The current definition of massive transfusion is replacement of 5 U of packed red blood cells in 3 hours because of uncontrolled hemorrhage or replacement of the entire blood volume within a 24-hour period. The prompt activation of a transfusion protocol can quickly restore hemodynamic stability. Effective teamwork and communication is critical for a favorable patient outcome. This case study demonstrates the effectiveness of using a massive transfusion protocol in an outpatient setting.

**Keywords:** Communication, intraoperative hemorrhage, massive transfusion protocol.

Clear communication and teamwork in an emergency are critical to improving patient outcomes. In the case of unexpected intraoperative hemorrhage, it is necessary to respond rapidly and work effectively as a team to restore hemodynamic stability. The traditional use of large-volume crystalloid support for volume resuscitation is associated with an increased volume of hemorrhage and lower survival rates. When a patient receives standard resuscitation fluids of packed red blood cells (RBCs) plus crystalloid (Ringer's lactate or normal saline) in large volumes, the plasma clotting factors and platelets are diluted (dilutional coagulopathy). This coagulopathy is worsened by the injury itself, which activates the clotting cascade.

Recent protocols for massive transfusion have been shown to decrease mortality. Although ideal ratios of RBCs, plasma, and platelets are still being developed, current recommendations are to give 1 U of plasma and 1 U of platelets for each 2 U of blood. Having a massive transfusion protocol (MTP) in place and using a massive transfusion box (Table 1) with a standardized supply of packed RBCs, plasma, and platelets where these blood products can be administered in predetermined ratios can help the anesthesia professional function in a critical situation. There are major variations among institutional practices of MTPs. The variations include the activation of the MTP, whether it is a verbal or written order, and administration procedures of blood products. The administration of blood products varies regarding the ratio of blood products given, the process of how the blood bank prepares and recycles the blood products as they are being used, and the use of laboratory values to guide the administration of products. Massive transfusion protocols with higher ratios of plasma and platelets to packed RBCs are associated with increased survival rates in patients with massive hemorrhage because of improved coagulation benefits from the early administration of these products. Although more research is needed in the area of standardizing the ratio of blood products for MTP based on the type of trauma, the following case study is an example of how an MTP can contribute to a positive outcome.

Massive transfusion is not without important clinical considerations, which include hypothermia, hypocalcemia, hyperkalemia, and acidosis. Prevention of hypothermia is critical during massive transfusion because the incidence of morbidity and mortality is greatly increased in the presence of hypothermia. This happens as the core body temperature decreases. Clinical signs may be cardiac arrhythmias and changes in the electrocardiogram (ECG) that can lead to hypotension and decreased cardiac output, further compromising the patient’s hypovolemic state. Blood products and the room temperature should be warmed. Use of warming devices is recom-

<table>
<thead>
<tr>
<th>Box No.</th>
<th>Red blood cells (U)</th>
<th>Plasma (U)</th>
<th>Platelets (U)</th>
<th>Cryoprecipitate</th>
<th>Factor VIIa (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6</td>
<td>4</td>
<td>2 (5 pooled)</td>
<td>—</td>
<td>7 (if requested)</td>
</tr>
<tr>
<td>2</td>
<td>10</td>
<td>10</td>
<td>2 (5 pooled)</td>
<td>2 5 U packs or 10 U pooled</td>
<td>7 (if requested)</td>
</tr>
</tbody>
</table>

Table 1. Product List in Mass Transfusion Box

* NovoSeven (Novo Nordisk Inc).
(Source: Cotton et al.5)
mended. Hypocalcemia will likely present as hypotension and occurs as the citrate in transfusion products binds to calcium, resulting in decreased calcium levels. Laboratory levels of ionized calcium should be used to guide replacement therapy. As potassium is released from stored RBCs, hyperkalemia may occur. This may present on an ECG as peaked T waves. Hyperkalemia can be treated with either 1 ampule of 10% calcium gluconate by intravenous (IV) injection over 10 to 15 minutes or 1 ampule of 10% calcium chloride by IV. Acidosis can occur from the additives used to store blood. Treatment should be based on blood gas analysis. A dose of 1 mEq/kg of sodium bicarbonate may be given and repeated depending on the response.

**Case Summary**

A 29-year-old woman presented to a university hospital outpatient operating room for an elective laparoscopy and hysteroscopy for endometrial resection. The patient's height was 1.6 m (5 ft 3 in) and weight was 47.6 kg (105 lb). A review of systems yielded normal findings, and results of the physical examination were within normal limits. She was classified as an ASA class 2. Her medical history included congenital didelphic uterus, unilateral (right) renal agenesis, previous uterine fibroids, past anxiety, and postoperative nausea and vomiting. Preoperative vital signs were within normal limits. The hematologic results were as follows: hematocrit, 44.3%; hemoglobin, 14.8 g/dL; and platelets, 195,000/mL.

Blood typing and screening samples were available in the blood bank the morning of surgery. The anesthesia care plan was for general anesthesia with endotracheal intubation. There was a discussion between the anesthesia provider and the surgical resident regarding the patient's previous laparoscopic surgeries. The surgical resident participated in previous gynecologic surgeries for this patient. The resident explained that the patient's gynecologic anatomy was mildly abnormal, and in previous surgeries the patient experienced more than expected blood loss. The anesthesia provider and the surgical resident decided that a type and screen with a cross-match was secured. An orogastric tube was inserted for gastric decompression. A second site for IV access was obtained with an 18-gauge catheter inserted into the left cephalic vein. Doxycycline, 100 mg, was administered before incision. The patient was placed in Trendelenburg with low lithotomy position. Anesthesia was maintained with 1.8% to 2.2% sevoflurane and a mixture of 50% oxygen and 50% air. During the universal time-out, preoperative hemoglobin and hematocrit concentrations, available blood products, and IV access were discussed between the surgical and anesthesia care teams.

Two and half hours after incision, during placement of a resectoscope, the patient sustained a uterine perforation with injury to the right internal iliac artery, resulting in massive blood loss and immediate hypotension. The anesthesia provider immediately requested additional anesthesia personnel and began volume resuscitation with hetastarch and lactated Ringer's solution. A vascular surgeon was called emergently to the operating room, and the MTP was initiated. Additional IV access was obtained with an 18-gauge catheter inserted into the left basilic vein and with a 14-gauge catheter into the left external jugular vein. A left radial arterial line was inserted, and a blood gas sample was sent for analysis. The patient's hemodynamic status was unstable, with blood pressures ranging from 48/32 mm Hg to 98/50 mm Hg. Sinus tachycardia ranging from 120/min to 150/min was noted. Phenylephrine was given in 100-µg boluses during volume resuscitation to support perfusion. The vascular surgeon repaired the right internal iliac artery simultaneously while the obstetrician-gynecologist repaired the perforated uterus.

The operating room was warmed, and the MTP continued with the administration of 7 U of packed red blood cells (PRBC), 3 U of pooled platelets, and 5 U of fresh frozen plasma (FFP). A total of 5 L of lactated Ringer's solution was given as well as 1 L of hetastarch. Total blood loss was calculated at 5 L. For correction of electrolyte abnormalities, 2 g of calcium chloride and 50 mEq of sodium bicarbonate were administered. The hematocrit level returned to 25.3% from a low of 12% before resuscitation. Hemodynamic measurements returned to baseline status, and the patient was prepared for transfer to the intensive care unit (ICU). Hydromorphone, 0.8 mg, was administered, as well as midazolam, 2 mg. Muscle relaxation was maintained with rocuronium. The orogastric tube was removed, and a nasogastric tube was inserted. The patient was transferred to the ICU with full hemodynamic monitoring in place. The patient remained hemodynamically stable and was extubated 2 hours later.

The hospital course was complicated by admission to the surgical ICU as well as postoperative fevers of unknown origin. On postoperative day 2, a fever developed, and the patient received antibiotic therapy. The infectious disease department was called to consult as the fevers continued despite multimodal antibiotic therapy,
normal computed tomographic scans of the abdomen, and negative blood cultures. The patient experienced idiopathic hepatitis, pancreatitis, and a rash in what was believed to be a reaction to cefazidime therapy, which was immediately discontinued. On postoperative day 18, the fever of unknown origin dissipated, and antibiotic therapies were discontinued. The patient was discharged to home on postoperative day 21.

**Discussion**

Massive transfusion is defined as replacement of 5 U of packed RBCs in 3 hours because of uncontrolled hemorrhage. It is most commonly observed in trauma patients, followed by patients undergoing liver transplantation, obstetric catastrophes, and intraoperative hemorrhage. In this case study, the patient was scheduled for an elective outpatient procedure and consequently required a massive transfusion. Massive transfusion is effective when carried out by personnel familiar with the protocol. It is essential to request additional resources because support staff is needed to check and administer blood products with a rapid infuser. Well-established IV access is crucial for massive volume resuscitation. An arterial line is useful for continued sampling of arterial blood gases and to monitor for electrolyte imbalances. Hypocalcemia, hyperkalemia, and metabolic acidosis are complications seen in cases of massive transfusion.

Blood product considerations are discussed here. **Packed Red Blood Cells.** Each unit of packed RBCs contains approximately 200 mL of red blood cells and will raise the hematocrit level by approximately 3% to 4% unless bleeding is not controlled. It is critical for the surgical team to control hemorrhage. Plasma potassium concentrations in stored blood increase approximately 1 mEq/L/d because of passive cellular leakage. Potassium is not actively transported back into the RBCs because membrane adenosine triphosphatase is inhibited. As a result, electrolyte analysis should be performed. The ECG should be monitored for signs and symptoms of hyperkalemia.

**Fresh Frozen Plasma.** During a massive transfusion there is a dilution of plasma clotting RBCs and FFP is recommended. Platelets lead to prolongation of the prothrombin time and the activated partial thromboplastin time. There is a 10% decrease in the concentration of clotting proteins for each 500 mL of blood loss that is replaced. After large blood loss and the replacement of 4 U or more of RBCs, dilutional thrombocytopenia and hypothermia can contribute to the development of coagulopathies in patients receiving massive transfusion. Platelets should be transfused in a 1:1:1 ratio alternating between RBCs, FFP, and platelets. Coagulation panels should be obtained during massive transfusion. Disseminated intravascular coagulation (DIC) panels need to be analyzed as well. DIC is a complication of massive transfusion.

**Cryoprecipitate.** Cryoprecipitate preparation is a concentrated form of antihemophilic factor. A dose of 10 single bags of cryoprecipitate derived from units of whole blood typically raises the plasma fibrinogen level by up to 1 g/L (60-100 mg/dL).

**Factor VIIa.** NovoSeven (Novo Nordisk Inc) is recombinant human coagulation factor VIIa, which promotes hemostasis by activating the extrinsic pathway of the coagulation cascade. Fresh frozen plasma, cryoprecipitate, and platelets need to be given before the administration of factor VIIa in order for it to have an effect on clotting. Factor VIIa should not be given without correcting the underlying hypovolemia using blood products first. The current recommended dose is 100 mg/kg. Factor VIIa is expensive and is ineffective in the presence of hypothermia and/or acidosis.

The MTP policy in this institution is activated by either ICU physicians or anesthesia personnel based on clinical judgment and the following criteria: the presence of life-threatening hemorrhage not expected to respond to crystalloid solution and/or uncontrolled major bleeding associated with hypotension in the ICU, trauma bay, or operating room. In the operating room setting, the anesthesia provider verbally orders the operating room nurse to notify the blood bank that the MTP is being activated. A designated operating room assistant picks up the transfusion box that is located in a centralized walk-in refrigerator. The mass transfusion boxes contain cold packs to maintain proper temperature when sent out. As the blood products are used, they are replaced and rotated to thaw for further availability. The blood bank and the anesthesia provider communicate regularly to expedite any laboratory testing that may be helpful in determining the status of the patient’s hemostasis. References, such as UpToDate, can be accessed in the operating room to help guide providers in blood transfusion therapy. This is a useful tool, especially when a protocol does not already exist, or clarity is needed. Ideally, a protocol is in place, so that the providers can activate the protocol and respond quickly. This protocol should be created using a multidisciplinary approach, and having a blood bank representative present in its creation is essential. Having a mass transfusion protocol in place with clear objectives can help focus the team on specific tasks and can provide a rapid response in the case of intraoperative hemorrhage (Table 2).

**Conclusion**

In this case, vigilance and prompt activation of the MTP along with additional anesthesia support allowed the team to quickly respond to and restore hemodynamic stability following an intraoperative hemorrhage. The surgical team simultaneously recognized the need for additional assistance. In conjunction with a vascular surgeon, they were able to control the hemorrhage. With the use of all available resources, the patient was quickly stabilized and
later discharged, with no long-term sequelae. The importance of communication and teamwork is vital during critical situations. Having an anesthesia provider familiar with the MTP assisted in the rapid response to a critical situation and led to a favorable outcome for this patient.

REFERENCES

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