Acute normovolaemic haemodilution — 2 case studies

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ABSTRACT

Acute normovolaemic haemodilution (ANH) is a technique used to preserve a patient's owns red blood cells and reduce the incidence of heterogeneous blood transfusion. This paper describes the use of the technique in a dog and a kitten. A significant benefit of ANH can be shown in the canine case presented. The dog lost 1800 mℓ of blood during surgery but the haematocrit was only reduced to 33 % 6 hours after the end of surgery. The kitten, however, did not benefit from ANH. It lost a small volume of blood during surgery and developed complications. This paper also describes some of the potential complications that may occur. To the best of my knowledge, this is the 1st clinical description of ANH in a dog and a cat.

Key words: acute normovolaemic haemodilution, blood loss, kitten, dog, haemodilution.

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INTRODUCTION

As blood is lost from the body during surgery, fluid is infused to maintain normovolaemia, and as a result, haemoglobin concentration decreases, corresponding with a drop in the oxygen carrying capacity of blood. Oxygen delivery in the body is dependent on cardiac output and oxygen carrying capacity[7]. With a decrease in oxygen carrying capacity an increase in cardiac output is required to maintain the same rate of oxygen delivery[7]. Surgery results in blood loss while anaesthetic agents reduce oxygen consumption. As a result, lower haematocrits may be tolerated under anaesthesia but on recovery the deleterious effects of anaemia may become evident. It should also be borne in mind that most anaesthetic agents depress cardiovascular function, and anaemia may not be tolerated under anaesthesia. Clinical signs of anaemia under general anaesthesia may not be evident.

In order to maintain optimal oxygen delivery by the maintenance of an adequate concentration of haemoglobin, a blood transfusion may be necessary after invasive surgery with massive haemorrhage. Concerns raised with the transfusion of blood include the transmission of disease, septicaemia, transfusion reactions, hypocalcaemia, hypothermia, coagulation defects and vomition[1]. A number of techniques have been described to conserve red blood cells in the peri-operative period. Acute normovolaemic haemodilution (ANH) is one such technique. As far as I can establish, ANH has not been reported in dogs and cats in a clinical setting.

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CASE 1

An 11-month-old, 2.9 kg female Burmese kitten with a history of a chronic nasal discharge, was presented to the Onderstepoort Veterinary Academic Hospital (OVAH). A full clinical examination, haematology, skull and nasal radiographs and a nasal biopsy were performed. A diagnosis of severe chronic active hyperplastic to ulcerative rhinitis was made. An exploratory ventral rhinotomy and curettage was planned. The kitten's haematocrit prior to surgery was 41 %. A 2.9-kg kitten has an approximate circulating volume of 240 mℓ. As blood loss during nasal surgery can be high, the kitten was cross-matched to a donor, and at the same time a decison was made to perform ANH. A 22-G catheter (Jelco, Johnson & Johnson) was inserted into the cephalic vein. The kitten was premedicated with diazepam intravenously (Valium, Roche Products) (0.2 mg/kg) and morphine subcutaneously (Intramed Morphine, Intramed) (0.1 mg/ kg). The kitten was then induced with propofol intravenously (Diprivan, Astra-Zeneca) (5 mg/kg) and maintained on halothane (Fluothane, Astra-Zeneca). A large-bore catheter (16-G Jelco) was inserted into the jugular vein from which 40 mℓ of blood was then collected in heparin (Sodium Heparin, Intramed). The blood volume removed was replaced with Hetastarch (Haessterile, Fresenius-Kabi) (40 mℓ) and Ringer's lactate (Ringers solution, SABAX, Adcock Ingram) (20 mℓ). The amount of blood removed was calculated according to Equation (1). It was calculated that the kitten would have a haematocrit of 35 % after ANH. The actual haematocrit recorded after ANH was 20 %. Surgery was then performed, which lasted approximately 55 minutes. Ringer's lactate was given to replace lost blood. Blood loss during surgery was approximately 40 mℓ. After surgery the kitten's haematocrit was 18 %. The blood drawn earlier was then transfused back into the kitten. A profuse haemorrhagic diathesis became evident shortly after the transfusion. Blood seeped from the nasal passages and from the rectum. The nasal loss of blood was estimated at 30 mℓ based on the weight of gauze swabs. The cause of haemorrhagic diathesis was iatrogenic due to heparin from the transfused blood. The kitten was treated with protamine sulphate (Protamine Sulphate, Glaxo-Welcome) at a dose rate of 0.5 mg protamine per 100 iu of heparin. It was estimated that the kitten received 2000 iu of heparin from the blood transfusion. The haemorrhagic episode stopped shortly after protamine was administered. The haematocrit post-transfusion was 22 % and 6 hours later it was 34 %. The kitten's haematocrits are illustrated in Fig. 1. During the anaesthetic and recovery periods the kitten was monitored continuously with an electrocardiograph (Datex Satellite Plus, Datex), pulse oximeter (Datex Satellite Plus, Datex) and capnograph (Capnomac, Datex).

Remarks

The blood lost during surgery was small (40 mℓ). Had the kitten lost this blood with his initial haematocrit of 41 %, at the end of surgery, after replacing the blood loss with fluid, the final haematocrit would have been ~35 %. This kitten lost an additional 30 mℓ due to heparinisation. Total blood loss was thus estimated to be 70 mℓ, and should all of this blood have been lost at a haematocrit of 41 %, the final haematocrit would have been 29 %. At 6 hours post-transfusion the kitten's haematocrit was 34 %, which represents a red blood

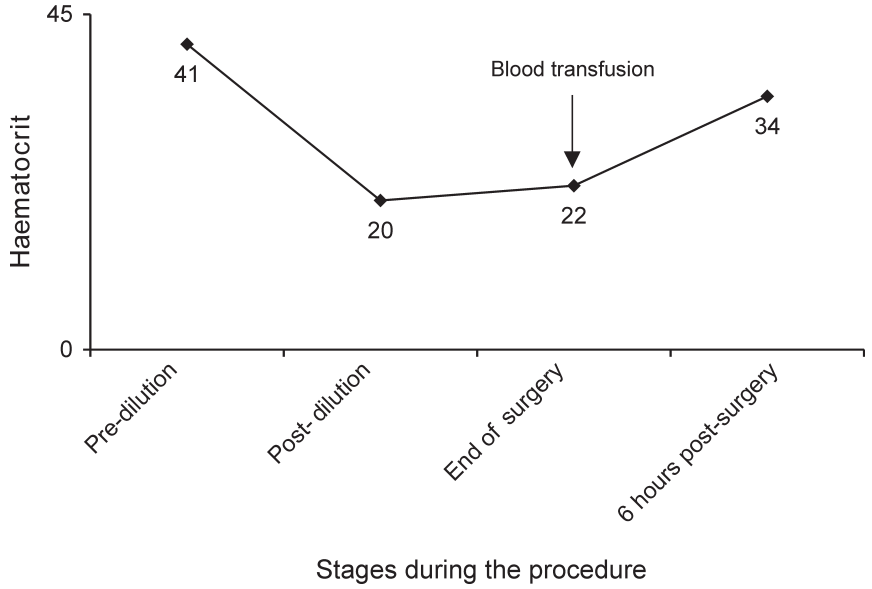

Fig. 1: **Haematocrits of the kitten during haemodilution and at various stages of surgery. The transfusion was given at the end of surgery.**

cell saving of 17 %. In reality, ANH in this case was unwarranted in view of the relatively small blood volume lost through nasal surgery. When planning an anaesthetic protocol of this nature the potential for blood loss should be the driving force behind the application of ANH. After blood collection and dilution the kitten's actual haematocrit was 20 % and not the desired level of 35 %. The decision to haemodilute the kitten to 35 % was an arbitrary one, mainly aimed at preventing haemoconcentration. The dilution of the haematocrit to below the calculated level is the result of volume expansion due to hetastarch and the administration of fluid. This represents hypervolaemic haemodilution.

There are a number of problems associated with the collection of blood in heparin, such as platelet aggregation and inhibition of coagulation factors[1]. A dose of 5–10 iu of heparin per mℓ of collected blood is recommended[1]. Heparin was chosen in this case because of its availability when the procedure was performed.

CASE 2

A 10-year-old, 25 kg female Labrador cross with a history of epistaxis over 2 months was referred to the OVAH. A full clinical examination, haematology, nasal, skull and lung radiographs and a nasal biopsy were performed. A diagnosis of telangiectatic osteosarcoma was made. A decision was made to perform a dorsal rhinotomy and to remove the tumour if possible. A 14-G Catheter (Jelco) was inserted into the cephalic vein. The dog was premedicated with diazepam intravenously (0.2 mg/kg) and morphine subcutaneously (0.1 mg/kg), induced with thiopentone intravenously (Intraval Sodium, Rhône-Poulenc) (10 mg/kg) and maintained on halothane. A large-bore catheter (12-G Intraflo, Vygon) was inserted into the jugular vein. The estimated circulating volume of blood in this dog was 2000 mℓ. The haematocrit immediately prior to induction was 43 %. The blood volume for removal was calculated as 900 mℓ to achieve a haematocrit of 25 %. The blood removed was divided into 2 units of 450 mℓ each. After each unit of blood had been removed, volume was replaced with hetastarch and Ringer's lactate. The 2nd unit of blood collected had a lower haematocrit than the 1st. The dog's haematocrit after the 1st unit of blood was drawn was 30 %, and after the 2nd unit it was 26 %. In total, 500 mℓ of hetastarch and 500 mℓ of Ringer's lactate was administered. Surgery then commenced and the tumour was removed within 45 minutes. During surgery, 1200 mℓ of blood was lost via suction and ~260 mℓ on swabs (swabs were weighed). This represents a total blood loss of 1460 mℓ. Blood lost during surgery was replaced with Ringer's lactate on a volume basis. Blood pressure (Capnomac II, Datex), electrocardiography, pulse oximetry and capnography were monitored throughout the anaesthetic period. Haematocrit and blood gas analyses were performed regularly. The haematocrit reached 18 % 10 minutes before the end of surgery and the unit of blood drawn last was transfused into the patient. This was followed by the 1st unit when the surgery had been completed. Six hours after the end of surgery the patient's haematocrit was 33 %. This patient's haematocrits are plotted in Fig. 2. In total, 2000 mℓ of Ringer's lactate was given. No specific blood gas abnormalities were observed.

Remarks

This dog lost almost its entire circulating blood volume during the anaesthesia. If this blood had been lost at the original haematocrit of 43 %, the dog's final haematocrit would theoretically have been 5 %. Fluid therapy during surgery to replace blood lost would, however, have diluted the blood in circulation, resulting in less haemoglobin being lost per millilitre of blood lost. What is certain, though, is that if haemodilution had not been performed, a blood transfusion would have been necessary. In this case, ANH served its purpose – saving red blood cells.

DISCUSSION

Haemodilution works on a very simple principle. If 1000 mℓ of blood is lost with a haematocrit of 45 %, a total of 450 mℓ of red blood cells are lost. However, if the haematocrit was only 25 %, only 250 mℓ of red blood cells are lost. This represents a saving of 200 mℓ of red blood cells. Two techniques have been developed to save red blood cells. The 1st is acute normovolaemic haemodilution in which blood is removed from the body and replaced with crystalloids and colloids. Normally the haematocrit is reduced to 25 % but in exceptional cases it is reduced to 20 %. The 2nd technique is hypervolaemic haemodilution, in which the patient is vasodilated and the blood diluted with crystalloids and colloids. What is more important regarding this concept is that haemoconcentration increases haemoglobin loss in a patient. Fluid deficits from fasting, 3rd-space losses, dehydration, diarrhoea and vomition should be corrected before surgery commences[5].

The amount of blood that can be lost during surgery can be estimated using the following equation:

$$ABL = EBV \times (Ht_0 - Ht_l)/(Ht_{ave}) \quad (1)$$

where ABL = allowable blood loss, EBV = estimated blood volume, Ht_0 = initial haematocrit, Ht_l = lowest allowable haematocrit, and Ht_{ave} = average haematocrit ($(Ht_0 + Ht_l)/2$). The estimated blood volume is usually determined as 8 % of body mass.

The allowable blood loss for each patient should be calculated prior to surgery. The lowest allowable haematocrit is usually 20 %. All blood lost during surgery needs to be replaced with fluids. Once the allowable blood loss level has been reached a blood transfusion should be considered. The allowable blood loss for case 1 was 165 mℓ and for case 2, 1460 mℓ.

The above equation is also used to determine the quantity of blood to be withdrawn for ANH. Ht_l is then the desired diluted haematocrit. This equation was

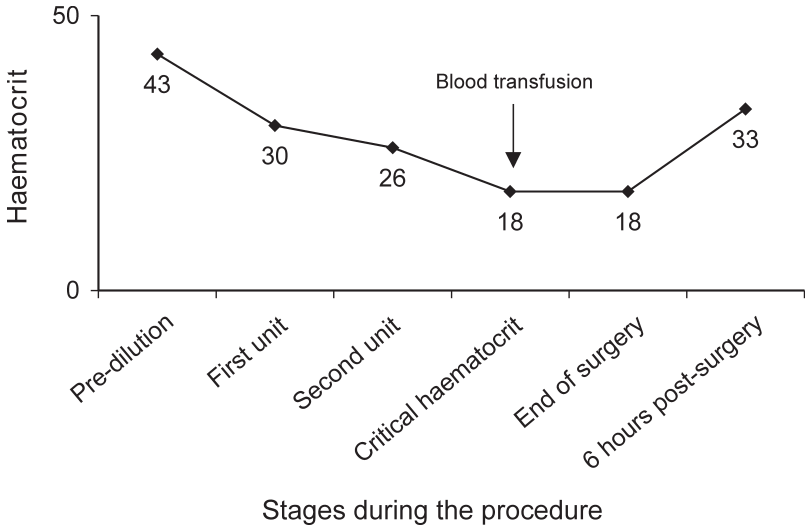

Fig. 2: **Haematocrits recorded for the dog during haemodilution and at various stages of surgery. 'First unit' and 'Second unit' = haematocrits after the 1st unit and 2nd unit of blood were drawn, respectively. 'Critical haematocrit' = transfusion of blood** (10 minutes before the end of surgery)**. The figures are the actual values recorded at each time interval.**

originally introduced by Gross[2].

As the haematocrit is reduced, blood viscosity is proportionally reduced. The reduction in blood viscosity is paralleled by a reduction in resistance to blood flow[7]. This enhances cardiac output if the heart maintains the same work rate. Thus the reduction in oxygen carrying capacity is compensated for by the 'automatic' increase in cardiac output[7,8]. Anaemic hypoxia is a potential complication of haemodilution if careful attention is not paid to oxygen delivery (haemoglobin concentration)[5]. The critical value of haemoglobin at which oxygen delivery is equal to oxygen utilisation has been shown to occur at 3.5–4.0 g/dℓ (haematocrit of ~10 %)[8]. Total oxygen extraction at this point is approximately 60 %, which correlates with values recorded during haemorrhagic shock[8]. The increased cardiac output during haemodilution is not necessarily distributed equally to all organ systems[8]. Renal blood has been shown not to increase during haemodilution, with renal hypoxia being a real risk[8]. Other organ systems that are affected include the liver and intestines[8]. Under anaesthetic conditions, cardiac output does not always increase in response to hypoxia[8].

The recommended level of haemodilution is to a haematocrit of 20–25 %[3,7]. Haemodilution to a haematocrit of 9 % has been reported[7]. A haemodiluted haematocrit of 16 % has been well tolerated by dogs[7]. The level of tolerance to haemodilution is determined by the margin of oxygen delivery in relation to cardiac output and oxygen carrying capacity[7]. The critical value for oxygen delivery appears to be 10 mℓ O_2/100g/min[4].

Under haemodiluted conditions, systemic oxygen extraction increases and this is reflected in a decreased mixed venous saturation[7]. A rise in arterial lactate and an unaltered pH have been recorded[7]. As blood loss occurs, and if this is not compensated for with adequate fluid resuscitation, the following events occur[7]:

a) Mixed venous saturation decreases rapidly to critical levels.
b) Arterial lactate concentration rises rapidly.
c) Arterial blood pressure drops owing to a reduction in cardiac output.

Shou *et al.*[7] reported that when haemodiluted (Ht 11 %), all pigs in their study that lost 40 mℓ/kg of blood died due to cardiovascular collapse[7]. Their control group of non-haemodiluted pigs (Ht 33 %) tolerated this blood loss with only 1 death in 6 pigs[7]. They concluded that hypovolaemia during haemodilution is not tolerated by pigs and adequate fluids should be given intra-operatively as blood loss occurs[7].

The intention of ANH is to reduce red blood cell loss. In so doing, the clotting factors, white blood cells and platelets are diluted as well. Evidence for changes in coagulation pathways is inconclusive. Hobisch-Hagen *et al.*[3] found no statistical difference in prothrombin time and activated partial thromboplastin time between the haemodiluted group and the control group[3]. They also studied fibrinolysis and concluded that there was no statistical difference between groups[3]. What they could conclude was that the degree of coagulation and fibrinolytic disturbances was correlated with the invasiveness of surgery[3]. This study is not alone in its conclusion concerning coagulation[3]. Refrigeration of blood destroys platelets[5]. Blood may be kept for 8 hours at room temperature after which it should be discarded[5]. Hetastarch may affect coagulation by inhibiting platelets, precipitating Factor VIII function and volume dilution of clotting factors[6].

Synthetic colloids exert an oncotic pressure and counteract the drop in protein oncotic pressure due to haemodilution[6]. Hetastarch 6 % may used on a volume to volume basis to replace blood withdrawn. Hetastarch 10 % is hypertonic and additional fluid may be required. Hetastarch 10 % results in a volume expansion of a 140 % of the infused volume such that 500 mℓ of hetastarch will increase plasma volume by 700 mℓ[6]. The maximum recommended dose of hetastarch is 20mℓ/kg[6].

Haemodilution is contraindicated in patients with lung disease with an associated desaturation of haemoglobin, increased oxygen consumption as occurs with sepsis and fever, myocardial and valvular disease and in patients with chronic anaemia[5]. Any disease process that affects the loading of oxygen onto haemoglobin or the transport of haemoglobin within the body, indicates that the patient has an impaired ability to tolerate anaemia[5]. In patients with severe cardiac disease, a haematocrit below 30 % is seldom tolerated[5].

Invasive monitoring should be performed when more than 20 % of circulating volume is removed from circulation[5], including central venous pressure and invasive blood pressure. Standard monitoring for ANH should also include haematocrit or haemoglobin concentration, urine output, electrocardiography, pulse oximetry, capnography, respiratory rate, heart rate and non-invasive blood pressure[5]. The nature of the surgery and the clinical status of the patient may indicate that additional monitoring is needed.

In pratice, ANH involves the following steps:

a) Determine the haematocrit to which haemodilution is allowed to drop.
b) Calculate the quantity of blood that can be removed.
c) Establish 2 ports for venous access with large-bore catheters (Fig. 3).
d) Collect blood from one catheter while administering crystalloids and colloids *via* the 2nd catheter to replace blood lost. Different venous drainage pools should be used to prevent excessive dilution of collected blood. Blood drawn should be clearly labelled. When surgery commences, use crystalloids and colloids to replace blood lost and monitor the haematocrit regularly (Fig. 4).
e) When the haematocrit reaches a

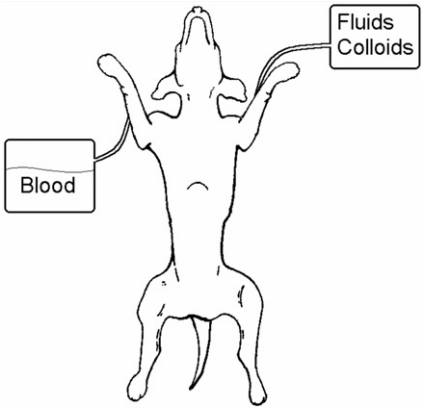

Fig. 3: **Blood collection – Blood collected during haemodilution should be drawn from a different venous drainage system as to what the crystalloids and colloids are administered to restore blood volume. The cephalic and external jugular veins may be used**.

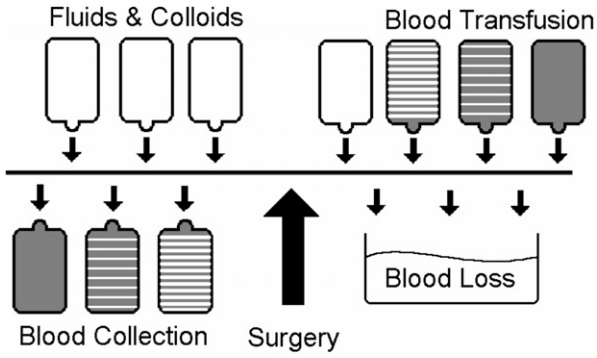

Fig. 4: **Blood collection and administration – As blood is collected, crystalloids and colloids are used to maintain normovolaemia. The 1st unit of blood has the highest haematocrit while the last unit of blood has the lowest haematocrit. Surgery commences and blood is lost. Initial circulating volume can be maintained with fluids and colloids but as the haematocrit reaches critical levels, blood is transfused. The last unit of blood drawn should be transfused 1st.**

critical level (≤18 %), transfuse the harvested blood into the patient. The unit of blood drawn last should be used 1st as it has the lowest haematocrit and therefore, if blood loss continues, the least amount of haemoglobin is lost. The unit of blood drawn 1st is given last (Fig. 4).

CONCLUSION

Acute normovolaemic haemodilution is an option to preserve a patient's own red blood cells. As with all procedures, a number of potential complications are associated with it. Any technique used to save red blood cells cannot compensate for poor surgical technique. Appropriate monitoring is indicated according to the clinical status of the patient and the degree to which the patient is haemodiluted.

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