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COMMENTARY

Management of massive blood loss: a template guideline

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The management of acute massive blood loss is considered and a template guideline is formulated, supported by a review of the key literature and current evidence. It is emphasized that, if avoidable deaths are to be prevented, surgeons, anaesthetists, haematologists and blood-bank staff need to communicate closely in order to achieve the goals of secure haemostasis, restoration of circulating volume, and effective management of blood component replacement.

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Complications of major blood loss and massive transfusion may jeopardize the survival of patients from many specialties, and challenge haematological and blood transfusion resources.

Avoidable deaths of patients with major haemorrhage are well recognized,[1 2] and locally agreed and/or speciality-specific guidelines[3] are needed to ensure effective management. Current UK published guidelines[4 5 6] are based on historical transfusion practice and are not easily referred to in an emergency situation. A symposium on massive transfusion was organized by the National Blood Service Northern Zone in December 1998 and was attended by anaesthetists, traumatologists, haematologists, nurses and blood-bank personnel. At the conclusion of the meeting, a number of key principles were agreed and, in consultation with delegates, a guideline document was produced and is now available in hospitals served by the Leeds, Liverpool, Manchester, Newcastle and Trent Blood Centres as a basis for local protocols.

The guideline is presented in this article (Table 1) as a simple template which may be modified to take into account local circumstances and displayed in clinical areas. The left-hand column of the template outlines the key steps or goals, the centre column adds procedural detail and the right-hand column provides additional advice and information.

The accompanying commentary is not intended to be an exhaustive review, but provides key references on which the recommendations are based.

The Hospital Transfusion Committee has a central role in ensuring the optimum and safe use of blood components. The development of protocols for the management of massive transfusion is an important part of the remit of such committees and it is hoped that this article will facilitate this process.

Commentary

Background

Massive blood loss is usually defined as the loss of one blood volume within a 24 h period,[7] normal blood volume being approximately 7% of ideal body weight in adults and 8–9% in children. Alternative definitions include 50% blood volume loss within 3 h or a rate of loss of 150 ml min^{-1}.[8] Such definitions emphasize the importance of the early recognition of major blood loss and the need for effective action to prevent shock and its consequences.

Priorities for treatment are:

- restoration of blood volume to maintain tissue perfusion and oxygenation;
- achieving haemostasis by:
  - treating any surgical source of bleeding;
  - correcting coagulopathy by the judicious use of blood component therapy.

A successful outcome requires prompt action and good communication between clinical specialties, diagnostic laboratories, blood-bank staff and the local blood centre. Blood component support takes time to organize and the blood centre may be up to 2 h away from the hospital.

Early consultation with surgical, anaesthetic and haematology colleagues is advisable, and the importance of good communication and cooperation in this situation cannot be

Table 1 Acute massive blood loss: template guideline

Goal	Procedure	Comments
Restore circulating volume	Insert wide-bore peripheral cannulae Give adequate volumes of warmed crystalloid, ?colloid, blood Aim to maintain normal blood pressure and urine output >30 ml h^{-1}	14 G or larger Monitor central venous pressure Blood loss is often underestimated Refer to Advanced Trauma Life Support guidelines Keep patient warm
Contact key personnel	Clinician in charge Duty anaesthetist Blood bank Duty haematologist	Nominated coordinator should take responsibility for communication and documentation
Arrest bleeding	Early surgical or obstetric intervention Interventional radiology	
Request laboratory investigations	FBC, PT, APTT, fibrinogen; blood-bank sample, biochemical profile, blood gases or pulse oximetry Ensure correct sample identity Repeat FBC, PT, APTT, fibrinogen every 4 h or after 1/3 blood volume replacement Repeat after blood component infusion	Take samples at earliest opportunity as results may be affected by colloid infusion Misidentification is commonest transfusion risk May need to give components before results available
Request suitable red cells	Un-crossmatched group O Rh negative In extreme emergency No more than 2 units Un-crossmatched ABO group-specific When blood group known Fully cross-matched If irregular antibodies present When time permits Use blood warmer and/or rapid infusion device. Employ blood salvage if available and appropriate	Rh positive is acceptable if patient is male or postmenopausal female Laboratory will complete cross-match after issue Further cross-match not required after replacement of 1 blood volume (8–10 units) Blood-warmer indicated if flow rate >50 ml kg^{-1} h^{-1} in adult Salvage contraindicated if wound heavily contaminated
Request platelets	Allow for delivery time from blood centre Anticipate platelet count $<50\times10^9$ $litre^{-1}$ after 2 × blood volume replacement	Target platelet count: $>100\times10^9$ $litre^{-1}$ for multiple/CNS trauma or if platelet function abnormal $>50\times10^9$ $litre^{-1}$ for other situations
Request FFP (12–15 ml kg^{-1} body weight= 1 litre or 4 units for an adult)	Aim for PT and APTT <1.5× control mean Allow for 30 min thawing time	PT and APTT >1.5× control mean correlates with increased surgical bleeding
Request cryoprecipitate (1–1.5 packs/10 kg body weight)	Replace fibrinogen and factor VIII Aim for fibrinogen >1.0 g $litre^{-1}$ Allow for delivery time plus 30 min thawing time	Fibrinogen <0.5 strongly associated with microvascular bleeding Fibrinogen deficiency develops early when plasma-poor red blood cells used for replacement
Suspect DIC	Treat underlying cause if possible	Shock, hypothermia, acidosis leading to risk of DIC Mortality from DIC is high

overemphasized. A member of the clinical team should be nominated to act as the coordinator responsible for overall organization, liaison, communication and documentation. This is a critical role for a designated member of the permanent clinical staff. The Hospital Transfusion Committee should provide a forum in which a rapid communication cascade can be agreed and massive transfusion episodes reviewed.

Resuscitation

Prolonged oligaemic shock carries a high mortality rate because of organ failure and disseminated intravascular coagulation. Restoration of circulating volume is initially achieved by rapid infusion of crystalloid or colloid through large-bore (14 gauge or larger) peripheral cannulae.[9] The use of albumin and non-albumin colloids versus crystalloids for volume replacement has recently been the subject of debate after two controversial meta-analyses,[10 11] and the use of colloid is not recommended in the latest American College of Surgeons Advanced Trauma Life Support Guidelines.[12] Further trials are required before firm recommendations can be made.

Red cell transfusion is likely to be required when 30–40% of blood volume is lost; the loss of over 40% of blood volume is immediately life-threatening.[12] Hypothermia

increases the risk of disseminated intravascular coagulation and other complications[12 13] and may be prevented by prewarming the resuscitation fluids, patient-warming devices such as warm air blankets, and the use of temperature-controlled blood warmers.

Blood loss is usually underestimated, and it must be remembered that haemoglobin and haematocrit values do not fall for several hours after acute haemorrhage.[9]

For acutely anaemic patients, the American Society of Anesthesiologists Task Force on Blood Component Therapy has concluded, on the basis of the available evidence, that transfusion is rarely indicated when the haemoglobin concentration is >10 g dl^{-1} but is almost always indicated when it is <6 g dl^{-1}.[14] Determination of whether intermediate haemoglobin concentrations justify red cell transfusion should be based on the patient's risk factors for complications of inadequate oxygenation, such as the rate of blood loss, cardiorespiratory reserve, oxygen consumption and atherosclerotic disease. Measured cardiological variables, such as heart rate, arterial pressure, pulmonary capillary wedge pressure and cardiac output, may assist the decision-making process, but it should be emphasized that silent ischaemia may occur in the presence of stable vital signs.

Intraoperative blood salvage may be of great value in reducing the requirement for allogeneic blood, but bacterial contamination of the wound is a relative contraindication.[15]

Investigations

Blood samples should be sent to the laboratory at the earliest possible opportunity for blood grouping, antibody screening and compatibility testing, as well as for baseline haematology, coagulation screening, including fibrinogen estimation and biochemistry investigations.

When dealing with an evolving process, it is important to check the parameters frequently (at least four-hourly and after each therapeutic intervention) to monitor the need for and the efficacy of component therapy.

Expert advice should be sought from a haematologist regarding appropriate investigations, their interpretation and the optimum corrective therapy.

Blood component therapy

Red cells

In an extreme situation it may be necessary to use group O un-crossmatched red cells if the blood group is unknown. In an emergency, premenopausal females whose blood group is unknown should be given ORh(D) negative red cells in order to avoid sensitization and the risk of haemolytic disease of the newborn in subsequent pregnancy. It is acceptable to give ORh(D) positive cells to males and postmenopausal females of unknown blood group.[16] Group-specific red cells should be given at the earliest possible opportunity as group O blood is a scarce resource.

It is important to bear in mind that most transfusion-related morbidity is due to incorrect blood being transfused.[17] It is therefore essential that protocols are in place for the administration of blood and blood components[18] and that these are adhered to even in an emergency situation.

All blood components supplied by the UK transfusion services are now leucodepleted and the blood bank will provide red cells in optimal additive solution, containing virtually no plasma, platelets or leucocytes. The benefits of leucodepletion include reduced non-haemolytic febrile transfusion reactions, reduced transmission of leucocyte-associated viruses, such as cytomegalovirus, and reduced immunosuppressive effects of transfusion.[19] An additional microaggregate filter is not necessary.

Platelets

Expert consensus argues that platelets should not be allowed to fall below the critical level of 50×10^9 $litre^{-1}$ in acutely bleeding patients.[20] A higher target level of 100×10^9 $litre^{-1}$ has been recommended for those with multiple high-energy trauma or central nervous system injury.[21 22] Empirical platelet transfusion may be required when platelet function is abnormal, as is found after cardiopulmonary bypass.

A platelet count of 50×10^9 $litre^{-1}$ is to be anticipated when approximately two blood volumes have been replaced by plasma-poor red cells,[23] but there is marked individual variation. In assessing the requirement for platelets, frequent measurements are needed, and it may be necessary to request platelets from the blood centre at levels above the desired target in order to ensure their availability when needed.

Fresh frozen plasma (FFP) and cryoprecipitate

Most clinical studies and guidelines have been based on the use of whole blood or plasma-reduced red cells, which contain some residual coagulation factor activity. Nowadays, red cell replacement is likely to be in the form of plasma-poor red cells suspended in optimal additive solution, in which coagulation factor activity is negligible. Under these circumstances, coagulation factor deficiency is the primary cause of coagulopathy. The level of fibrinogen falls first; the critical level of 1.0 g $litre^{-1}$ is likely to be reached after 150% blood loss, followed by decreases in other labile coagulation factors to 25% activity after 200% blood loss.[23] Prolongation of activated partial thromboplastin time (APTT) and prothrombin time (PT) to 1.5 times the mean normal value is correlated with an increased risk of clinical coagulopathy[24] and requires correction.

Laboratory tests of coagulation should be monitored frequently and interpreted with advice from a clinical haematologist; laboratories should have in place standard operating procedures to ensure that clinical staff are

contacted appropriately. Experienced laboratory staff should be empowered to issue blood components in the first instance using a locally agreed algorithm. It may be necessary to request components before results are available, depending on the rate of bleeding and the laboratory turnaround time. Although 'formula replacement' with fresh plasma is not recommended, it has been suggested that infusion of FFP should be considered after one blood volume has been lost.[25] The dose should be large enough to maintain coagulation factors well above the critical level, bearing in mind that the efficacy may be reduced because of rapid consumption.[21 25]

FFP alone, if given in sufficient quantity, will correct fibrinogen and most coagulation factor deficiencies, but large volumes may be required. If fibrinogen levels remain critically low (<1.0 g litre^{-1}), cryoprecipitate therapy should be considered.[21 25]

The Guidelines on Oral Anticoagulation of the British Committee for Standards in Haematology recommend prothrombin complex concentrate as an alternative to FFP when major bleeding complicates anticoagulant overdose.[26] It should be remembered, however, that these preparations are potentially thrombogenic and the role of specific coagulation factor concentrate outwith hereditary bleeding disorders is unproven.

Disseminated intravascular coagulation (DIC)

DIC is a feared complication in the acutely bleeding patient. It carries a considerable mortality rate, and once established it is difficult to reverse. At particular risk are: patients with prolonged hypoxia or hypovolaemia; patients with cerebral or extensive muscle damage; and patients who become hypothermic after infusion of cold resuscitation fluids. Laboratory evidence of DIC should be sought before microvascular bleeding becomes evident so that appropriate and aggressive action can be taken to address the underlying cause. Frequent estimation of platelet count, fibrinogen, PT and APTT is strongly recommended; measurement of fibrinogen degradation products or D-dimers may be useful. Prolongation of PT and APTT beyond that expected by dilution, together with significant thrombocytopenia and fibrinogen of <1.0 g litre^{-1}, are highly suggestive of DIC.

Treatment consists of platelets, FFP and cryoprecipitate, given sooner rather than later, in sufficient dosage but avoiding circulatory overload.

Discussion

A guideline has been defined as 'a systematically developed statement that assists in decision-making about appropriate health care for specific clinical situations'.[27] Successful implementation will depend on local ownership by adaptation to local circumstances and accessibility at the point of clinical activity.

In developing this template guideline, we have examined such sound scientific evidence as is available, reviewed the relevant literature and professional consensus statements, and taken into account discussion and comment from contributors and delegates at the National Blood Service Northern Zone Symposium on Massive Transfusion.

The recommendations contained in these guidelines must be regarded as Grade C, based as they are on uncontrolled observational studies and a consensus of expert opinion (Level 3 evidence). Well-designed case–control studies and randomized clinical trials are lacking in this important area of transfusion medicine.

A recent cohort study[28] shows a significantly improved survival rate in massively transfused patients over a 10-yr period and associates this with more effective and efficient rewarming techniques, aggressive resuscitation and component therapy, and improved blood-banking.

There is a need for further studies to clarify these issues and provide firm evidence on which future recommendations can be based.

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