TITLE: Twelve autologous blood transfusions in eight cats with haemoperitoneum

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Abstract

Objective: The objectives of this study were to describe the clinical use and outcome of autologous transfusions in cats with intracavitary haemorrhage
Methods: A retrospective descriptive study was performed. Computerised medical records of a single referral centre were searched for cats receiving an autotransfusion. Medical records were evaluated for underlying disease process, autotransfusion technique, autotransfusion volume, time period over which the autotransfusion was given, packed cell volume (PCV) pre and post autotransfusion, percentage rise in PCV, use of other blood products and any complications of the procedure. Survival to discharge and survival at 2 months was documented.
Results: Between July 2012 and March 2018 a total of 12 autotransfusions were performed in 8 cats. All patients were diagnosed with haemoperitoneum. Four of the 8 cats were diagnosed with abdominal neoplasia, 3 had post-operative haemorrhage and 1 had a traumatic haemoperitonuem. Three cats received more than one autotransfusion. Blood was collected using a 23g butterfly catheter and 20ml syringe in 7/12 collections, a 23g needle and 20ml syringe in 2/12 collections and directly into syringes from the open abdomen at the time of surgery in 3/12 collections. A median volume of 50ml (range 25-80ml) was collected and administered, meaning a median volume of 16.5ml/kg (range 9-26ml/kg) was administered. The autologous transfusions were given over a median of 3 hours (0.25-6 hours). Five cats were given another blood product alongside the autotransfusion. Median percentage PCV increase was 5% (range 1-7%). Anti coagulant was used in 5/12 autotransfusions. No clinically relevant adverse effects were reported. Six of the 8 cats survived to discharge. Two month survival was 60% (3/5).
Conclusions and relevance: Autologous transfusion appears to be a safe and effective technique for stabilising cats with haemoperitoneum. This technique allows rapid and cheap provision of blood and avoids the need for an allogenic blood donor.

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Introduction

The transfusion of blood products to anaemic patients is an important part of critical care. However, access to feline blood products can be limited due to technical difficulties in collecting and storing feline blood products and difficulties in recruiting feline blood donors. [1] Both haemoglobin based oxygen carriers (HBOCs) and xenotranfusion with canine blood products have been used as alternative strategies for the anaemic cat. [2,3,4] However, HBOCs have well documented adverse effects and transfused canine red blood cells have a short life span a result of intravascular haemolysis. [2,5] An alternative method to allogenic transfusion, that is well described in the human literature, is autotransfusion. [6] Autotransfusion has been reported in dogs with intracavitary haemorrhage in the veterinary literature, but there are no clinical reports in cats. [7,8,9,10,11,12] In these canine studies minor, non-clinically significant adverse effects were reported and autotransfusion appeared to be a successful management option. This study aimed to investigate the frequency and efficacy of feline autotransfusion in a referral hospital setting, as well as describing the reasons for performance of autotranfusion and the methods used.

Materials and methods

Inclusion criteria

The electronic clinical and surgical records from the Queen Mother Hospital for Animals (Hatfield, UK). were searched for cats that were administered an autotransfusion between July 2012 and March 2018.

Retrieved data

The following data was extracted from the clinical records; signalment, underlying disease, technique of blood collection, volume of blood collected, use of anticoagulant, volume of autologous blood transfused, transfusion time period, pre and post transfusion PCV, serum calcium, prothrombin time and partial thromboplastin time post transfusion and administration of other blood products. Survival to discharge and 2 month survival were also documented.

Results

A total of 8 cats had at least one autotransfusion during the time period. Six were female (5 neutered) and 2 were male (1 neutered). Five were Domestic short hairs and 3 were pure breeds (British short hair, Ragdoll and Bengal). The median weight of the cats was 3.67Kg (range 1.38-5.5Kg). All cats were blood typed. Six cats were blood type A and 2 cats were blood type B.

Four of the 8 cats had spontaneous hemoperitoneum secondary to abdominal neoplasia (2 cats had splenic haemangiosarcoma, 1 cat had both splenic and liver haemangiosarcoma and one cat had liver and splenic lesions consistent with neoplasia on ultrasound but histological diagnosis was not made). Three of the 8 cats required an autotransfusion for management of post-operative

haemorrhage (the surgical procedures were routine ovariohysterectomy performed at the primary care vets in two cats, and extra-hepatic shunt ligation and liver biopsy in the other cat). One cat presented with a traumatic haemoperitoneum. Six out of 8 cats required surgery for management of their condition.

A total of 12 autotransfusions were performed over the study period. Three cats had an autologous transfusion performed on more than one occasion. Case 1, a cat with a traumatic haemoperitoneum, required autotransfusion on presentation and 12 hours later due to continuing haemorrhage. Surgical exploration revealed a splenic fracture with bleeding splenic artery. An autotransfusion was performed on case 3 prior to surgery for removal of a poorly differentiating splenic haemangiosarcoma and it required repeat autotransfusion 10 days post discharge to due recurrence of the haemoperitonuem. Case 5 received an autotransfusion during cardiopulmonary arrest suspected to be due to haemorrhage post surgery for extra-hepatic portosystemic shunt ligation and liver biopsy. Autotransfusion was performed again at the time of revision surgery (0.5 hours later) and also in the post-operative period (2 hours later).

Autotransfusion was performed in all cats to treat their anaemia and hypovolaemia. Three of the 12 autotransfusions were performed intra-operatively, 1/12 was performed post-operatively and 2/12 were performed peri-cardiopulmonary arrest.

Out of the total 12 autotransfusions performed, blood was collected using a 23g butterfly catheter and 20ml syringe in 7 collections, a 23g needle, three-way tap and 20ml syringe in 2 collections and directly into syringes from the open abdomen at the time of surgery in 3 collections. Ultrasound guided sampling was performed in all cases except collection at the time of surgery.

Anti-coagulant acid citrate dextrose (ACD-A, USA) was used in 5/12 of the autotransfusions performed with 0.14ml of ACD used per 1ml of blood collected as described in previous studies.[13] In all cases the collected blood was transfused through an 18μm blood filter (Utah Medical Products, USA). A median volume of 50ml (range 25-80ml) was collected and administered, equivalent to median volume of 16.5ml/kg (range 9-26ml/kg) over a median of 3 hours (range 0.25-6 hours, the time over which the autotransfusion was administered was not recorded in one case). Three autotransfusions were given in one hour or less at a rate from 0.28ml/kg/min-1.2ml/kg/min.

The median PCV pre-autotransfusion was 12% (range 7-20%, n = 11). Post autotransfusion, the median PCV was 18% (range 9.5-23%, n = 11) with the median percentage PCV increase being 5% (range 1-7%, n =10).

During the administration of the autotransfusions there were no documented report of urticaria, erythema, increased rectal temperature or other signs consistent with transfusion reaction. Post-transfusion ionised calcium levels were available after 7/12 autotransfusions. The median ionised calcium value

was 1.22mmol/L (range 0.92-1.3mmol/L). Total calcium was measured in 1 patient and this was 2.03mmol/L (RI 2.07-2.8mmol/L). Out of these 8 patients 2 were documented as having a mild hypocalcaemia of which one received anticoagulant. No patient showed clinical signs of hypocalcaemia.

Five of the 8 cats received other blood products. Case 2 and case 8 who presented with haemoperitonuem post routine ovariohysterectomy received both packed red blood cells and type specific fresh frozen plasma. Case 8 received type specific feline packed red blood cells and case 2 received canine packed red blood cells due to the lack of availability of feline blood at the time of admission. Case 5 received feline whole blood and oxyglobin and case 4 and 7 received feline packed red blood cells (Table 1).

Coagulation tests were assessed in three cats prior to the first autotransfusion and were found to be within normal limits. Two cats had prothrombin time (PT) and activated partial thromboplastin time (aPTT) measured post autotransfusion; one had had mild prolongation of aPTT and one had moderately prolonged PT and aPTT as well as a severe thrombocytopaenia of $40x10^9$/l (RI $200\text{-}800x10^9$/L). This cat (case 2) had received canine packed red blood cells and autologous transfusion in less than 2 hours. A total of 10ml/kg fresh frozen plasma transfusion was given for management of the coagulopathy. Four hours post all transfusions the patient was found to have an increased respiratory effort and documented pleural effusion, suspected to the result of fluid overload. The patient was treated with oxygen and 2mg/kg frusemide (Diamzon, MSD Animal Health).

Gross haemolysis was detected in one cat (case 3) post autotransfusion on examination of serum, but this had also been present prior to autotransfusion. This patient's PCV increased by 2 and 2.5% after each autotransfusion.

Three cats had cytology performed on the abdominal fluid and 2 cats had culture of the abdominal fluid used for autotransfusion. None of these cases had cytological evidence of bacteria. One cat out of the 2 (case 6) that had culture of the abdominal fluid cultured positive for *Enterococcus faecalis.* This case was given an autologous transfusion after respiratory arresting and was euthanased due to progressive neurological deterioration.

Outcome

Six of the 8 cats survived to discharge. No delayed adverse reactions to the autotransfusions were reported in any patient. Both of the patients that died in hospital were given an autotransfusion peri-cardiopulmonary arrest. Case 5 arrested post operatively after extra-hepatic portosystemic shunt ligation and hepatic biopsy. This patient regained spontaneous circulation and had repeat surgery to performed isolate the bleeding vessel. The patient was euthanased on recovery from general anaesthesia due to severe hypoxaemia, despite further autotransfusion, whole blood, crystalloid and colloid and vasopressor therapy. Case 6 neurologically deteriorated and was euthanased post respiratory arrest.

Two-month survival was 60% (3/5). Two patients (cases 3 and 4) were diagnosed with splenic and liver haemangiosarcoma and were euthanased 4 and

6 weeks post discharge respectively. Both patients re-presented collapsed and pale, one with a recorded PCV of 9%. This latter patient was presumed to have had a repeat abdominal haemorrhage. The other case (case 7) diagnosed with splenic haemangiosarcoma was lost to follow up. Case 1 with traumatic hemoperitoneum and case 2 and case 8 with haemoperitoneum post ovariohysterectomy are reported to be well on follow up.

Discussion

The aim of this case series was to examine the use of autotransfusion in feline patients in a referral hospital setting. We report eight cats, which had an autotransfusion to aid treatment of their anaemia. Given the high caseload of the hospital, this is not a frequently performed procedure, probably helping to explain the lack of literature on the use of autotransfusion in cats. A recent survey of canine and feline transfusion practice found that autotransfusion is performed in 36% of both primary care and tertiary referral centres in the USA. [13]

Three main autotransfusion techniques have been described in man; pre-operative autologous donation (PAD) whereby blood is collected in advance of an elective procedure, stored in the blood bank and transfused back to the patient when required, acute normovolaemic haemodilution where blood is collected immediately prior to surgery and blood volume restored by crystalloid or colloid, and cell salvage in which blood is collected from suction, surgical

drains, or both and re-transfused back to the patient after filtration or washing. [6] There is one experimental report of autologous transfusion in cats and one clinical report of PAD in cats performed prior to planned craniotomy surgery. [15, 16] There are various reports of canine cell salvage in the veterinary literature. [8,9,10,11,12]

Autotransfusion can be considered an underused method in cats as it has several advantages when compared to the use of allogenic blood products. The blood is readily available and is cheaper than allogenic blood products as there is no need for blood typing or cross matching. This is particularly useful outside large referral hospitals in the UK as there is no commercial feline blood bank and access to blood donors, particularly type B and AB cats can be limited. Autotransfusion has the proposed advantage of reducing the risk of transmission of disease or isoimmunisation associated with allogenic blood transfusion. A meta-analysis in man found that red cell salvage reduced exposure to allogenic blood by 40%. [16] In this case series 40% of cats did not require allogenic blood products, compared to 30% dogs undergoing autotransfusion. [10]

Cell salvage in man has been predominantly used intra-operatively in cardiothoracic, vascular, orthopaedic, neurological and transplantation surgery and there are rare reports of its use in the emergency department. [6,17] In dogs autotransfusion has been used primarily for resuscitation in emergencies, the management intra-operative haemorrhage and coagulopathy, post operative haemorrhage and bleeding secondary to neoplasia where surgical intervention

may or may not be required. [8, 10,12] In this case series, autotransfusion was a key part of stabilisation in all 8 of the cats as well as providing intra-operative support and included similar causes as the aforementioned studies. Surgery was performed as well as autotransfusion in 66.7% (8/12) autotransfusion events, similar to the number requiring surgery in dogs undergoing an autotransfusion. [10]

Techniques for red cell salvage in man and dogs include direct collection from the abdomen using a syringe or suction device and the use of a cell saver device whereby shed blood is collected, anticoagulated and washed or filtered prior to re-transfusion via a filter. [6,8, 9, 11] A cell salvage device has the advantage of washing and filtering the blood and thus removing potentially antigenic cells such as leukocytes, neoplastic cells. [18] However, most cell salvage systems require a predetermined volume of erythrocytes prior to washing, making it less suitable for most cats were collected blood volumes are usually small. The techniques described for autotransfusion in the cats of this case series were percutaneous collection by ultrasound guidance using a butterfly catheter connected to 20ml syringe or direct collection via a 20ml syringe at the time of surgery, similar to that reported in the case series of 25 dogs. [10]

In 5 out of the 12 autotransfusion cases blood was collected into acid citrate (ACD-A). The use of anticoagulant in autotransfusion is controversial. Some literature suggests that blood in contact with peritoneal surface greater than one hour become defribinated and thus systemic anti-coagulant is unnecessary and the citrate itself may lead to hypocalcaemia. [18] In 2/8 autotransfusion events

where ionised or total calcium was available post transfusion there was a documented mild non-clinically significant hypocalcaemia. Acid citrate was used only in one of these cases. Hypocalcaemia has been reported in dogs undergoing autotranfusion via cell saver device and direct collection. [10,11] In one study of autotransfusion in dogs, 50% of the cases were administered blood with anticoagulant and 50% without and there was no association seen between the use of anticoagulant and survival. [10] Further studies are required to investigate the clinical relevance of anti coagulant use in autotransfusion in cats.

The use of a blood filter is recommended for re-delivery of blood in attempt to remove microaggreates that could promote an inflammatory reaction. Platelets and platelet products have been found to incite an inflammatory reaction, which can lead to the development cutaneous oedema and acute respiratory distress syndrome. [19] The filter size of 18 micron used in the cats of this case series has a high microaggregatory retention preventing platelet and leukocyte passage. However, this size filter will not filter serotonin, histamine or catecholamine, which are reported to lead to an increase risk of system inflammatory response. [20] No patient in this case series showed any clinical signs consistent with an inflammatory response post transfusion.

Each patient, where recorded, received between 9-26ml/kg of autologous blood during each transfusion. Two cats cases received in in excess of 30ml/kg total blood product in 4-6 hours and thus by definition underwent a massive transfusion. [20] The one patient who received a massive transfusion, and

293 survived, was found to have prolonged PT and APTT and severe
294 thrombocytopenia post transfusion requiring fresh frozen plasma therapy.
295 Autotransfusions have been previously documented to cause consumptive
296 coagulopathy; PT and APTT were prolonged post transfusion in 80% of cases of
297 canine autotransfusions where post transfusion PT and APTT were measured
298 in one study.[10] This hypocoagulability is thought to occur as a result of
299 widespread activation of coagulation system and secondary fibrinolysis when
300 the blood is re-infused.[21] The cat in this case series that had a prolonged PT and
301 APTT post transfusion received a large volume of crystalloid, massive
302 transfusion of canine packed red blood cells and autologous blood. It is
303 therefore difficult to determine the contribution of the autotransfusion to this
304 coagulopathy. Only one other patient, diagnosed with a traumatic
305 haemoperitoneum had coagulation values measured post the transfusion and
306 this revealed a mild coagulopathy, which could be the result of continual
307 bleeding or the effect of the autotransfusion, or a combination of both. Ideally
308 post transfusion platelet count and clotting times should be assessed to
309 monitor for development of a consumptive coagulopathy.

310

311 Other reported complications of autotransfusion include haemolysis secondary
312 to prolonged exposure to serosal membrane and mechanical injury during
313 collection and re-infusion.[10, 22, 23] Haemolysis results in the release free
314 haemoglobin that can lead to acute kidney injury. To minimise the risk of
315 mechanical injury to the red blood cells aspiration was performed gently using
316 low suction pressure to minimise cell damage during the retrieval. One cat,

317 diagnosed with a haemangiosarcoma , was reported to have haemolysed serum
318 post autotransfusion, compared to 5/19 (26%) of dogs in a previous study. [10]
319 This patient was also shown to have haemolysed serum pre transfusion and no
320 evidence of worsening post transfusion suggesting it was likely part of the
321 patients disease state. This patient's PCV showed a mild increase in (PCV
322 increase 2-2.5%) post the transfusions, which could have been the result of
323 ongoing haemolysis. Larger studies of feline autotransfusions are required to
324 assess the true prevalence and consequence of haemolysis in these cases.
325
326 One patient suffered from suspected transfusion associated circulatory overload
327 (TACO). This patient had received massive transfusion of canine packed red
328 blood cells and autologous blood products alongside crystalloid therapy and
329 fresh frozen plasma. It is therefore likely it was due to the volume of product
330 versus the type of transfusion. This patient responded well to therapy and went
331 on to make a complete recovery.
332
333 Reported contraindications for autotransfusion in man are surgeries for
334 malignancy, bacterial contamination and contamination of the blood with
335 products that can cause haemolysis such as hypotonic fluids. [6] The use of
336 autotransfusion for management of haemorrhage secondary to neoplasia is
337 controversial. It is unclear how well malignant cells are removed by filtration
338 and it has been suggested that autotransfusion can contribute to metastatic
339 spread of the tumour. [24] However, autotransfusion has been described in dogs
340 with haemoperitoneum secondary to neoplasia with no reported complications
341 and studies in man have not shown an increased metastatic rate when auto

342 transfusions have been performed in patients with neoplasia. [8, 10, 25] In this study
343 50% of patients (4/8) had an autotransfusion due to a ruptured neoplasm, of
344 which 3/4 died within 6 weeks of the autotransfusion. These patients likely
345 already had metastatic disease so we cannot elucidate if the transfusion
346 contributed to disease progression. In this case transfusion itself was life saving
347 treatment and prevented the use of feline blood products, a scare resource, in a
348 terminal patient.
349
350 In one cat the autotransfusion may have involved infusion of blood contaminated
351 with bacteria. Microbiological culture was performed on the abdominal fluid of 2
352 cats and in 1 case this led to a positive culture for *Enterococcus faecalis.* Bacterial
353 growth of salvaged blood has not previously been reported in the veterinary
354 literature but has been reported in up to 12.7% of blood salvaged in humans. [26]
355 Patients in this study were followed up for 2 months post autotransfusion and no
356 statistically significant correlation between bacteriologic results of
357 autotransfused blood and infectious complications could be found. The cat with
358 the positive culture in this case series was euthanased shortly after its
359 autotransfusion and therefore it was not possible to determine its clinical
360 significance.
361

362 Two-month survival was 75% for cats available for follow up in this study. In
363 the cats that died the cause of death was euthanasia due to underlying disease
364 and continued haemorrhage, similar to that reported in dogs. [10] This case series

supports other studies in man and veterinary species that autotransfusion does not appear to adversely affect mortality or lead to significant complications. [10, 16]

This case series describes the successful use of a simple cost effective autotransfusion technique using 23g needle or butterfly catheter, 20ml syringe and a blood filter to manage life threatening abdominal haemorrhage and to provide intravascular support under general anaesthesia. This technique is cheap and requires minimal equipment with no clinically significant adverse effects and should be considered in unstable cats with a confirmed non-septic haemoperitoneum. Monitoring for post transfusion haemolysis, coagulopathy and hypocalcaemia are recommended post transfusion.

In conclusion autologous transfusion appears to be a safe and effective technique for stabilising cats with haemoperitoneum. This technique allowed rapid and cheap provision of blood and avoids the need for an allogenic donor.

Statement of conflict of interest

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