Overview of massive transfusion practice

Irena Seferi[1], Erind Cafi[1]

[1]National Blood Transfusion Centre (NBTC), Tirana, Albania.

Corresponding Author: Irena Seferi, MD, PhD;
Address: National Blood Transfusion Centre, Rr. Lord Bajron, Tirana, Albania;
Telephone: +35542389907; E-mail: iqendro@yahoo.com

Abstract

Aim: Recently reported experiences suggest that early use of FFP together with RBC in 1:1 ratio in massive transfusion is associated with improved outcome. Our aim was to investigate the current situation of massive transfusion in our country.
Methods: We analyzed retrospectively data from trauma patients hospitalized during January 2012-August 2013. We included in the study trauma patients that received more than 5 units of red cells in 4 hours, 23 in total. The transfusion therapy of these patients was evaluated by registering all the components transfused. The RBC:FFP ratio was calculated for each patient. According to the value of this ratio the patients were divided in three groups: patients with RBC:FFP ratio above 1.1, with RBC:FFP ratio 0.9-1.1, RBC:FFP ratio under 0.9. The mortality rate for each group was calculated and groups were compared with each other for transfusion therapy used, and mortality rate.
Results: The overall mortality rate was 21.7%. The mortality rate was higher in the groups transfused either with higher or with lower RBC:FFP ratio, the difference between them was not statistically significant, p=0.536. No death was registered in the group transfused with RBC:FFP ratio of 0.9:1.1. The mortality rate was 25% in patients transfused with high RBC:FFP ratio and 40% in patients transfused with low RBC:FFP ratio.
Conclusion: Literature data suggest for an early aggressive treatment of coagulopathy in trauma patients by keeping a RBC:FFP ratio of 1:1. We also observed better outcome for patients treated with 1:1 RBC:FFP ratio with no deaths registered. Well defined and updated protocols are needed for the correct treatment of trauma patients with blood components. These protocols should include most recent recommendations on ratios between blood components (RBC, FFP and PC) used in trauma patients, as well as the proper use of fibrinogen and tranexamic acid for better patient outcome.

Keywords: massive transfusion, trauma patients.

Introduction

Worldwide, approximately five million people die from injuries every year. Early trauma-related mortality is dedicated to head injury (40-50% of causes of death) or hemorrhage (20-40%), whilst late mortality is usually secondary to multiorgan failure (7-9%). Furthermore, massive transfusion is associated with high mortality rate in trauma patients: patients who received 10 or more RBC units in their hospital stay had a mortality rate of 39% and patients who received 50 or more units of blood products in the first 24 hours had a mortality rate of 57% (1-4).

Another important problem that should be addressed with appropriate attention is the coagulopathy present upon admission of traumatic patient. Coagulopathy upon admission is reported in 25% of patients with traumatic injury, and it increases the risk of hemorrhage and death in this population. Coagulopathy is probably induced by endothelial injury, ischemia, tissue factor activation, inflammation and exacerbated by factor consumption, hypocalcaemia, haemodilution, hypothermia and acidosis. Normalization of coagulation abnormalities is an area where significant advances have been made. The most important product at the center of the research has been plasma, and to a lesser degree platelets. A lot of studies stress the role of haemostatic resuscitation which includes the early use of plasma (5-7). Military experiences suggest that early use of FFP (Fresh Frozen Plasma) together with Red Blood Cell Concentrate (RBC) in 1:1 ratio in massive transfusion is associated with improved outcome. In the same time military and civilian trauma centers report decreased mortality by using also high quantities of Platelet Concentrate (PC) and cryoprecipitate in massive transfusion. In 2005, a symposium of surgeons, anesthesiologists, hematologists and transfusion medicine specialists achieved a general consensus to create guidelines for the use of FFP, RBC and PC in the ratio 1:1:1 for massive transfusion in severely injured patient (8). Another important parameter recently studied is the level of fibrinogen in trauma patients. It has been also shown that fibrinogen may be one of the most vulnerable coagulation factors. A recent study reports worsened outcomes in trauma patients with decreasing fibrinogen levels (9). The strong association between fibrinogen levels and mortality shown from this study and other authors (10,11) warrants further evaluation and research.

Our aim in this study was to investigate the current situation of massive transfusion by focusing in transfusion ratios used in our country, and in the actual follow up of important clinical parameters.

Methods

We analyzed retrospectively data from multiply injured patients that were hospitalized in our trauma center in Tirana during January 2012–August 2013. There are two definitions of massive transfusion: one defining as massive transfusion the transfusion of more than five units of red cells in four hours and the other defining the massive transfusion as transfusion of more than ten units of blood in 24 hours. Most of studies use the second definition for massive transfusion. We had to choose the first definition in our study because the number of patients receiving more than ten units in 24 hours was very small (8), but the mortality rate has been evaluated by us separately for the whole group and for the group with more than ten units in 24 hours. The patients that matched our criteria for massive transfusion were 23. Patients were initially chosen from the registry of the blood bank and then the personal files and clinic parameters were evaluated. The parameters monitored by us were: transfusion therapy, PT (Prothrombin Time), and fibrinogen. According to several evidences, use of above mentioned ratios among blood components, close monitoring of coagulation (PT, fibrinogen), platelet count, and use of tranexamic acid are very important in the successful treatment of trauma patient. In order to enable the comparison among our patients we took in consideration the situation of the parameters (blood components ratio, PT, fibrinogen level, platelet count) upon admission to

ICU (Intensive Care Unit). There are different authors reporting that use of aggressive FFP therapy, and close monitoring of coagulation in the early phase of trauma before admission to ICU is significant in patient survival (5-8).

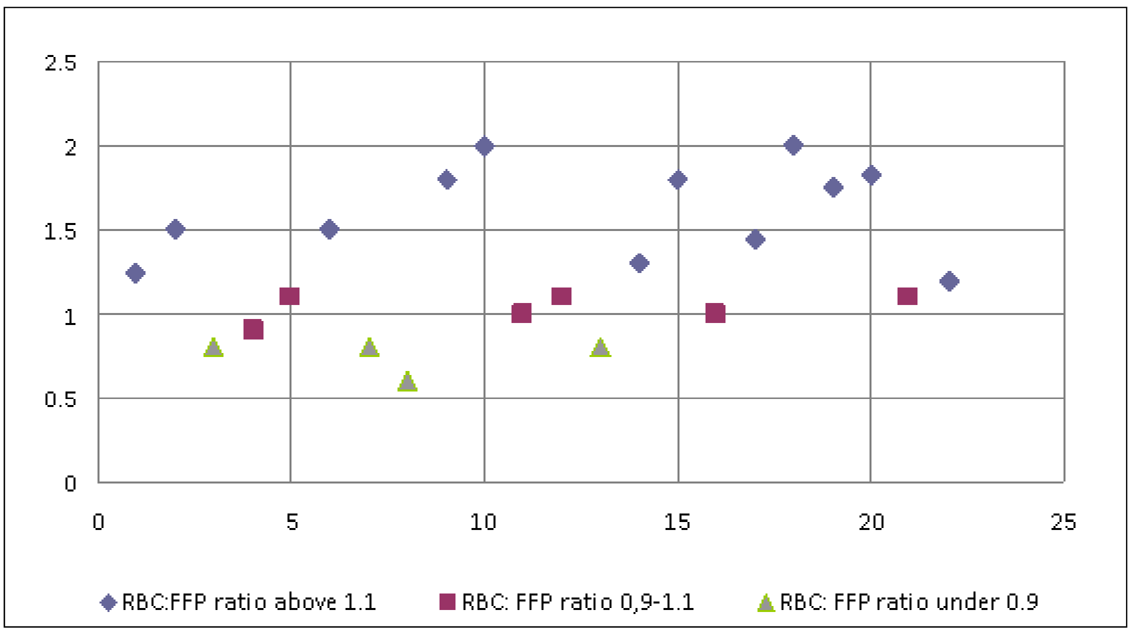
There were 23 patients that fulfilled the above mentioned criteria of massive transfusion, with an average age 37.65 years (range: 13-68 years) and with a male/female ratio = 21/2. This study includes all the trauma patients hospitalized for more than one year in the only one trauma center at national level, therefore is enough to show us the situation of treatment of this patient group at national level, which was our main goal with this study. Moreover, since we analyze here the mortality rate in trauma patients which is reported very high from the literature (20-40%), we consider that even small groups of patients are enough to draw appropriate conclusions.

According to transfusion therapy received, the patients were divided in three groups that is: patients transfused with RBC:FFP ratio of more than 1.1, patients transfused with RBC:FFP ratio 0.9-1.1 and patients transfused with a RBC:FFP ratio of <0.9. Mortality rate was estimated and groups were compared with each other for mortality rate.

Results

Transfusion therapy of 22 out of 23 patients included in the study is shown in the following graphs. Only for one of them has not been possible to calculate the RBC: FFP ratio.

Figure 1. RBC:FFP ratio upon admission to ICU for 22 patients



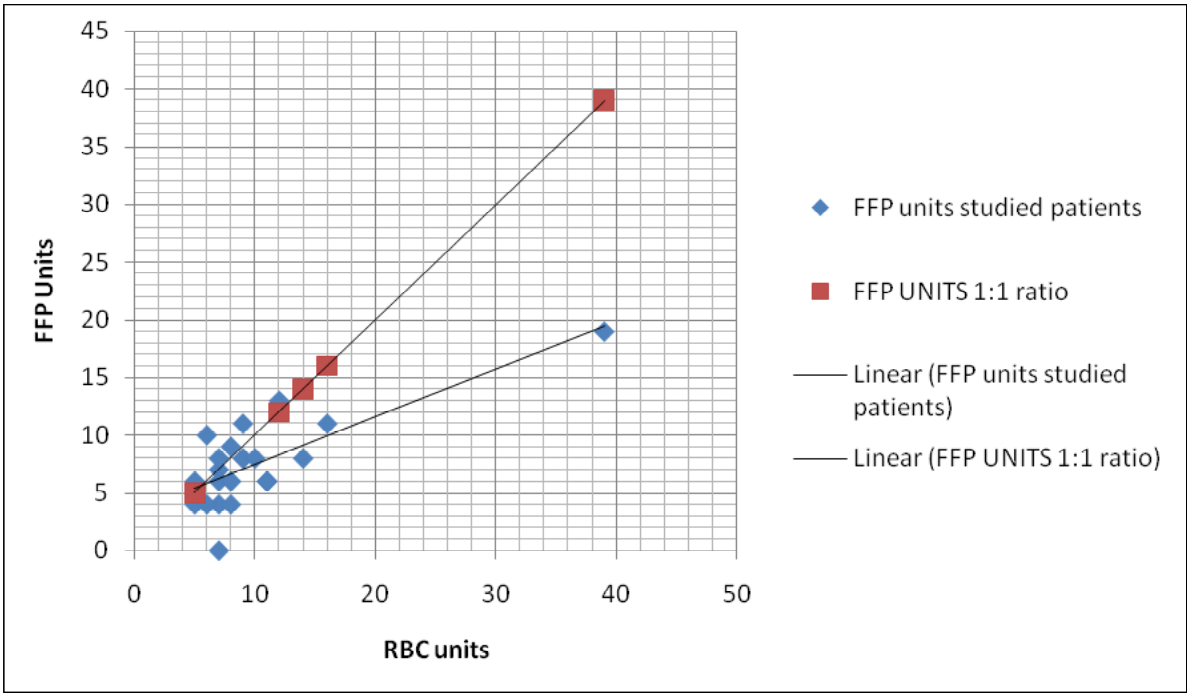
The mortality rate in this study is defined as the percentage of patients that died during hospitalization. The overall mortality rate was 21.7%.

According to the RBC:FFP ratio of transfusion we had:

- Twelve patients (56.52%) transfused with an RBC:FFP ratio of more than 1.1.
- Six patients (26%) transfused with RBC:FFP ratio of 0.9-1.1.
- Five patients (17.39%) transfused at a RBC/FFP ratio of less than 0.9.
- The mortality rate according to transfusion ratio was as following:
- Three patients (25%) transfused with high RBC: FFP ratio died (8;17;19 days after admission).
- None of the patients transfused with RBC:FFP ratio of 0.9-1.1.

Two patients (40%) transfused at a low RBC:FFP

Figure 2. Distribution of RBC:FFP transfusion ratios among patients under study



ratio (less than 0.9). One of them died nine hours after admission, whereas the other one died two days after admission.

When we compared the mortality rate among these groups we found that the difference in the mortality rate was not statistically significant, P=0.536. We could not include in this comparison the group transfused with RBC:FFP ratio of 0.9:1.1 because no death was registered in this group. However it is clear that the rate of death in the group of patients transfused with 1:1 ratio was much lower compared to the other groups.

The transfusion of platelets has been used only in one case. In the group of patients under study, transfusion of platelets has not been used even in patients with platelet count less than 75 x 10^9/ l upon admission to ICU.

We found a PT measured upon admission to ICU, in 13 out of 23 patients, with values less than 70% in seven of them. As far as fibrinogen measuring is concerned, we could find it measured in eight out of 23 patients with abnormal critical level in one of them.

Discussion

Our aim in this study was to observe the current situation of treatment of trauma patients subject to massive transfusions. A lot of studies demonstrate that the ratio of blood products transfused, affects mortality both in the military and civilian settings. Early aggressive correction of coagulopathy by using FFP has resulted beneficial for survival following massive transfusion in patients that have undergone trauma (5-7,9-11). In contrast, our data show that most of our patients receiving massive transfusion, 13 out of 23 (56.52%), are transfused with a RBC:FFP ratio of more than 1.1 which testifies that during massive transfusion in our country more RBC than plasma are used, which is also demonstrated in Figures 1 and 2. We could not conclude if the small quantity of plasma used in massive transfusions in these patients was related to a protocol that uses more RBC or to the fact that plasma has not been distributed because not available. These are of course limitations related to the retrospective study.

The overall mortality rate in our group was 21.7%, which is low compared to mortality rate reported from several studies (5-7,12,13). It is important to mention here that these studies define as massive transfusion, the transfusion of more than ten units of blood in 24 hours and in this group very high mortality rate, up to 39% is reported. In our study we used another definition for massive transfusion (more than five units in four hours) and the included patients are those with more than five units in four hours because the number of patients with more than ten units in 24 hours was very small (eight patients). Therefore we evaluated the mortality rate separately for the last group which resulted very high 37.5%, showing in this way a strong association between number of red cell units transfused and severity of trauma and patient outcome. We found a higher but not statistically significant mortality rate in the group transfused with RBC:FFP ratio of less than 0.9 compared to 0,9-1,1 group and to >1.1 group (40% vs. 0 vs. 25%). This is also confirmed by other authors (12,13).

One of the limitations of this study was the fact that among groups of patients compared, has not been taken in consideration the degree of trauma upon admission but only the number of transfusions for judging the situation of the patient. Therefore the death in all five patients, might have been related also to the degree of trauma. In future studies, in order to achieve accurate results, it is also very important to include as a parameter for grouping patients the degree of trauma, by using different indicators such as ISS (Injury Severity Score) etc. together with the number of transfusions.

The platelet transfusion seems not to be a practice for massive transfusion in our country. The transfusion of platelets has been used only in one case out of 23 patients studied. Again being evaluated retrospectively, we could not conclude whether it is related to lack of request or lack of available products. According to transfusion guidelines, transfusion of platelets must be considered when platelet count falls below 75x109/l in traumatic hemorrhage. Whereas according to several studies (9-13), regardless of platelets count during the early phase of treatment of trauma patient, a ratio of FFP:RBC:PLT 1:1:1 or 5:5:2, reduces mortality in massively transfused patients. In our group of patients we could find an estimation of platelet count upon admission to ICU in 17 out of 23 patients, and in 5 of them there was a platelet count of less than 75x109/l. Transfusion of platelets has been used only in one of these patients.

Hypofibrinogenemia is common in massive hemorrhage. Fibrinogen levels of <1g/l are likely after 1-1.5 times blood volume replacement (14-16) and bleeding will be exacerbated by a plasma fibrinogen of <1.5g/l. Cryoprecipitate (as two five-unit pools) has been widely used for replacement therapy. In none of the patients included in our study has been used transfusion of cryoprecipitate. Furthermore a recent study reports the level of fibrinogen of less than 100 mg/dl was a strong independent risk factor for death (17). We could find a determination of the level of fibrinogen upon admission to ICU only in 8 out of 23 patients, and a determination of PT in 13 out of 23 patients. Fibrinogen and PT are very important parameters in monitoring trauma patients and need close monitoring and adequate correction in case of abnormal values.

The use of tranexamic acid, according to randomized controlled trial (18) reduces significantly the mortality in patients with or at risk for significant bleeding after trauma. The drug was shown to be efficacious in reducing death whilst also being safe with no increased thrombotic events. Further analysis showed that benefit was greatest the earlier that tranexamic acid was given after injury with a possibility of harm if given more than three hours after injury. In none of our patients has been used tranexamic acid.

Our data show that a high RBC:FFP ratio is used in most trauma patients, in contrast with recommendations and conclusions of several studies for an early aggressive correction of coagulopathy by using a RBC:FFP ratio of 1:1. We also found that the group of patients that showed better outcome was the one transfused with 1:1 RBC:FFP ratio. Platelet transfusions seem not to be a practice in our country, in trauma setting. These findings suggest that well-defined and updated protocols in the treatment of trauma patients are needed. These protocols should include most recent recommendations on ratios between blood components (RBC, FFP and PC) used in trauma patients, as well as the proper use of fibrinogen and tranexamic acid for better patient outcome.

Conflicts of interest: None declared.

References

1. Peden M, McGee K, Sharma G. The injury chart book: a graphical overview of the global burden of injuries. WHO; 2002.
2. Heron MP, Hoyert DL, Murphy SL, Xu JQ, Kochanek KD, Tejada-Vera B. Deaths: final data for 2006. National vital statistics reports; vol.57, no.14. Hyattsville, MD: National Center for Health Statistics; 2009.
3. Como JJ, Dutton RP, Scalea TM, Edelman BB, Hess JR. Blood Transfusion rates in the care of acute trauma. Transfusion 2004;44:809-13.
4. Vaslef SN, Knudsen NW, Neligan PJ, Sebastian MW. Massive transfusion exceeding 50 units of blood in trauma patients. J Trauma 2002;53:291-6.
5. 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 transfusion at a combat support hospital. J Trauma 2007;63:805-13.
6. Gonzalez EA, Moore FA, Holcomb JB, Miller CC, Kozar RA, Todd SR, Cocanour CS, Balldin BC, McKinley BA. Fresh frozen plasma should be given earlier to patients requiring massive transfusion. J Trauma 2007;62:112-9.
7. Gonzalez EA, Jastrow K, Holcomb JB, Kao LS, Moore FA, Kozar RA. Early achievement of a 1:1 ratio of FFP:RBC reduces mortality in patients receiving massive transfusion. J Trauma 2008;64:247.
8. Holcomb JB, Hess JR. Early massive trauma transfusion: state of the art. J Trauma 2006;60:S1-S2.
9. Inaba K, Karamanos E, Lustenberger T, Schöchl H, Shulman I, Nelson J, Rhee P, Lam L, Demetriades D. Impact of Fibrinogen Levels on Outcomes after Acute Injury in Patients Requiring a Massive Transfusion. J Am College of Surgeons 2013;216:290-7.
10. Johannson PI, Hansen MB, Sorensen H. Transfusion practice in massively bleeding patients: time for a change? Vox Sang 2005;89:92-6.
11. Holcomb JB, Wade CE, Michalek JE, Chisholm GB, Zarzabal LA, Schreiber MA, Gonzalez EA, Pomper Gj, Perkins JG, Spinella PC, Williams KL, Park MS. Increased plasma and platelet to red blood cell ratios improves outcome in 466 massively transfused civilian trauma patients. Ann Surg 2008;248:447-58.
12. Gunter OL Jr, Au BK, Isbell JM, Mowery NT, Young PP, Cotton BA. Optimizing outcomes in damage control resuscitation: identifying blood product ratios associated with improved survival. J Trauma 2008;65:527-34.
13. Maegele M, Lefering R, Paffrath T, Tjardes T, Simanski C, Bouillon B. Red blood cell to plasma ratios transfused during massive transfusion are associated with mortality in severe multiply injury: a retrospective analysis from the Trauma Registry of the Deutsche Gesellschaft für Unfallchirurgie. Vox Sang 2008;95:112-9.
14. Zink KA, Sambasivan CN, Holcomb JB, Chisholm G, Schreiber MA. A high ratio of plasma and platelets to packed red blood cells in the first 6 hours of massive transfusion improves outcomes in a large multicenter study. Am J Surg 2009;197:565-70.
15. Hirchberg A, Dugas M, Banez EI, et al. Minimizing dilutional coagulopathy in exsanguinating hemorrhage: a computer simulation. J Trauma 2003;53:454-63.
16. Spahn DR, Rossaint R. Coagulopathy and blood component transfusion in trauma. Br J Anaesth 2005;95:130-9.
17. Shaz BH, Dente CJ, Nicholas J, MacLeod JB, Young AN, Easley K, Ling Q, Harris RS, Hillyer CD. Increased number of coagulation products in relationship to red blood cell products transfused improves mortality in trauma patients. Transfusion 2010;50:493-500.
18. CRASH-2 trial collaborators, Shakur H, Roberts I, et al. Effects of tranexamic acid on deaths, vascular occlusive events and blood transfusion in trauma patients with significant hemorrhage: a randomized placebo-controlled trial. Lancet 2010;376:23-32.