Emergency Transfusions

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KEYWORDS

• Transfusion • Blood • Resuscitation • Coagulopathy

KEY POINTS

- In the setting of bleeding, crystalloid should be limited and blood transfusions should be initiated early.
- Blood products should be utilized in a balanced ratio and should be guided by viscoelastic assays and endpoints of resuscitation.
- It is essential to urgently address the cause of the hemodynamic instability or coagulopathy to maximize the benefit of any transfusion.

INTRODUCTION

Trauma is the leading cause of life-years lost throughout the world, with hemorrhage accounting for 30% to 40% of trauma mortalities.[1–3] The ability to recognize and treat acute blood loss and trauma-induced coagulopathy (TIC) is a skill for all emergency providers. There are numerous approaches to emergency transfusion resuscitation but they each center on the early utilization of blood products while allowing for permissive hypotension and minimizing crystalloid administration. Together, these factors have been shown to improve outcomes and decrease complications.[4,5] This article approaches the major principles of emergency transfusions, starting with obtaining access and advancing through resuscitation approaches and concluding with special considerations and endpoints of resuscitation.

CONSIDERATIONS IN EMERGENT TRANSFUSION

Once a patient is identified as needing an emergent transfusion, the focus should be on establishing hemostasis and correcting coagulopathy in a timely manner. The time to hemostasis consistently has been associated with outcome and, therefore, must be a primary focus alongside initial stabilization maneuvers and airway securement.[6]

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The decision to transfuse a patient should coincide with multiple other considerations (Box 1).

OBTAINING ACCESS

Intravenous (IV) access is a critical first step in addressing emergency transfusions. Although obtaining large-bore IVs is taught in courses, such as advanced trauma life support (ATLS), it is easily overlooked until it is difficult to obtain.[7] This article addresses 4 different approaches: prehospital IV placement, central venous catheter (CVC), intraosseous (IO) access, and rapid infusion catheter.

Prehospital Intravenous Access

Obtaining IV access prior to decompensation can be life-saving. Large-bore peripheral IVs are the preferred access for rapid delivery of resuscitative fluids in an unstable patient. One unique situation that warrants special attention is in the prehospital setting. Paramedics are very capable of placing IVs under difficult situations; however, prehospital IV placement does not appear to improve patient outcomes significantly.[8] When assessed in a study of 200 participants, prehospital time was prolonged in patients when IV access was obtained in the prehospital setting.[9] Additionally, there was no improvement in the time to transfusion upon hospital arrival.[9] Therefore, it is recommend that, particularly in situations with short prehospital times, the goal should be to expedite transportation, with a scoop-and-run approach.

Central Venous Catheter

CVC placement is a viable option in the emergent setting, particularly when placed under ultrasound guidance.[10] On average, placing a CVC requires more than 3 minutes to place; however, this may take longer based on operator experience, collapsed vessels from hypovolemic shock, and variant anatomy.[11] When selecting the type of CVC, a CVC with an 8-French or 9-French sheath is preferred because larger diameter and shorter catheter length limit resistance and facilitate rapid infusion.[12]

Box 1
Considerations in resuscitation

Does the patient have sufficient IV access?
- Does the patient require additional access? If so, what resources are available?

Will the patient benefit from blood transfusion?
- How much blood loss occurred in the prehospital setting?
- Is the patient currently bleeding? If so, what is the safest method to achieve hemostasis?

How urgent is this transfusion?
- Is it appropriate to use uncrossmatched or type-specific blood?
- Are multiple units of blood expected? If so, is massive transfusion anticipated?

What other factors are contributing to ongoing bleeding or hemodynamic instability?
- Is the patient on anticoagulation or antiplatelet therapy?
- Are there signs and symptoms of coagulopathy from other causes, such as acute hemorrhagic or septic shock?
- Are these factors correctable?

What are the endpoints of resuscitation?
- Is the patient hemodynamically stable after the resuscitation?
- What laboratory values are available to determine resuscitation status?

Not all CVCs are compatible for contrast power injectors for computed tomography scans, if that is deemed necessary. It is important that providers are familiar with their available equipment to help expedite patient care. With respect to patient complications, there is a risk of unintended arterial injury, line infection, and deep venous thrombosis, especially when placed in an urgent situation. It generally is recommended that these lines should be replaced under sterile conditions within 48 hours.[13,14]

Intraosseous Device

IO device placement offers a rapid alternative to IV access that most physicians, nurses, and paramedics are trained to place.[15,16] The timing for the placement of an IO device is equivalent to the timing for a peripheral IV and is faster than placement of a CVC.[11] Although an IO device does have a slower transfusion rate compared with an IV, in animal models, the time to return blood pressure to baseline is comparable. Furthermore, IO devices have been shown to be safe for administration of blood products.[17]

Rapid Infuser Catheter

A rapid infuser catheter can be a valuable tool to secure adequate access for massive transfusion when a CVC or IO is not readily available. This initially requires a 20-gauge IV access in a superficial peripheral vein, typically in the upper or lower extremities, which then can be exchanged into a large bore sheath over wire.[18]

PERMISSIVE HYPOTENSION

Most patients who require emergency transfusions have some degree of hemodynamic instability. It is important that this is not corrected too abruptly, because it can result in platelet disruption and ongoing bleeding. There are numerous studies that have demonstrated the importance of permissive hypotension. Bickell and colleagues[19] showed that delaying fluid resuscitation in patients with a systolic blood pressure (SBP) less than or equal to 90 mm Hg until they reached the operating room for penetrating torso injuries resulted in an 8% improved survival. Morrison and colleagues[20] demonstrated that targeting a mean arterial pressure of 50 mm Hg, rather than 65 mm Hg, resulted in lower rates of death and coagulopathy in the early postoperative setting. Schreiber and colleagues performed a feasibility study in patients with prehospital SBPs of less than or equal to 90 mm Hg. This study compared administering 2 L of crystalloid initially and additional fluid to maintain an SBP greater than or equal to 110 mm Hg to those patients who received 250-mL boluses of crystalloid to maintain a radial pulse of an SBP greater than or equal to 70 mm Hg. This study demonstrated a 10% improvement in mortality in the permissive hypotension group.[21]

MASSIVE TRANSFUSION AND CRITICAL ADMINISTRATION THRESHOLD

The American College of Surgeons Committee on Trauma (ACS-COT) mandates that trauma centers develop a massive transfusion protocol (MTP). The goal of the MTP should be to meet the transfusion requirements of the patient rapidly. The MTP is centered on identifying triggers for activation of MTP, product availability and delivery, continuation of the MTP during procedures and in the intensive care unit (ICU), transfusion targets, and termination of the MTP.[22]

There are numerous criteria that may be used to trigger an MTP, ranging from blood transfusion requirement in the trauma bay to the Assessment of Blood Consumption (ABC) score (**Box 2**). The ABC score assigns a score of either 0 or 1 to 4

Box 2
Assessment of blood consumption

Penetrating mechanism (no = 0 points; yes = 1 point)

Heart rate (≤120 = 0 points; >120 = 1 point)

SBP (≥90 = 0 points; <90 = 1 point)

FAST examination (negative = 0 points; positive = 1 point)

Abbreviation: FAST, focused assessment with sonography for trauma.

Data from Nunez TC, Voskresensky IV, Dossett LA, Shinall R, Dutton WD, Cotton BA. Early prediction of massive transfusion in trauma: simple as ABC (assessment of blood consumption)?. J Trauma. 2009;66(2):346-352. https://doi.org/10.1097/TA.0b013e3181961c35.

components that are easily assessed in the trauma bay. The ABC score has been validated in a multicenter study, with a score of 2 or more resulting in a sensitivity of 75% to 90% and a specificity of 67% to 88% for predicting the need for massive transfusion.[23]

The initiation of the MTP must be accompanied by a plan for administering blood products and recognizing when the MTP may be discontinued (described later); uncrossed blood products should be utilized until group-matched products are available. The ACS-COT recommends the MTP should be administered in a ratio-driven fashion until all surgical bleeding is controlled in the operating room or there is radiographic and physiologic evidence of bleeding control after angioembolization.[22]

Massive transfusion historically has been defined as administration of 10 U of packed red blood cells (pRBCs) over a 24-hour period. This definition can be problematic, because it does not account for patients who die early within this fixed time period and fails to recognize the difference between patients who are acutely unstable and those who require transfusions from slow persistent bleeding.[24,25] Alternatively, the critical administration threshold, defined as requiring 3 U of pRBC transfusion per hour, is believed to better reflect the severity of hemorrhagic shock and a better predictor of mortality.[26]

FIXED RATIO RESUSCITATION

Over the past decade, there has been increased focus on how to deliver blood products in the order and ratio that are best suited to meet the physiologic demands associated with hemorrhagic shock. In general, the goal is to "replace what the patient is losing." In other words, the bleeding patient is losing red blood cells as well as clotting factors and platelets, and the resuscitation plan must account for each component.

The Prospective, Observational, Multicenter, Major Trauma Transfusion (PROMMTT) study was a landmark trial looking at transfusion ratios. This was a prospective cohort study that included 10 level 1 trauma centers. All patients were adult trauma patients who survived at least the first 30 minutes after admission and who received at least 1 U of pRBCs within the first 6 hours and at least total 3 U of blood products within 24 hours. The primary outcome was in-hospital mortality with a focus on the number and type of transfusions as well as the timing they were administered. The PROMMTT study highlighted that at 30 minutes after admission, 67% of patients had not received plasma and 99% had not received platelets. Although the resuscitation was more likely to become balanced with more time after admission, across multiple level 1 trauma centers, there was no constant ratio of blood products

administered during the period of active resuscitation. It also recognized that higher plasma and platelet ratios were associated with decreased 6-hour mortality.[27]

The follow-up Pragmatic, Randomized Optimal Platelet and Plasma Ratios (PROPPR) trial was designed to address the effectiveness of using plasma:platelets:pRBC ratios, 1:1:1 versus 1:1:2. This phase 3 multicenter trial compared 24-hour and 30-day mortality between patients who received platelets first and then alternative plasma and pRBCs in either a 1:1 or a 1:2 ratio. The PROPPR trial showed the 1:1:1 group achieved hemostasis and experienced fewer deaths related to exsanguination by 24 hours. There was no difference found between the groups with respect to 24-hour and 30-day mortality. This study recognized that 1:1:1 resulted in hemostasis and fewer deaths within the first 24 hours.[5]

VISCOELASTIC ASSAY GOAL-DIRECTED THERAPY

The use of viscoelastic assays (VHAs), such as thromboelastography (TEG) and rotational thromboelastometry, has offered an alternative to the use of traditional coagulation laboratory panels. Unlike conventional coagulation assays, such as the international normalized ratio and partial thromboplastic time, VHAs give more insight into which steps of coagulation are either deficient or hyperactive. In this way, VHAs allow for early recognition of TIC and provide a goal-directed path to the correction of TIC.[28,29] VHA-guided resuscitation has resulted in improved survival with decreased transfusion requirements compared with MTP resuscitation guided by the more conventional coagulation assays.[30,31] There is an ongoing debate about the use of VHA versus fixed ratio transfusions.[32]

TRANSFUSION CONSIDERATIONS AND ADJUNCTS

Limiting Crystalloid Infusions

Crystalloids are relatively inexpensive and convenient fluid of choice for resuscitation. For this reason, ATLS recommends judicious administration of no more than 1 L of crystalloid while allowing permissive hypotension during the initial phase of emergent resuscitation.[7] Aggressive crystalloid resuscitation fell out of favor, however, because it is associated with several complications. One major concern is that crystalloid can worsen the trauma triad that consists of acidosis, hypothermia, and coagulopathy. Specifically, most crystalloid solutions have a low pH resulting in metabolic acidosis and are not sufficiently warmed, which contributes to hypothermia. Additionally, because crystalloid solutions do not contain clotting factors, dilution coagulopathy may develop. Although crystalloid infusions may be more easily available, liberal use of crystalloid can be detrimental to patients.[4,33]

Aggressive early fluid resuscitation also has been associated with numerous complications beyond the initial mortality. In a prospective multicenter study that contained approximately 2000 patients, the volume of crystalloid resuscitation was associated with ventilator days as well as both days in ICU and hospital length of stay.[34] Additionally, crystalloid volume was associated, in a dose-dependent fashion, with the development of acute lung injury, acute respiratory distress syndrome, multiple organ failure, bloodstream infections, surgical site infections, and abdominal and extremity compartment syndromes.[34]

Plasma First

Damage control resuscitation in trauma is based on the premise of preventing and correcting coagulopathy. Given that plasma has been shown to decrease coagulopathy and limit endothelial inflammatory response, it is reasonable to consider starting

resuscitation efforts with plasma, as opposed to pRBCs.[35] The Prehospital Plasma during Air Medical Transport in Trauma Patients at Risk for Hemorrhagic Shock (PAMPer) study evaluated approximately 500 patients in a multicenter phase 3 superiority trial. This study compared prehospital use of thawed plasma with standard care. In this case, the standard-care group may have received crystalloid solution, which was available at all sites, and/or pRBCs, which were available at 13 of 27 sites. The PAMPer study showed a 9.8% decrease in 30-day mortality for patients who received plasma.[36]

Unfortunately, not all studies have shown a clear improvement in patient outcomes. One study in an urban setting with short prehospital times was stopped early due to the lack of improvement in the setting of a high financial burden of providing prehospital plasma.[37] A separate study that included a large number of air transport showed an improvement in TEG studies but failed to show a significant outcome improvement.[38]

Uncrossmatched Blood

In the emergency setting where crossmatched blood is not immediately available uncrossmatched type O blood should be used for resuscitation.[39] The goal in these instances is to provide blood that is compatible, even if not type-specific. Ideally, uncrossmatched O blood should be available in the emergency department to allow for an effective way to transfuse pRBCs.[40] In settings where there is a high rate of injury recidivism in the trauma population, frequent use of uncrossmatched blood transfusion may increase the likelihood of receiving multiple transfusions over the course of their lifetime, increasing the risk of hemolytic transfusion reactions (HTRs). Approximately 30% to 40% of patients who receive uncrossmatched blood meet some criteria for HTRs, although it is rare for a patient to develop clinically significant adverse effects.[41,42] A high index of suspicion should be maintained for HTRs when transfusing an unstable patient with acute hemorrhage nonetheless.

One area of concern with using uncrossmatched blood is the development of anti-Rh antibodies. This is a concern especially in women of childbearing age. Women with Rh-negative or unknown Rh status should receive Rh-negative blood. Alloimmunization occurs in approximately 20% of Rh-negative patients who receive Rh-positive blood. Most of these patients develop anti-D antibodies with transfusions of 2 U to 4 U of blood.[43] Although RhD alloimmunization may not pose immediate risks during the acute transfusion period, this may affect a woman's subsequent pregnancy or future transfusion. It is recommended that Rh-negative women who receive Rh-positive transfusions should receive treatment. One option is to administer Rh immunoglobulin (RhIg) within 72 hours of the initial transfusion. One vial of RhIg contains 300 μg of the immunoglobulin and is effective at neutralizing 15 mL of erythrocytes. Approximately 14 vials of RhIg are required to neutralize a single pRBC transfusion, but a single vial is sufficient to neutralize a single Rh-positive platelet transfusion.[44–46]

Whole Blood

The goal with all resuscitation is to restore physiologic balance, resulting in a hemodynamically stable patient. One way to do this is to transfuse whole blood. Recently, there has been an increase in civilian research assessing the safety and feasibility of whole blood. In multiple studies, whole-blood has shown similar or improved survival compared with traditional ratio-based MTP resuscitation. Additionally, patients who received whole blood have required fewer transfusions to obtain higher hemoglobin goals. Importantly, low-titer whole blood has shown either similar or decreased transfusion reaction profiles.[47–51] Taken together, this suggests a benefit to using whole

blood but most studies at this point are relatively small and additional work is required before its clinical utility and safety can be fully endorsed.

Tranexamic Acid

Tranexamic acid (TXA) is an adjunct to massive transfusion in the setting of hyperfibrinolysis. The Clinical Randomisation of an Antifibrinolytic in Significant Haemorrhage 2 (CRASH-2) trial concluded that TXA safely reduces the risk of death in bleeding trauma patients without significantly increasing the risk of vascular occlusive events.[52] As understanding of the variations of fibrinolysis continues to develop, there has been ongoing work to assess outcomes related to TXA administration. CRASH-2 presumed a hyperfibrinolytic state occurred in severely injured trauma patients, but with VHAs it is now recognized that patients may be in a hyperfibrinolytic, physiologic fibrinolytic, or shutdown fibrinolytic state. There is no known benefit for TXA use in patients in a physiologic fibrinolytic state.[53]

COMPLICATIONS OF MASSIVE TRANSFUSIONS

Massive transfusion carries risks similar to routine transfusions while also having complications associated with large-volume resuscitations.[54] Management of these conditions is beyond the scope of this article but should be considered (**Box 3**).

SPECIAL CONSIDERATIONS

Emergent transfusion must be tailored to individual patients' comorbid conditions. In addition to traumatic causes of hemorrhage, gravid patients with obstetric hemorrhage may impose further challenges in management. Patients with advanced heart failure or end-stage renal disease undergoing large-volume resuscitation are highly susceptible to hypervolemia-induced respiratory and cardiac failure. Patients with advanced liver failure present with variety of hemostatic abnormalities, which increases risks for both bleeding and thrombotic events.[55]

ENDPOINTS OF RESUSCITATION

It is important to be able to recognize when the goals of a resuscitation have been met. A key component of this requires that any ongoing bleeding has been addressed.

Box 3
Complications of massive transfusion

Acute complications
- Acute transfusion reactions
- Transfusion-related acute lung injury
- Transfusion-associated circulatory overload
- Dilutional coagulopathy
- Electrolyte abnormalities, including hypocalcemia
- Metabolic alkalosis
- Bacterial sepsis
- Hypothermia

Delayed complications
- Delayed transfusion reactions
- Transfusion-related immunomodulation
- Microchimerism

Once satisfied, there are numerous endpoints that include hemodynamic findings (eg, mean arterial pressure, central venous pressure, and cardiac output) as well as chemical markers (eg, base deficit and/or lactate), or end-organ function (eg, urine output).[22] VHA is a newer tool that also may serve a role to demonstrate correction of any coagulopathy.[56]

SUMMARY

Successful emergency transfusions require early recognition and activation of resources to minimize delays in treatment. Obtaining access fast is key to allow efficient delivery of resuscitative fluids. The initial goals should focus on replacement of blood in a balanced fashion. There is an ongoing debate regarding the best approach to transfusions, with some advocating for resuscitation with a fixed ratio of blood products and others preferring to use VHAs to guide transfusions. Whole-blood transfusion also is a debated strategy. It generally is accepted that transfusions should be started early and crystalloid infusions should be limited. As hemodynamic stability is restored, endpoints of resuscitation should be used to guide the resuscitation.

DISCLOSURE

The authors have nothing to disclose.

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