

MASSIVE TRANSFUSION AND CONTROL OF HEMORRHAGE IN THE TRAUMA PATIENT

Introduction

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Priorities in trauma patient management are to ensure adequate ventilation and oxygenation, control hemorrhage, and maintain tissue perfusion to vital organs. The most familiar means to control hemorrhage are surgical ligatures and clips. Other means include transcatheter embolization, appropriate blood component therapy, maintenance of normothermia, and pharmacologic agents. Finally, attention must also be directed toward treatment of the hypercoagulable state that follows major traumatic injury and can lead to deep venous thrombosis and pulmonary embolism.

The first edition of a monograph on the topic of “Massive Transfusion and Control of Hemorrhage in the Trauma Patient” was developed by the International Trauma Anesthesia and Critical Care Society following two special ITACCS seminars in 1999 during which leading experts discussed this subject. The 12 reports of these updated articles that comprise this issue of *TraumaCare* summarize the state-of-the-art knowledge and clinical practice issues regarding surgical and nonsurgical management of massive transfusion and control of hemorrhage in the injured patient.

In the section on “Etiology and Pathophysiology,” Dr. Scalea reviews the physiologic importance of recognizing and restoring hemostasis following injury and discusses the American College of Surgeons’ classification scheme for hemorrhage, as well as operative and nonoperative (e.g., embolization) techniques for treatment of bleeding. He emphasizes that embolization is the preferred technique for most pelvic bleeding, and that embolotherapy plays a major role in nonoperative management of solid visceral injuries within the abdomen and in patients with vascular injuries in relatively inaccessible areas. Dr. Dutton discusses the four phases of traumatic shock and reviews the macro- and microcirculatory responses to traumatic shock, responses that ultimately determine patient outcome.

The “Therapeutic Strategies” section begins with a report on surgical perspectives to control bleeding in trauma. In his article, Dr. Plaisier describes the benefits and risks of topical hemostatic agents such as oxidized cellulose, collagen sponges, thrombin, gelatin matrix, denatured Gelfoam, and fibrin glue. He reviews the concept

of damage control, and reports on the use of recombinant activated human factor VII (rFVIIa) for trauma patients. Drs. Satkurunath and Royston review the hemostatic and anti-inflammatory effects of a variety of drugs in trauma such as aprotinin, epsilon-aminocaproic acid, tranexamic acid, desmopressin, and rFVIIa. There appears to be a significant benefit of high-dose aprotinin therapy to reduce blood loss and the need for blood and blood product transfusion. However, aprotinin has been withdrawn from the market. The main theoretical risk of hemostatic drugs is excess coagulation forming thrombosis in the venous or arterial system. Drs. Shander, Gandhi, and Goodnough discuss the etiology and pathophysiology of anemia in the critically ill. Most trauma patients develop anemia because of ongoing blood losses, occult losses, and/or decreased red cell production in the intensive care unit. Phlebotomy is one of the major contributors to these ongoing blood losses. The benefits and risks of erythropoietin therapy to correct anemia in trauma are discussed as well as the risks of allogeneic transfusion. Several randomized, prospective studies support the use of recombinant human erythropoietin in critically ill patients to overcome the blunted endogenous erythropoietin response to anemia.

In their article, Drs. Rubens, Mujoomdar, and Tien advocate the use of cell salvage in trauma and hemorrhage. Advantages and disadvantages of cell salvage are reviewed. Evidence supports that salvaged red cells have normal functioning and survival as compared with blood simultaneously collected by venipuncture, and there is supportive evidence that this collected blood has a greater oxygen-carrying capacity than banked blood. Centrifugal washing is extremely effective at hemoconcentrating the blood product. Centrifugal washing also removes most soluble proteins and nonerythrocyte particulate matter, such as interleukin-6, tumor necrosis factor, thrombin antithrombin III complex, and free hemoglobin.

The section on “Transfusion: Clinical Practice” begins with a review of fluid and blood component therapy in trauma by Drs. Novikov and Smith, and addresses various issues such as delayed fluid resuscitation, hypertonic fluids, end points of fluid and blood resuscitation, complications of transfusion therapy, and clinical strategies to reduce complications. In his article on fluid choice for resuscitation, Dr. Boldt states that choice of fluid should take into account effects on inflammation, perfusion, and tissue oxygenation. An important aspect of fluid therapy in the traumatized patient is the risk of inducing interstitial edema. This risk is reduced with certain colloids (e.g., low-molecular-weight hetastarch) that are associated with beneficial effects beyond their volume-replacing properties (e.g., improving microperfusion, capillary integrity, inflammatory response, and endothelial activation/integrity). Dr. Waters reviews the scientific literature in his article pertaining to trauma surgery and transfusion options, with the concept of “decreasing the amount of blood transfused to trauma patients” in light of transfusion-related immunomodulation, transfusion-related acute lung injury, and other risks. The known risks of allogeneic blood can be decreased by lowering the transfusion trigger and using cell salvage. The principles of warming intravenous fluid and blood are reviewed by Drs. Smith and Wagner, with special emphasis on the thermal stress of infusing cold or inadequately warmed fluids, and the safety and

efficacy of fluid warmers and rapid infusion devices.

In the final section, "New Horizons in Synthetic Blood Substitutes," Drs. Como and Malangoni review the complex issues surrounding the use of hemoglobin solutions in trauma in their article on hemoglobin-based oxygen carriers. They report on the experience with PolyHeme (human hemoglobin-based temporary red cell substitute), the only hemoglobin-based oxygen carrier that has been evaluated in severely injured patients in the United States. Final results of the PolyHeme study, if favorable, may herald the introduction of hemoglobin-based oxygen carriers to patient care. Dr. Schubert concludes this issue by examining the potential clinical uses and effectiveness of hemoglobin-based oxygen carriers and perfluorocarbons. The long shelf life, long circulation half-life, and

good oxygen-carrying capacity and tissue oxygen delivery make these compounds particularly attractive in patients with high blood loss, that is, trauma patients. In his article, Dr. Schubert evaluates the different hemoglobin solutions and the pitfalls associated with their clinical use.

As editors and principle organizers of this special issue, we have attempted to provide a concise, up-to-date reference on massive transfusion and management of hemorrhage in the trauma patient, a reference that integrates both basic science and clinical practice. We sincerely hope that you, the reader, will obtain essential knowledge from this publication that will enable you improve your clinical practice when caring for trauma patients.

SECTION I. ETIOLOGY AND PATHOPHYSIOLOGY

Trauma, A Disease of Bleeding

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Learning Objectives: 1) To describe alternatives to the use of vital signs in determining depth of shock. 2) To define a newer resuscitation scheme that may limit the blood loss. 3) To describe the role activated factor VIIa may have as an adjunctive hemostasis agent.

Abstract

Acute blood loss is the most common life-threatening problem immediately after injury. Diagnosis is obvious in some patients but can be far more subtle in others. Vital signs often underestimate the degree of hemorrhage. Other parameters such as measuring the degree of metabolic acidosis can be helpful. In addition, newer technology can noninvasively measure the adequacy of perfusion by measuring blood flow in vascular beds that are particularly sensitive to blood loss. Certainly some patient populations, such as the elderly, are more sensitive than others to loss of circulating blood volume. Rapid diagnoses are essential in these patients to avoid cardiovascular collapse. Resuscitation strategies have changed recently as well. Limited fluid resuscitation may be better than large-volume crystalloid resuscitation. Transfusion therapies have evolved with more liberal use of fresh-frozen plasma. Finally, factor VIIa can be extremely helpful as adjunctive homeostasis. These issues will continue to require refinement in order to provide optimum care.

Acute blood loss is a very common problem following injury. Rapid recognition and restoration of homeostasis is the cornerstone of the initial care of any badly injured patient. Untreated, hemorrhage robs the cardiovascular system of the preload necessary to ensure adequate cardiac output and peripheral oxygen delivery. Inadequate perfusion, even if it is not associated with overt hypotension, can set off the neurohumoral cascade, ultimately leading to sequential organ failure.¹ This is especially important, as the mortality from established organ failure has not changed since it was first described almost 25 years ago.² Thus, it is imperative that hemorrhage is recognized and treated early.

The recognition of acute hemorrhage can be difficult. The American College of Surgeons has developed the classification scheme for hemorrhage, stratifying blood loss from stage 1 (<15% of total circulating blood volume) to stage 4 (>40% of total circulating blood volume).³ Changes in various physiologic parameters as hemorrhage volume increases are listed in Table 1. Unfortunately, many of these signs and symptoms are nonspecific. In addition, a number of other parameters will affect the patient's vital signs and physical findings. For instance, the rapidity of volume loss may be as important as the total volume of hemorrhage.³ Underlying cardiovascular reserve also plays a role. Young people with very compliant blood vessels may compensate extremely well for large-volume blood loss, even as much as 40% to 50% of total circulating blood volume.⁴ They then develop sudden cardiovascular compromise when compensatory mechanisms fail. Elderly people, on the other hand, will develop cardiovascular insufficiency and hypotension with much smaller blood loss.⁵ Prescription medication and/or illicit drugs will also influence the cardiovascular response to injury.^{6,7} The amount of resuscitation, if any, the patient received in the field will affect cardiovascular response as well.⁴

Data from the past 15 years strongly suggest that normally followed vital signs are a very poor indication of the depth of hemorrhage.⁸ In particular, blood pressure and pulse rate, the two vital signs often used in the emergency department to gauge hemorrhage, are tremendously nonspecific. Central venous oxygen saturation and mixed venous oxygen saturation are far more sensitive and reliable measurements of acute volume loss.^{8,9} Degree of metabolic acidosis, as measured by the base deficit from an arterial blood gas, is also extremely helpful in gauging the degree of shock.¹⁰ Base deficit has been shown to correlate with transfusion