. There is clinical evidence in humans to suggest that administration of blood products compared to crystalloid resuscitation in the face of massive blood loss maintains endothelial integrity and reduces SIRS, coagulopathies and the need for volume (Gaunt and Woolley 2014). However, blood transfusions in people are associated with increased mortality, postoperative infection, and sepsis (Stainsby et al, 2000). In a retrospective study (953 transfusions in dogs), there was a 15% incidence of transfusion reactions, most commonly fever and vomiting (Bruce et al, 2015). Mortality rates were less than 1%, with dogs usually dying from an underlying disease process rather than as a direct

Table 1. Arterial blood sample values at different times

	A	B	C	D
pH (7.35–7.45)	7.287	7.283	7.340	7.123
$PaCO_2$ 35–45 mmHg)	53.1	45.6	44.3	76.4
PaO_2 (80–500 mmHg)	70.9	240	374	247.1
HCO_3- (20–24 mmol/L)	24.8	21.1	23.4	24.4
Base excess (- 5–0)	-1.9	-5.1	-2.1	-5.3
$Sp0_2$ (90–100%)	91.7	99.9	99.7	99.5
Na^+ (139–150 mmol/L)	140.4	140	140.1	140.3
K^+ (3.4–4.9 mmol/L)	3.37	3.61	3.2	2.88
Ca^{++} (1.12–1.4 mmol/L)	1.33	1.15	0.74	1.18
Cl^- (106–127 mmol/L)	111	112	114	115
Anion gap (8–25 mmol/L)	8	10.5	5.9	3.7
Haematocrit (35–50%)	24	18	13	26
Total haemoglobin (12–17 g/dL)	8	6	4.4	8.9
Glucose (3.3–6.4 mmol/L)	6.5	8.2	7.8	6.5
Lactate (0.6–2.0 mmol/L)	6.5	4.22	2.5	1.35

A,B,C,D correspond to time points in minutes during the general anaesthesia (GA); A = T20 (20 minutes after initiation of GA), B = T90, C = T180, D = T240

result of blood product administration (Bruce et al, 2015). If blood products are used, there are logistical considerations with stock availability, requirements for early blood typing, and organisation within the veterinary hospital, as well as the cost of the products.

Case description

A 2-year-old male neutered American Staffordshire Terrier, weighing 30 kg, was presented with tachycardia, dyspnoea and acute collapse with pale mucous membranes. He had been presented to the hospital 2 weeks previously with a haemothorax and similar clinical signs. At that time, computerised tomography (CT) revealed a right thoracic mass, considered most likely to be a thymic involution causing haemorrhage. He improved following fluid therapy and rest, and was discharged from the hospital.

At re-presentation, manual packed cell volume (PCV) and total solids (TS) were 45% and 52 g/l respectively. A blood smear revealed mild thrombocytopenia, which was interpreted as being due to increased platelet consumption in the face of haemorrhage. On thoracic focused assessment with sonography for trauma (TFAST) a small amount of free fluid was seen, but the volume was too small to sample. Intravenous (IV) fluid therapy (Hartmann's solution) was started, and a nasal cannula was fitted for administration of oxygen. Overnight the dog became tachypnoeic, tachycardic (160–200 beats per minute (bpm)), and his oxygen saturation (SpO_2) dropped to 90%. Ongoing intrathoracic haemorrhage was suspected, and confirmed by thoracocentesis, which yielded a sample with a PCV of 36% and TS of 52 g/l. This matched a blood sample taken from his jugular vein. Radiographs revealed a large mass in the right thorax. Within a few hours his PCV had dropped to 22% and TS to 42 g/l. Coagulation tests were normal (activated partial thromboplastin time (APTT) 88 seconds, prothrombin time (PT) 155 seconds). He was blood typed (DEA 1.1 negative) and given half a unit of pRBC. Due to the continued blood loss and lack of clinical improvement, emergency surgical resection of the mass via a sternotomy was planned.

Both cephalic veins were cannulated. The pre-anaesthetic clinical examination revealed a pulse rate of 120 bpm synchronous with the heart, hyperdynamic peripheral pulses, pale mucous membranes and a capillary refill time (CRT) of <3 seconds. The dog was tachypnoeic, and required supplementation of inspired oxygen to maintain his SpO2 above 90%.

Methadone (0.3 mg/kg IV) was administered and a facemask used for preoxygenation. Anaesthesia was induced IV with ketamine (0.5 mg/kg) followed by alfaxalone given to effect (1.5 mg/kg required). After endotracheal intubation with a cuffed tube, intermittent positive pressure ventilation (IPPV) was started using a Nuffield 200 Ventilator with a flow rate set at 0.3 L/s, inspiratory time of 1 second, expiratory time of 4 seconds and peak inspiratory pressure (PIP) of 12 cmH_2O. Antibiotics (cefuroxime) were given before the start of surgery and every 90 minutes thereafter. General anaesthesia (GA) was maintained with sevoflurane vaporised in oxygen, using a rebreathing system (circle). In addition to visual monitoring of respiratory rate and tactile monitoring of pulse quality, monitoring was carried out using electrocardiography, pulse oximetry, capnography, oesophageal temperature, and non-invasive arterial blood pressure measurement (oscillometric) until cannulation of the right dorsal pedal artery with a 22 G catheter enabled direct arterial blood pressure measurement. The first arterial blood gas (ABG) (*Table 1*, column A) revealed an acidaemia, respiratory acidosis, severe hypoxaemia and a haemoglobin concentration of 8 g/dL. Hartmann's solution was administered IV at a rate of 10 mL/kg/h and tranexamic acid (10 mg/kg) was given IV.

In theatre, a GE Aespire S5 Anesthesia Machine with 7900 Smartvent was used on a volume-controlled pressure limited mode: a tidal volume (TV) was set a 10 mL/kg, inspiration:expiration ratio of 1:2, respiratory rate (RR) at 12, PIP at 20 mmHg and positive end expiratory pressure (PEEP) 0 mmHg. Continuous rate infusions (CRI) of ketamine (10 µg/kg/minute) and fentanyl (10 µg/kg/h) were started. A second ABG (*Table 1*, column B) just before start of the sternotomy revealed an acidaemia with a hyperlactaemia, but an improved partial pressure of oxygen with a haemoglobin of 6 g/dL.

As surgery began, the heart rate (HR) and mean arterial pressure (MAP) increased from 100 to 160 bpm and from 85 to 110 mmHg respectively. The changes were interpreted as responses to nociception, therefore sequential boluses of 3 µg/kg of fentanyl (12 µg/kg total) were administered and the ketamine CRI was

increased to 20 µg/kg/min. This reduced the heart rate (90 bpm) and MAP (65 mmHg). Once the thorax was opened, severe active bleeding was seen. The heart rate increased to 180 bpm and the MAP decreased to 50 mmHg. Two boluses of 10 mL/kg Hartmann's solution and one gelatin based colloid bolus (Geloplasma, Fresenius Kabi, Runcorn) of 15 mL/kg were administered while blood products were prepared for administration. Blood pressure and heart rate (HR) returned to values seen after induction of GA. Due to the position of the mass in the dorsal thorax, the surgeons closed the sternotomy and started a right lateral thoracotomy. At the end of the first surgery, a 50% blood volume loss was estimated using the measurements described in *Table 2*. Packed red blood cells and fresh frozen plasma (FFP), one unit each and both DEA 1.1 negative, were administered at an initial rate of 0.5 mL/kg for 10 minutes, although due to the massive blood loss this was rapidly increased to 60 mL/kg/h. Once the thoracic cavity was entered for second surgery, the dog became mildly hypotensive and tachycardic (MAP 55 mmHg, HR 130 bpm). Three fluid boluses of 10 mL/kg Hartmann's solution improved the MAP and reduced the HR. An ABG (*Table 1*, C) revealed an improved pH with mild acidaemia, an improved hyperlactaemia, hypocalcaemia and hypokalaemia, with a severely low haemoglobin. Given the continuing blood loss, low haemoglobin concentration and no further DEA 1.1 negative products being available, the decision was made to administer a unit of DEA 1.1 positive pRBC. No immediate haemolytic reactions or anaphylaxis were seen. During the last 30 minutes of the surgery, the HR decreased from 100 to 40–50 bpm and MAP was 75 mmHg. Although a heat mat (at 39°C) was placed under the dog during the procedure, the dog's body temperature dramatically reduced from the start of the surgery, to between 32–34°C by the end of surgery. A thoracostomy tube was placed. During the skin closure, the ketamine CRI was reduced to 10 µg/kg/min and the fentanyl to 5 µg/kg/h.

During the surgery, haemoglobin oxygen saturation was maintained above 95% and no arrhythmias were observed.

At the end of surgery, fluid loss equivalent to 100% blood volume loss was estimated (*Table 2*). During this time, the dog had received a total volume of 3750 mL of fluids (*Table 3*).

At the end of surgery, sevoflurane administration was discontinued and spontaneous ventilation resumed. The dog was transferred to the Intensive Care Unit (ICU) while receiving oxygen via the endotracheal tube, and this was continued in the ICU. A urinary catheter was placed. The fourth ABG, with the trachea still intubated (*Table 1,* column D) revealed significant acidaemia with a severe respiratory acidosis, an improved ionised calcium, hypokalaemia, normal lactate and an improved haemoglobin. The manual PCV was 33% and TS 32 g/L. Postoperative analgesia was give: ketamine CRI at 10 µg/kg/min, fentanyl 5 µg/kg/h and paracetamol 10 mg/kg IV every 8 hours. Hartmann's solution supplemented with 28 mmol/L potassium chloride was administered (4 mL/kg/hr) and tranexamic acid (10 mg/kg IV every 8 hours). Recovery from anaesthesia was smooth, and the dog was discharged from the hospital 5 days later.

Unfortunately, histopathology performed on the biopsies of the mass revealed an aggressive soft tissue cell sarcoma, and euthanasia was performed by the referring veterinary surgeon.

Discussion

It was estimated that the dog lost his entire blood volume during the 3 hours of surgery, which is considered to be a massive haemorrhage (*Table 2*). The published UK guidelines for people emphasise the importance of restoring blood volume to maintain tissue perfusion and oxygenation; and of achieving haemostatis by treating the source of bleeding and permitting coagulation (Stainsby et al, 2000; Kisielewicz and Self, 2014). There is no evidence for the optimal fluid and timing of administration for dogs when treating acute haemorrhage (Jutkowitz et al, 2002; Kwan et al, 2014). The dog initially received a large volume of crystalloids and colloids in response to tachycardia, hypotension and increased serum lactate, which are indicators of hypoperfusion and inadequate delivery of oxygen to the organs (*Table 3*). These fluids are effective at correcting hypotension, but can lead to acidosis, hypothermia and coagulopathy. Furthermore, they do not provide oxygen carrying capacity and although they can improve microcirculatory perfusion by reducing blood viscosity, they can exacerbate the failure of oxygen delivery to the tissues by diluting the residual erythrocytes.

In response to fluid therapy the dog's vital parameters (HR, MAP, lactate) improved, but the haemoglobin concentration dropped to 4.4 g/dL. There is no consensus in the veterinary literature about when to administer blood products based on haemoglobin levels. In people, current guidelines from the American Association of Blood Banks (AABB) have a conservative approach to blood transfusion, with a transfusion not given until haemoglobin falls below a 'trigger' of 7 g/dL rather than 8–9 g/dL (Carson et al, 2016). This level was based on 31 randomised control trials (RCT) showing that a conservative RBC transfusion threshold was not associated with higher rates of adverse clinical outcome,

Table 2. Theatre blood loss record from this dog during general anaesthesia

	Total weight of swabs (g) (A)	Number of swabs (B)	Weight of dry swabs (g) (C)	Volume of blood (mL) (1g = 1 mL) (= A – C)
Small swabs (6 g each) (D)	208	21	126	82
Laparotomy swabs (20 g each) (E)	1411	22	440	971
Amount contained within suction			+	1650
Estimated amount on drapes			+	10
Volume of saline used in surgery (e.g. to clear the operating field)			–	15
Total blood loss (mL)			=	2698
Estimated percentage of blood volume* lost (total blood loss/estimated blood volume x 100)				100%
*Estimated blood volume calculated as 90 mL/kg (dog)				

KEY POINTS

- Massive blood loss, defined as more than 50% blood volume in three hours, leads to physiological responses including increased sympathetic tone and tachycardia.
- Normal physiological responses may be masked during anaesthesia, so anticipating surgical haemorrhage, careful monitoring of blood loss, and communication with the surgeons are essential.
- Management of blood loss should be based on the amount of volume lost and the patient's physiological response, with the aim of maintaining the circulating volume, tissue oxygen delivery and haemostasis.
- It is important to know the implications of the treatments: large volumes of crystalloids (such as Hartmann's solution) may result in haemodilution, electrolyte imbalances and coagulopathies, while administration of blood products can cause transfusion reactions.
- Volume replacement and maintaining oxygen carrying capacity are the priorities during acute blood loss, but the consequences of rapid fluid replacement, such as electrolyte abnormalities, coagulopathies and hypothermia, also need to be monitored and treated.

Table 3. Fluid replacement in this dog during acute blood loss during general anaesthesia

Hartmann's solution	2000 mL	66.6 mL/kg
Gelatin-based colloid	500 mL	16.6 mL/kg
pRBC DEA 1.1 +	350 mL	11.6 mL/kg
pRBC DEA 1.1 -	550 mL	18.3 mL/kg
FFP	350 mL	11.6 mL/kg
Total volume replacement	3750 mL	125 mL/kg

FFP: fresh frozen plasma. pRBC: packed red blood cells

mortality or post-operative complications (Lier et al, 2008). Recommendations for resuscitation from haemorrhagic shock in people advocate a 1:1 ratio of FFP:pRBC to restore the lost blood cells and coagulation factors (Gaunt and Woolley, 2014). During the surgery the dog received non-compatible blood products. The clinical decision to give incompatible blood was based on severe ongoing haemorrhage, a very low haemoglobin concentration (4.4 g/dL) and evidence of inadequate oxygen delivery and increased anaerobic respiration (lactate >2 mmol/L). The benefits and needs were considered to be greater than the risk of acute haemolytic reaction and anaphylaxis (Chodan and Davidow, 2015; Redding and Plews, 2016); furthermore, since dogs lack isoantibodies, the first transfusion is unlikely to cause an immune reaction. Fresh whole blood would have been more appropriate and ideally would have been gven in this situation, as this includes platelets, which are not found in pRBC or FFP.

Using a cell salvage device to permit autologous blood transfusion might have been a useful strategy in this case. The autologous RBC have antigenic compatibility and have not undergone cellular associated changes to reduced function and duration (oxygen delivery capacity). The use of a cell salvage device might also have reduced costs associated with pRBC transfusion (Kellett-Gregory et al, 2013). In people, their use is rarely associated with complications apart from coagulopathies and electrolytes abnormalities (Esper and Waters, 2011; Kellett-Gregory et al, 2013). The presence of neoplasia in this case complicates the decision on whether to use cell salvage techniques. There is the theoretical potential for disseminating neoplastic cells via the vascular system, although controlled trials have not reported an increase in metastasis or mortality compared to transfusions of previously-collected autologous blood (Esper and Waters, 2011). Retrospectively, since we had access to a limited immediate supply of blood products, and in view of the size of the dog and the high risk of bleeding, using a cell salvage device should have been considered.

Hypocalcaemia and hypokalaemia were observed after transfusion of two units of pRBC and one unit of FFP alongside the administration of Hartmann's solution and gelatin based colloids. This can be caused by dilutional effects, citrate overload, hypoproteinemia and re-entry of electrolytes into transfused cells (Blain and Paterson, 2016). There were no changes on the electrocardiogram, such as a prolonged QT interval or inversion of the T wave (Chodan and Davidow, 2015). Calcium is important in coagulation, contractility and heart rate. Reduced activation of coagulation on platelets and disruption of haemostatis is clinically evident if the ionised calcium falls below 0.6 mmol/L and the pH below 7.3 (Lier et al, 2008). The low calcium may have contributed to the bradycardia at the end of surgery, although this is likely to have been multifactorial, in combination with severe hypothermia, bradycardia due to myocardial hypoxia, and reduced nociceptive stimuli (Korner and Edwards, 1960; Grimm, 2015). The calcium levels returned to normal by 1 hour after recovery from anaesthesia, while the potassium continued to decrease, so the dog's crystalloid fluids were supplemented with potassium chloride. Due to the complexity of the case and concerns regarding the potential for accidental administration of fluid containing excessive amounts of electrolytes, potassium and calcium were not administered intraoperatively, although retrospectively responding to these electrolyte abnormalities more rapidly may have been beneficial. A more proactive approach to the management of electrolyte abnormalities in animals receiving large volumes of fluids and blood products will be adopted in the future.

Tranexamic acid (TA) is an antifibrinolytic drug. In people there is evidence that when administered during active bleeding it reduces blood loss and requirements for blood transfusion (Blain and Paterson, 2016). Tranexamic acid has been evaluated in healthy dogs and has been reported to be safe at clinical doses of 10 mg/kg (Kelmer et al, 2013). Assessment of its anti-fibrinolytic properties using thromboelestography were inconsistent (Kelmer et al, 2013; Kelmer et al, 2015). A retrospective evaluation of the efficacy on TA in bleeding dogs showed that dogs receiving TA received less volume of blood products than those that were not treated with this drug (Kelmer et al, 2015). Prospective studies are

warranted to determine its efficacy intraoperatively. Because of its potential benefits and apparent absence of adverse effects in dogs, TA is being used more commonly in veterinary medicine.

Conclusions

This case was challenging and underlines the need for further studies and consensus in dealing with massive blood loss. Retrospectively, the dog could have benefitted from supplementation of electrolytes, although at the time volume replacement and oxygen carrying capacity were prioritised. The dog's young age may have contributed to him tolerating such a significant physiological stress well. Volume replacement was only just adequate, and in hindsight the dog should have received whole blood, with closer attention paid to electrolyte levels. CA

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