Haemorrhagic Shock

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1. Introduction

Haemorrhagic shock is a common and life-threatening consequence of whole blood loss. As a form of hypovolaemic shock, it results in impaired oxygen delivery from reduction in cardiac preload. Additionally, it results in the loss of red blood cells, platelets, and coagulation factors. If red bloods cells are not adequately replaced during treatment, the resultant decrease in haemoglobin concentration will further impair oxygen delivery. Failure to adequately replace platelets and coagulation factors will promote a hypocoagulable state, which may perpetuate bleeding. Progressive hypocoagulability, haemorrhage, and shock can become a vicious cycle leading to increased morbidity and mortality. Prompt recognition and appropriate treatment of haemorrhagic shock is vital.

2. Assessment of the Haemorrhagic Shock Patient

Haemorrhagic shock is diagnosed when there is evidence of impaired perfusion (vasoconstrictive shock) in combination with evidence of bleeding. These features may be recognized in several ways:

- Obvious bleeding, e.g., external haemorrhage, may prompt evaluation of perfusion
- Detection of vasoconstrictive shock may prompt diagnostic evaluation that reveals evidence of haemorrhage
- Monitoring of perfusion may detect the development of shock in a patient known to be at risk of haemorrhage, such as a postoperative patient

Regardless of what prompted the initial diagnosis of haemorrhagic shock, all affected patients should subsequently have assessment of the source of haemorrhage, the severity of perfusion impairment, and the systemic effects of the shock.

Determining the source of haemorrhage confirms the diagnosis of haemorrhagic shock and allows determination of whether bleeding is controlled or ongoing. Sometimes the source of haemorrhage is obvious, such as a wound or epistaxis, but internal haemorrhage can be more difficult to detect. Careful physical examination is invaluable in localizing haemorrhage. Gastrointestinal haemorrhage often manifests as melaena and/or haematochezia, which can be detected with rectal examination. Haematemesis may also be visualized or reported in the history. Haemorrhage into a long bone fracture site is often detected as severe swelling and skin tension at the site. Some fracture site haemorrhage produces no clear external evidence of the severity of bleeding, however, especially with

pelvic fractures. Thoracic haemorrhage may lead to tachypnoea, a shallow respiratory pattern, and dull breath sounds. Abdominal haemorrhage may be detected as progressive abdominal distension, sometimes with a fluid wave. Cullen's sign, appearing as bruising in the umbilical area, is strongly suggestive of haemoperitoneum.

Internal haemorrhage of sufficient severity to cause shock most commonly occurs in the pleural or peritoneal space. Point-of-care ultrasound is invaluable in identifying effusions. Paracentesis to confirm the haemorrhagic nature of the fluid is recommended before committing to treatment of haemorrhagic shock, as the discovery of a different type of fluid (e.g., modified transudate) should prompt diagnostic re-evaluation. Evidence of gastrointestinal, urinary, mediastinal, retroperitoneal, or fracture site haemorrhage may also be detected by astute sonographers.

Haemorrhage in any location may be secondary to trauma, a coagulopathy, or spontaneous haemorrhage from diseased tissue, most commonly neoplasia. Determination of the reason for haemorrhage is an important parallel to determining the source, as different treatment may be required to control haemorrhage of different underlying aetiologies. This determination is aided by history of trauma, known congenital coagulopathy, access to rodenticide, or known neoplasia. Physical examination may detect other evidence of trauma or neoplasia. Imaging and assessment of coagulation are helpful additional steps. Point-of-care ultrasound is again the preferred initial modality, though additional imaging such as radiography or computed tomography with IV contrast may be necessary in some patients. Assessment of coagulation is discussed later.

Assessment of perfusion allows for determination of shock severity and response to treatment. These will help determine the required intensity of treatment. Haemorrhagic shock is a form of vasoconstrictive shock, leading to the following expected abnormalities in perfusion parameters: reduced mentation (obtunded to comatose), cooler peripheries than core, pale mucous membranes, prolonged capillary refill time, tachycardia, and reduced pulse quality. Bradycardia may be found in severe haemorrhagic shock in dogs, or haemorrhagic shock of any severity in cats. As well as allowing for rapid diagnosis of shock, monitoring of these parameters allows for assessment of response to treatment.

In emergency patients presenting with haemorrhagic shock, a small number of readily available point-of-care diagnostic tests may complement the perfusion parameter assessment of perfusion. Blood pressure measurement is commonly performed. However, caution should be taken as normotension may be maintained despite moderate haemorrhagic shock. Severe haemorrhagic shock is usually associated with progressive hypotension, though in this setting the accuracy and reliability of non-invasive methods of blood pressure measurement are suboptimal. Increased plasma lactate concentration, especially in conjunction with metabolic acidosis, is supportive of shock and can be used to monitor shock progression and treatment. Some caution should be taken, as hyperlactatemia is a non-specific finding that may be confounded by concurrent disease states. Point-of-care ultrasound is also growing in popularity for assessment of intravascular volume status, though training is necessary to perform it with competence and more research is required to optimize its utility. As well as these simple tests, a variety of other

advanced modalities may be available for a more thoroughly instrumented patient in the ICU.

Assessment of the source of haemorrhage and the severity of perfusion impairment aids in categorizing haemorrhagic shock patients into two broad groups: controlled/mild haemorrhage and severe uncontrolled haemorrhage. This distinction is important as an aggressive approach to treatment is necessary to save the life of a patient with severe uncontrolled haemorrhage. Severe uncontrolled haemorrhage can be diagnosed by examination or imaging evidence of severe ongoing bleeding, evidence of severe shock, and lack of substantial response to an initial fluid bolus. The treatment for each of these scenarios is discussed separately below.

Haemorrhagic shock is associated with a 'lethal triad' of hypothermia, coagulopathy, and acidosis. These factors can perpetuate shock and ongoing bleeding and should be proactively avoided. Close monitoring of body temperature and proactive use of warming devices should be prioritized. Close monitoring of blood gases is also warranted, and additional factors contributing to acidemia such as hypoventilation or high-chloride fluid administration should be avoided. Rapid assessment of coagulation is recommended to rapidly identify coagulopathy and direct appropriate treatment. Viscoelastic testing is superior to traditional coagulation tests in this setting. In addition to the more established viscoelastic modalities of thromboelastography (TEG) and rotational thromboelastometry (ROTEM), a small point-of-care device for the veterinary market is now available (Entegrion VCM VET™). If viscoelastic testing is not available, coagulation assessment may include platelet count, coagulation times (PT and aPTT), and plasma fibrinogen concentration.

Organ injury, such as acute kidney or liver injury, is common following haemorrhagic shock. Collection of a pre-treatment CBC, biochemical panel, and urinalysis allows for establishment of a baseline. These tests should be then periodically monitored to assess for progressive organ injury. Monitoring of plasma electrolytes, GI function, and respiratory parameters is also warranted.

3. Management of Controlled or Mild Haemorrhage

Management of controlled or mild ongoing haemorrhage typically involves first restoring adequate preload with bolus synthetic 'clear' fluid, followed by transfusion to replace red blood cells and/or coagulation factors if necessary.

Clear fluids include isotonic crystalloids, hypertonic crystalloids, and synthetic colloids. Isotonic crystalloids form the mainstay of treatment of hypovolaemia in controlled haemorrhagic shock. Buffered crystalloids should be prioritized over 0.9% NaCl, as the latter is associated with hyperchloremic metabolic acidosis and potential subsequent acute kidney injury. As well as containing a lactate buffer, Hartmann's solution also contains some calcium which may aid in prevention of hypocalcaemia. Some authors recommend avoiding acetate-buffered fluids in vasoconstrictive shock due to the potential vasodilatory and pro-inflammatory properties of this anion, though we did not see any evidence of this in our canine haemorrhagic shock model.

Hypertonic crystalloids can aid in rapid but temporary blood volume expansion. They are most useful for treatment of haemorrhagic shock in large patients (followed by subsequent isotonic fluid administration), treatment of patients with concurrent traumatic brain injury, or prior to massive transfusion in patients with severe uncontrolled haemorrhage (see below). There is some concern that hypertonic crystalloids may impair coagulation, though the evidence for this is primarily from in vitro mixing studies that do not allow for the effects of fluid redistribution that occurs *in vivo*. The routinely administered hypertonic crystalloid is hypertonic NaCl, which is a high-chloride fluid. Thus, the same concerns over hyperchloraemic metabolic acidosis exist for this fluid. There is some research into the use of other hypertonic crystalloids. It should be noted that undiluted sodium bicarbonate solution is a hypertonic crystalloid, and it can be mixed with hypertonic sodium chloride (e.g., in a 1:4 ratio) to make a buffered hypertonic crystalloid. Concentrated sodium bicarbonate should only be administered to patients that are able to increase their minute volume to excrete the carbon dioxide produced by buffering, with concern of the risk of paradoxical CNS acidosis.

Synthetic colloid fluids include macromolecules aimed at increasing plasma colloid osmotic pressure and retaining infused fluid within the vasculature. The major concern over synthetic colloid fluid administration in haemorrhagic shock is that they contribute to impairment of coagulation through multiple mechanisms, including platelet dysfunction, impairment of coagulation factors, weaker fibrin meshwork, and enhanced fibrinolysis. Evidence for coagulation impairment in dogs exists for the two most common synthetic colloid fluid types: hydroxyethyl starch and gelatin. Thus, I generally avoid synthetic colloid fluids in haemorrhagic shock. They could be considered for individual patients on a risk/benefit analysis if shock cannot be resolved with crystalloids and blood products are not readily available.

Circulating haemoglobin concentration is often either normal or mildly reduced in controlled haemorrhagic shock prior to clear fluid resuscitation. However, restoration of blood volume often ‘unmasks’ anaemia. Thus, transfusion of red blood cells is often necessary in patients that do not sufficiently respond to initial clear fluid resuscitation. If shock is mostly resolved but substantial anaemia is present, a slow transfusion may be given. If signs of shock persist despite adequate blood volume replacement (e.g., 20-40 mL/kg of isotonic crystalloid in a patient that was not initially anaemic, or 10-20 mL/kg in a patient that was initially anaemic), then a more rapid transfusion of packed red blood cells or whole blood is recommended. Plasma products should also be considered if there is evidence of coagulopathy or a large volume (>10 mL/kg) of packed red blood cells is needed.

4. Management of Severe Uncontrolled Haemorrhage

Severe uncontrolled haemorrhage is immediately life threatening and must be treated aggressively. It should be recognized in patients that have obvious severe ongoing bleeding, severe shock, or do not adequately respond to an initial crystalloid bolus. In practice, for logistical reasons, treatment of haemorrhagic shock usually begins with some amount of bolus administration of crystalloid (isotonic or hypertonic). The response to this initial bolus is an important trigger for switching to a more aggressive treatment approach. Treatment of

severe uncontrolled haemorrhage requires massive transfusion, rapid definitive haemostasis where possible, and appropriate adjunct therapies.

Definitions of massive transfusion in the literature include transfusion of an entire blood volume within 24 hours, 50% of blood volume within 3-4 hours, or administration at 1.5 mL/kg/min for 20 minutes. Whilst useful for research, these definitions are not very practical clinically as they refer to what has happened after the fact, rather than a prospective treatment approach. I conceptually think about massive transfusion in this setting as bolus administration of blood products to rapidly treat hypovolemia whilst preventing anaemia and coagulopathy, in contrast to the traditional approach of slower transfusion. Another term to describe this, frequently used in the human trauma literature, is 'haemostatic resuscitation', as it is designed to actively support haemostasis. Fresh whole blood is the ideal transfusion product but is usually not rapidly available in sufficient volumes. Thus, massive transfusion typically involves administration of packed red blood cells, plasma, and platelets (if available). These are either administered in a fixed ratio (e.g., 1:1:1 units), or with guidance by serial viscoelastic testing. Refrigerated plasma or whole blood products provide alternatives to traditional stored components. This treatment approach puts substantial strain on blood bank resources. Blood bank managers should be notified immediately. Patient selection is important, as administration of large amounts of blood product to an animal with a non-survivable illness or injury may strain resources. However, it is often difficult to know whether a patient may survive in the acute setting, as aggressive treatment can resuscitate many patients with very severe shock. Autotransfusion of cavitary provides a readily available alternative to use of stored blood products that is appropriate in many scenarios.

Massive transfusion of room temperature (or cold) blood products contributes to hypothermia, which is often already severe due to the shock. Rapid fluid warmers are often used in human trauma centres but are typically not available in veterinary practice. A combination of a warm air warming device and a sealed foil 'blizzard' blanket is highly effective at maintaining normothermia.

Rapid administration of blood products causes ionized hypocalcaemia due to chelation by the citrate anticoagulant. Calcium plays vital roles in haemostasis and the cardiovascular response to shock. There is not substantial evidence for any specific calcium management strategy in severe haemorrhagic shock. I am very aggressive in maintaining normocalcaemia, by monitoring plasma ionised calcium concentration closely. As patients receiving massive transfusion invariably become hypocalceamic, I often empirically administer 0.5 mL/kg of 10% calcium gluconate following every 10-20 mL/kg of blood product if a current ionised calcium measurement is not available.

Massive transfusion must continue until definitive control of severe haemorrhage is achieved and cardiovascular stability is restored. Rapid interventions to control haemorrhage should be pursued whenever possible. General anaesthesia in patients with haemorrhagic shock carries increased risk, but a careful multimodal approach with minimal cardiovascular depressant drugs is often successful. With sufficient doses of opioid and benzodiazepine, often minimal or no other induction or maintenance agent is necessary.

Surgery may be definitive, where a single surgical procedure resolves the surgical lesion. However, in complex lesions, 'damage control surgery' to control haemorrhage and contamination may be initially pursued, with later definitive surgery once cardiovascular stability has been restored. Some haemorrhaging lesions are amenable to minimally invasive (endoscopic or fluoroscopic) treatment. However, experience of the operator must be considered, as in some circumstances an open technique may be quicker or more reliable.

Adjunct therapies may aid in haemorrhage control in severe uncontrolled haemorrhage. Systemic administration of an antifibrinolytic agent should be considered. I typically administer 20 mg/kg of tranexamic acid IV as an initial bolus; the slightly higher dose than typical recommendation based on synthesis of canine pharmacokinetic data. I pre-treat with IV maropitant to prevent vomiting. Aminocaproic acid is an alternative if tranexamic acid is not available. Antifibrinolytics may also be applied topically for oral lesions or epistaxis. For oral lesions, a paste made from tranexamic acid tablets can be effective. For epistaxis, I typically administer the injectable formulation through a mucosal atomization device (MAD). Catecholamines can also be applied topically. Systemic desmopressin can be given in cases where a thrombocytopathia is suspected.

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