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Journal club critique

Black Hawk Down: The evolution of resuscitation strategies in massive traumatic hemorrhage

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Expanded Abstract

Citation

Borgman MA, Spinella PC, Perkins JG, Grathwohl KW, Repine T, Beekley AC, Sebesta J, Jenkins D, Wade CE, Holcomb JB: The ratio of blood products transfused affects mortality in patients receiving massive transfusions at a combat support hospital. J Trauma 2007, 63:805-813 [1].

Background

Patients with severe traumatic injuries often present with coagulopathy and require massive transfusion. The risk of death from hemorrhagic shock increases in this population. To treat the coagulopathy of trauma, some have suggested early, aggressive correction using a 1:1 ratio of plasma to red blood cell (RBC) units.

Methods

Objective: To determine whether the ratio of plasma to RBCs transfused would affect survival by decreasing death from hemorrhage.

Design: Retrospective chart review.

Setting: United States Army combat support hospital in Iraq.

Subjects: 246 patients who received a massive transfusion (≥10 units of RBCs in 24 hours) from November 2003 to September 2005. Three groups of patients were constructed according to the plasma to RBC ratio transfused during massive transfusion.

Intervention: None.

Outcome: Hospital mortality rates and the cause of death were compared among groups. Multivariable logistic regression was used to determine the independent association between plasma to RBC ratio and hospital mortality.

Results

For the low ratio group the plasma to RBC median ratio was 1:8 (interquartile range (IQR), 0:12-1:5), for the medium ratio group, 1:2.5 (IQR, 1:3.0-1:2.3), and for the high ratio group, 1:1.4 (IQR, 1:1.7-1:1.2) ($p<0.001$). Median Injury Severity Score (ISS) was 18 for all groups (IQR, 14-25). For low, medium, and high plasma to RBC ratios, overall mortality rates were 65%, 34%, and 19%, ($p<0.001$); and hemorrhage mortality rates were 92.5%, 78%, and 37%, respectively ($p < 0.001$). Upon logistic regression, plasma to RBC ratio was independently associated with survival (odds ratio 8.6, 95% confidence interval 2.1-35.2).

Conclusions

In patients with combat-related trauma requiring massive transfusion, a high 1:1.4 plasma to RBC ratio is independently associated with improved survival to hospital discharge, primarily by decreasing death from hemorrhage. For practical purposes, massive transfusion protocols should utilize a 1:1 ratio of plasma to RBCs for all patients who are hypocoagulable with traumatic injuries.

Commentary

On 3 October 1993, two hundred American soldiers caught during a daytime raid participated in a firefight in the streets of Mogadishu, Somalia. In the hours before extraction, fourteen men died of their wounds in the field; more succumbed first at the combat hospital and later in Germany. That single event prompted a review by military

medical personnel of existing resuscitation practices, rekindling debates begun at the time of World War I [2]. As difficult as it is to imagine today, during World War I there was commonly no preoperative resuscitation in combat trauma. By World War II, resuscitation with colloid and blood had become the standard approach. Only during Vietnam did the work of Moyer, Shires, Moss, and others [2] lead to the widespread use of large-volume resuscitation with isotonic crystalloids, with guidelines recommending the infusion of crystalloid and blood in a ratio of three to one. As pre-hospital care improved, attention shifted to consideration of other interventions that might decrease mortality among those suffering massive blood loss, fixing on the so called "bloody lethal triad" of hypothermia, acidosis, and coagulopathy [3], the later of which is due in part to both dilution and consumption of coagulation factors [4].

The 1980s saw the advent of damage control surgery, in which the restoration of normal anatomy is deferred to limit the progression of coagulopathy and blood loss. This approach improved survival rates for patients with massive traumatic hemorrhage from 30% to around 50% to 60%, where they remained to the turn of the century [3]. When John Holcomb issued a statement on behalf of the United States Armed Forces in January 2007 announcing a change in field practices to incorporate the use of plasma as the primary resuscitation fluid [5], he articulated an impatience of the trauma community at the failure to make greater progress in reducing mortality among those at "the outer limits of survivability."

This apparent paradigm shift drew on an emerging body of work suggesting that management of the coagulopathy of trauma required a proactive, rather than reactive, approach. Using a computer model based on data from severely injured trauma patients, Hirschberg and colleagues found that patients who arrived to the emergency department with a systolic blood pressure of 70 mmHg had already lost 67% of their blood volume [6]. Preventing the development of profound and often refractory coagulopathy in these patients required plasma infusion before, instead of after, the patient became coagulopathic. Gonzalez and colleagues studied the existing trauma massive transfusion protocol at Memorial Hospital in Houston, which at that time required the infusion of six units of RBCs prior to use of plasma [7]. The authors found that coagulopathy, which was present on admission, remained after the initial pre-ICU resuscitation and that even after the administration of a mean of 10 units of plasma in the ICU, patients remained coagulopathic. The authors suggested that to correct coagulopathy and decrease RBC requirements, plasma should be given earlier and in a plasma to RBC ratio of 1:1. In a retrospective review of trauma patients who underwent emergent surgery at an urban Level I trauma center, Duchesne and colleagues found a significant mortality difference in patients who were transfused with >10 units of RBCs when plasma accompanied the RBCs in a 1:1 as opposed to 1:4 ratio (26% vs. 87.5%, p=0.0001) [8]. In a before and after study, Johansson and colleagues compared survival of patients undergoing surgery for a ruptured abdominal aortic aneurysm after implementing a transfusion strategy that included proactive administration of platelets together with plasma given in a 1:1 ratio with RBCs [9]. The authors found that patients treated under the new strategy had fewer postoperative transfusions (RBC units, 2 vs. 6, p<0.01), and higher 30-day survival (66% vs. 44%, p=0.02).

In the current study, Borgman and colleagues examined the use of plasma and RBCs in severely injured patients in a combat support hospital in Iraq between November 2003 and September 2005 [1]. In this retrospective cohort study, the authors identified 246 patients that received massive transfusion, ≥ 10 units of RBCs in 24 hours, in the Joint Theater Trauma Registry; a database that prospectively captures data from the point of injury through discharge from military treatment facilities. Patients were grouped based on the ratio of plasma to RBCs received during massive transfusion: a low ratio group (median ratio 1:8); a medium ratio group (median ratio 1:2.5); and a high ratio group (median ratio 1:1.4). Initial Injury Severity Scores were similar between groups as was the proportion with either blunt or penetrating trauma. However, severe thoracic injuries were more common in the low ratio group. All baseline vital signs and laboratory results were comparable, with the exception of hemoglobin, which was lower in the low ratio group compared with the medium and high groups (9.4 mg/dL vs. 10.8 mg/dL vs. 10.9 mg/dL, p<0.05). Not surprisingly, there were differences in hourly infusion rates and total volume of various resuscitation products given. Low ratio patients received higher hourly rates of crystalloids and RBCs, lower hourly rates and total volume of plasma, and were less likely to receive platelets, cryoprecipitate, and recombinant Factor VIIa (fFVIIa). In univariate analysis, as the ratio of plasma to RBCs received increased, hospital mortality decreased in an apparent dose-response fashion (65% vs. 34% vs. 19%, p<0.001). Nonsurvivors in the low and medium ratio groups died significantly sooner than those in the high ratio group (median time to death, 2 hours vs. 4 hours vs. 38 hours, p<0.001). The relationship between plasma to RBC ratio and overall mortality persisted after adjusting for potential confounders, including Abbreviate Injury Scale subscores, systolic blood pressure, base deficit, hemoglobin levels, and when patients with thoracic trauma, neurotrauma, or those receiving fFVIIa were excluded from the analysis.

As with any observational study, this work can only show associations between exposure and outcome and cannot prove cause and effect. The excess early deaths observed in the low ratio group might a product of having received less plasma. Conversely, dying early might prevent subjects from having a chance to receive large quantities of plasma, which typically must be thawed prior to use. Though the authors have considered a large number of patient and treatment-related variables and adjusted for differences between groups in their analyses, residual confounding due to unmeasured factors associated with survival may still exist. It would have been helpful for the authors to have

included a propensity score for the ratio of plasma to RBCs received in their analyses, though even this would not completely remove the possibility of indication bias. Finally, the most problematic challenge to this work is one of generalizeablity, since the patient population consisted of young, otherwise healthy men suffering primarily penetrating injuries from combat trauma. Whether these findings translate to civilian trauma settings or to non-traumatic cases of massive hemorrhage, such as post-operative patients or medical patients with gastrointestinal hemorrhage, remains to be seen.

Since publication of this manuscript, additional work published in abstract form supports its findings. In a single center study, Gonzalez and colleagues found a reduction of hospital mortality from 30% to 15% in trauma patients receiving massive transfusion after the institution of an early goal directed therapy protocol calling for a 1:1 ratio of plasma to RBCs within the first 6 hours of injury [10]. Sperry and colleagues retrospectively examined plasma to RBC ratios in a multi-center prospective cohort study evaluating clinical outcomes in blunt injured adults with hemorrhagic shock. In those requiring at least 8 units of RBCs within the first 12 hours post-injury, higher plasma to RBC ratio was associated with significantly reduced hospital mortality in a dose-response relationship [11]. Additional analysis of these data revealed that a ratio of ≥ 1:1.5 was independently associated with lower hospital mortality, but higher risk of acute respiratory distress syndrome [12], the latter of which may be a product of increased survival or of the additional plasma itself.

It is important to note that transfusion of plasma is not without risk, including infection, transfusion-related acute lung injury, acute allergic and anaphylactic reactions, hemolysis, and fluid overload [4]. Furthermore, wide-scale adoption of 1:1 plasma to RBC ratios would have important implications for the blood supply. Yet, only 1% of civilian trauma patients require massive transfusion, so perhaps the impact would be less than anticipated.

Recommendation

In massively injured patients, the prevention and/or treatment of coagulopathy with plasma administered in a 1:1 ratio with RBCs has a certain degree of face validity and growing support in observational studies. The increased use of plasma, however, is not without risk and may have important implications for blood supply management. Whether similar associations might also be seen in patients bleeding from non-traumatic injuries is unknown, with the exception of those bleeding from ruptured abdominal aortic aneurysms. Prospective trials investigating the optimal plasma to RBC ratio in patients requiring massive transfusion are warranted.

Competing interests

The authors declare no competing interests.

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