The Journal of Emergency Medicine, Vol. 39, No. 2, pp. 253–260, 2010

0736-4679/$–see front matter

doi:10.1016/j.jemermed.2009.02.034

Clinical Reviews

TRANSFUSION OF BLOOD PRODUCTS IN TRAUMA: AN UPDATE

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□ **Abstract—Background: Blood transfusion in the management of severely injured patients can be lifesaving. These patients are susceptible to developing early coagulopathy, thus perpetuating bleeding. Objectives: This article presents recent advances in both the civilian and military clinical arena to improve the treatment of trauma patients with severe hemorrhage, the use of agents to support coagulation, perspectives on restrictive transfusion strategies, and transfusion-related risks. Discussion: Massive blood transfusion is an adjunct to surgical care. The volume of blood products transfused and the ratio of blood components have been associated with increased morbidity and mortality rates. The adverse clinical effects of transfusion and the limited supply of blood products have resulted in modern resuscitation protocols to limit the volume of blood transfused. Conclusion: A restrictive blood transfusion strategy and the use of hemostatic agents may decrease morbidity and mortality in trauma patients, but insufficient data are available for their use in trauma patients. Massive transfusion should reflect an equal ratio of packed red cells and plasma to limit coagulopathy. Prospective randomized trials are needed to standardize an effective protocol. © 2010 Elsevier Inc.**

□ **Keywords—Blood components; Massive transfusion; Red blood cell; Coagulopathy; Trauma**

INTRODUCTION

Trauma is a major global health problem and the leading cause of death worldwide in individuals aged 1 to 44 years (1,2). Hemorrhage after trauma is the second most frequent cause of death, exceeded only by traumatic brain injury, and remains the leading cause of potentially preventable and early in-hospital deaths (2–6). The modern approach to trauma care, including effective prehospital care, development of trauma systems, and appropriate resuscitation, have improved the outcomes of critically injured patients (2,3,6–8).

Approximately 12 million units of packed red blood cells are transfused each year in the United States; 40% are used for emergency resuscitation, with 10–15% of that used in treating trauma patients (9). In civilian practice, 8–11% of trauma patients receive blood products as part of treating acute injury (10,11). Upon patient arrival to the emergency department (ED), initial clinical evaluation based on Advanced Trauma Life Support (ATLS®) principles and assessment of the extent of bleeding should occur along with identification of patients who need urgent surgical interventions. Initial resuscitation is essential to restore and support tissue oxygenation and perfusion, therefore the need for blood transfusion should be considered early. In hemodynamically stable patients, blood transfusion may be a significant therapeutic adjunct to non-operative management (4).

The acquired coagulopathy of trauma is responsible for a large number of deaths and is a major cause of battlefield mortality. An aggressive approach to treating post-traumatic coagulopathy has the greatest potential to improve outcomes in trauma patients (12–14). The ideal

RECEIVED: 24 July 2008; FINAL SUBMISSION RECEIVED: 10 February 2009;
ACCEPTED: 26 February 2009

ratio between different transfused blood components remains controversial. The early use of packed red blood cells (PRBCs), fresh frozen plasma (FFP), and platelets still offers the best chance of limiting coagulopathy in the early phases of care (15–19). However, transfusion can have an immunomodulatory effect, by decreasing cell-mediated immunity, increasing a proinflammatory state, augmenting the risk of infection, increasing the risk of acute respiratory distress syndrome, and leading to multi-system organ failure (MOF) (10,12,14).

Our purpose was to review the current literature on blood transfusion, evaluate recent strategies for blood replacement, and review the battlefield experience with resuscitation strategies. We reviewed the existing literature based on a MEDLINE search for the past two decades ending July 2008. Keywords searched included "massive transfusion" and "coagulopathy," and were limited to "trauma" and "injury." Even though we present a comprehensive and balanced review, we recognize the limitation of existing data, further underscoring the need for future investigation.

TRAUMA RESUSCITATION

The current ATLS® protocol defined by the American College of Surgeons calls for the replacement of each milliliter of blood lost with 3 mL of isotonic crystalloid. In patients presenting with hypovolemic shock and an unidentified source of bleeding, aggressive fluid resuscitation may be detrimental, as it may increase blood loss, leading to hemodilution, coagulopathy, and recurrent hypotension. The "hypotensive resuscitation" strategy advocates that aggressive fluid infusion should be held until surgical control of bleeding can be achieved. This principle is based on the concept that active surgical bleeding (bleeding from injured vessels or organs) is exacerbated if a patient is aggressively resuscitated with crystalloid solution to maintain intravascular volume and pre-injury systolic blood pressure. This concept is of particular interest in battlefield injuries, where medical personnel are often faced with a prolonged pre-hospital phase in an acutely hemorrhaging patient. In a study of 598 hypotensive penetrating torso trauma patients, those receiving immediate resuscitation had a slightly lower overall survival (62%) compared to patients in whom resuscitation was delayed (70%) (20). There was no difference in the rate of organ failure or infectious complications in either group. This has led to a minority of trauma centers adopting a strategy of hypotensive resuscitation in a select group of patients despite other investigators having equivocal results (6,12,18,21). For now, hypotensive resuscitation remains mostly theoretical in its benefit, with a paucity of evidence reflected only in animal models and in limited human trials (20,22).

Hypotension is frequently used as a marker of significant hemorrhage, but it is a late sign consistent with $>$ 30% blood loss. Hemoglobin (Hb) levels obtained shortly after trauma may be confounded by crystalloid-related dilution. Frequently, Hb may be fictitiously high, not yet equilibrating to actual blood loss. In a recent study, Bruns et al. obtained three Hb measurements within the first 30 min of patient arrival to the ED and identified that an early decrease in Hb level ($\leq$ 10 g/dL) was associated with the need for emergent interventional procedures (surgical or angiographic) to stop bleeding in 87% of patients (23). They concluded that an initial Hb $\leq$ 10 g/dL can be used as a trigger to prompt an aggressive search for sources of bleeding.

Massive transfusion protocols are beneficial in trauma patients with severe hemorrhage, with varying definitions identifying these patients (Table 1) (5). In lethal hemorrhagic shock, transfusion of blood products is performed empirically, not guided by laboratory tests, but based on clinical parameters otherwise known as "blind" transfusion (24).

Resuscitation fluids used in trauma are not innocuous, and may exacerbate the initial cellular injury caused by hemorrhagic shock. An ideal fluid should be efficacious, safe, inexpensive, easy to store and transport (especially in the military setting), assist in carrying oxygen and nutrients to the cells, and have beneficial immunomodulatory properties (Table 2) (12,21,25).

Blood recovery techniques can be used to reduce blood loss and to minimize the need for transfusion. Cell savers are the most commonly employed technique in the operating room. This device collects, filters, and returns patient blood loss throughout surgery. However, there are no randomized trials of cell saver use in trauma patients to support routine autotransfusion (3,26). Autotransfusion of blood after thoracostomy tubes in the ED for a hemothorax may be an effective method of returning patient blood volume and limiting transfusions, however, no definitive trial exists proving that this improves outcome.

One important development in modern trauma management is distinguishing surgical and non-surgical

Table 1. Definitions of Massive Hemorrhage

Loss of an entire blood volume equivalent within 24 h; or
Loss of 50% of blood volume within 3 h; or
Continuing blood loss of 150 mL/min; or
Continuing blood loss of 1.5 mL/kg/min over 20 min; or
Rapid blood loss leading to decompensation and circulatory failure despite volume replacement and interventional treatment