Early Massive Trauma Transfusion: State of the Art

EDITORS' INTRODUCTION

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A report on a symposium held at the U.S. Army Institute of Surgical Research, 26–27 May 2005.

Injury is the most important cause of years of productive life lost world-wide. Uncontrolled hemorrhage causes much of that morbidity and mortality and is the critical factor most susceptible to treatment in injured patients. In highly developed trauma systems, supported by the best in blood-banking, early massive transfusion buys time for surgeons and interventional radiologists to get bleeding stopped. In recent years, however, the epidemiologic association of massive transfusion with poorer outcomes has raised important questions about the meaning of this statistical association and its possible physiologic basis. Given the importance of early interventions in the care of the critically injured, understanding the physiology of and true indications for early massive transfusion in trauma care has the potential to save many lives. The U.S. Army Institute of Surgical Research (USAISR) symposium on early massive trauma transfusion focused on what is known and what is unknown about all components of massive transfusion, to aid in the design of standardized research protocols and clinical practice guidelines in hemostasis and transfusion. Forty-six surgeons, anesthesiologists, hematologists, transfusion medicine specialists, epidemiologists, basic scientists, regulatory experts and administrators from Europe and North America were identified by their previous contributions to the literature or their ability to comment critically based on their current position and knowledge. They were divided into teams of two to four, assigned one of twelve topics to research, and asked to pay special attention to the quality of the supporting evidence. Each team produced a manuscript that was circulated to discussants in advance. The group was then brought to San Antonio, TX, site of the USAISR, and met to present and discuss the papers in plenary sessions. Discussion was lively but resulted in broad consensus.

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The first presentation, by Kauvar, Levering, and Wade described the epidemiology of injury and the general clinical issues associated with presentation and treatment of massive hemorrhage in trauma. The paper and the resulting discussion set out the key issues that would guide the group over the next day and a half: the international burden of trauma mortality and morbidity; the critical importance of coordinated, early, intervention; the differing concerns but tight links between initial trauma presentation and care and, in those who survive the immediate effects of their injuries, subsequent complications and outcome; the risks and benefits of various approaches to blood and blood product use.

This was followed by Hess and Lawson discussing the coagulopathy of trauma: the roles of blood loss, dilution, hypothermia, acidosis, component consumption, and fibrinolysis in coagulopathic bleeding and the pathologic dissemination of coagulation. The coagulopathy of trauma was compared with disseminated intravascular coagulation (DIC) from brain, fat, amniotic fluid, and diffuse tissue injury in trauma patients and DIC in non-trauma patients.

In the next session, Eastridge, Malone, and Holcomb examined the literature for published data-based predictors of the need for massive transfusion and of mortality in trauma patients. In large, retrospective studies, pre-hospital and presentation physiologic markers, measures of oxygen debt, coagulopathy, and hypothermia predict the need for transfusion. The association between transfusion in the first 24 hours and subsequent multiple organ failure (MOF) is clear in these data. This was followed by Napolitano's review of published literature on cumulative risks of early red blood cell (RBC) transfusion as demonstrated in retrospective surgical cohort and basic immunologic studies. Blajchman, in turn, presented data from the trauma subset of the prospective Trauma Requirements in Critical Care (TRICC) study, which show no additional risk from single RBC transfusions to hemodynamically stable trauma patients in the critical care phase.

Carson and Dutton then presented data on the indications for early RBC transfusion, emphasizing the mortality seen with increasing anemia in surgery on Jehovah's Witnesses, and the contribution of anemia to acidosis.

The next two sessions addressed the use of non-RBC blood products. First, MacLennan and Norda reviewed the risks of plasma and platelet transfusions and the U.K. and European organizational responses to these risks. Ketchum, Hess, and Hiippala examined the benefits of and rationale for

earlier and more aggressive use of these products than is now generally practiced. Cumulative risk of further injury, inflammatory and infectious, from plasma and platelets as measured in the European hemovigilance studies appears to be at least 2 orders of magnitude below the risk of developing coagulopathy in massively injured and massively transfused individuals.

Military, civil, regulatory, and technical issues that impact the safety of massive transfusion were addressed in the next four sessions. Repine, Perkins, Blackbourne, and Kauvar described the use of fresh whole blood as a field expedient to treat trauma coagulopathy in casualties in Iraq. Lefering, Dutton, and Lynn presented data on risk factors for mortality observed in large civilian trauma system databases. Holness and Vostal from the U.S. Food and Drug Administration (FDA) discussed regulatory aspects of blood safety and blood product licensure, using transfusion-related lung injury and pathogen-reduced platelets as recent examples. Blajchman reviewed the data on the contribution of universal leukoreduction of RBC and platelets to transfusion safety.

Finally, Malone, Hess, and Fingerhut reviewed massive transfusion protocols from well-developed trauma systems in Denver, Houston, Helsinki, Sydney, and Baltimore. Despite superficial differences, all deliver similar amounts of the various blood components in similar circumstances and with similar triggers. This group then presented a massive transfusion protocol based on the best data from their review.

Over the day and a half of meetings, the most contentious issue was the significance of the identification of blood transfusion as an independent risk factor for multiple organ failure and death in multivariate analysis of large retrospective series of trauma patients. Some felt strongly that the association suggested causation. Others noted that the most severely injured both required the most blood and had the highest risk of bad outcomes. The statistical independence of transfusion and injury severity scores in predicting bad outcome may mean that blood use is more linearly related to injury severity than the quadratically modified injury severity scores. In addition, in the literature reviewed, blood transfusion was not separable from blood loss. All agreed that better evidence is needed to explore these issues.

Despite this controversy, general consensus was reached that, in the most severely injured patients, early use of RBC, plasma, and platelets still offers the best chance of limiting the coagulopathy of trauma in early phases of care. Further, the practical problems of initiating venous access, delivering initially uncross-matched RBC, and obtaining further RBC, thawed plasma, and platelets from a transfusion service mean that most of these patients will be receiving these components on an approximately 1:1:1 ratio in an effort to make up early deficits that occur when only crystalloid and RBC are available. These facts allow standardized guidelines for massive transfusion that use the 1:1:1 ratio and accept the number of units of transfused RBC as a surrogate for the amount of blood lost to become guidelines for clinical practice and clinical research.

The conveners wish to thank all of the participants for their hard work, thoughtful comments and attention to detail. We also thank the sponsors, NovoNordisk and the U.S. Army for the support that allowed the assembly of this symposium and the production of this supplement to *The Journal of Trauma*. We hope that the results of this effort are better understanding and more generally applicable protocols for research and improved care of the injured.

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