Journal of Blood & Lymph
ISSN: 2165-7831

Cohn and Keric, J Blood Lymph 2014, 4:1
DOI: 10.4172/2165-7831.1000118

Review Article Open Access

Impact of the Age of Transfused Red Blood Cells in the Trauma Population

Stephen Cohn* and Natasha Keric

Division of Surgery, University of Texas Health Science Center, USA

Abstract

Following injury, transfusion of Red Blood Cells (RBCs) of greater storage duration has been associated with anincreased morbidity and mortality. Prospective trials focusing on the impact of the storage age of RBCs in severely bleeding trauma patients have typically failed to accrue patients. This has been attributed to both inability to maintain a large inventoryof fresh RBCs, and the difficulties in obtainingconsent in severely bleeding trauma patients. To address theissue of the impact of old blood on the injury victim, we reviewed the literature on this topic.

Keywords: Transfusion practices (surgical); Red blood cells; Storage lesion; Age of blood; Trauma; Injury

Introduction

There is a well-established association between transfusion of red blood cells and increased morbidity and mortality in trauma patients [1-5] and in the critically ill population in general [6,7]. Hebert et al. in 1999 reported that a restricted red cell transfusion strategy was at least as effective and possibly superior to a liberal transfusion strategy in the critically ill population [8]. It remains unclear as to why infusion of red blood cells would be harmful and numerous investigators have reviewed the literature in order to understand the influence of duration of storage in the blood bank on outcome in the critically ill [9-11]. In the largest study to date, focusing upon the impact of duration of red cell storage and complications after cardiac surgery, Koch and colleagues suggested that individuals given exclusively older red blood cells (median 20 days old, n=2872 patients) appear to have a greater morbidity (25.9% vs. 22.4%, p=0.001), hospital and one year mortality (one year: 11.0% vs. 7.4%, p<0.001), when compared to those receiving exclusively younger red cells (median 11 days old, n=3130 patients) [6]. In the trauma patient population, data relating duration of red cell storage to complications and death is quite limited [9-11]. Following injury, transfusion of older aged red cells has been identified in retrospective trauma studies to be associated with an increased morbidity and mortality [1,2,5,11]. This detrimental effect of old red cells on tissue perfusion has not been demonstrated in normal volunteers [12] or seen in other critically ill populations [13], however. The results of existing clinical studies comparing old and young RBCs suggest that prospective clinical trials investigating the risks and benefits of prolonged red cell storage are feasible and should be performed [14].

In the trauma patient population, little work has been published relating duration of red cell storage to complications and death [9-11] (Table 1). Following injury, transfusion of RBCs of increased storage duration has been suggested in retrospective trauma studies to be associated with a greater likelihood of pneumonia [15,16] and other major infections [17], renal failure [15] andvenous thrombosis [5]; and has been possibly associated with an increased incidence of multiple organ dysfunction [18], longer ICU [19] and hospital [20] stays, and death [1,2,5,15]. Interestingly, tissue oxygenation is negatively impacted when critically injured patients [21] and those with traumatic brain injury [22] receive old blood. This detrimental effect of old red cells on tissue perfusion has not been demonstrated in normal volunteers [12] or seen in other critically ill populations [13], however. The results of these clinical studies comparing old and young RBCs suggest that prospective clinical trials investigating the risks and benefits of prolonged red cell storage should be performed.

While randomized controlled trials are currently being performed to determine if the transfusion of RBC of increased storage duration increases the risk of morbidity and mortality in adult critically ill patients and in adults requiring complex cardiac surgery, no trials are being performed in patients with traumatic hemorrhagic shock [23]. This is despite the fact that the trauma population may be at the highest risk of RBC storage lesion effects[11]. Logistical difficulties in maintaining the availability of very large quantities of RBCs of decreased storage duration for study patients appears to be the predominant reason that age of red blood cell trials are not being conducted in patients with traumatic hemorrhagic shock. By current standards of care, when a patient is to receive a transfusion, the blood bank provides the oldest unit of blood available. Despite this practice, in areas where type O RBC donors are prevalent, an abundance of fresher RBCs is often available in stock. We performeda short survey of blood age, prior to conducting a trial at our trauma center at University Hospital in San Antonio. In a retrospective analysis of all type O and type A Red Blood Cells transfused between July 2005 and June 2006, we found that patients with type O blood typically received younger RBC units (17.5 ± 8.7 days) than type A blood patients (24.3 ± 9.9 days).

We previously attempted to perform a pilot trial examining the impact of age of blood on patient outcomes in severely bleeding trauma patients but were prevented from completing the study due to a lack of blood bank resources [24]. The methods in our previous trial differed in that we required a large inventory of both "young" and "old" blood available in the blood bank prior to randomizing a patient.We found that that having a sufficient inventory of RBCs (particularly of "young" RBC of less common ABO types) was a major impediment to conducting our trial.In fact, we were only able to enter 17 patients during one year at a very busy trauma center.Recently we published a randomized trial of "young" type O blood (median age 6 days) compared to the usual

***Corresponding author:** Stephen Cohn, Professor of Surgery, University of Texas Health Science Center, 7703 Floyd Curl Drive, San Antonio, Texas 78229, USA, Tel: 2102602620; E-mail: cohn@uthscsa.edu

Received February 12, 2014; **Accepted** February 27, 2014; **Published** March 03, 2014

Citation: Cohn S, Keric N (2014) Impact of the Age of Transfused Red Blood Cells in the Trauma Population. J Blood Lymph 4: 118. doi:10.4172/2165-7831.1000118

Copyright: © 2014 Cohn S, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Author (ref)	Design	No.	Study Population	ISS	Blood age	Major Conclusions
Zallen et al. [18]	Retro single	63	Trauma patients with 6 to 20 units PRBC	~30	24 vs. 31 days	Older PRBC associated with organ failure (>14 or >21 days)
Schulman et al. [24]	Pros single	17	RCT Type A trauma patients ≥ 2 units PRBC	NA	<11 vs. >20 days	Lack of accrual due to PRBC bank inventory
Offner et al. [17]	Retro single	61	Trauma patients with 6 to 20 units of PRBC	~30	27 ± 1 day	>14 or 21 days old PRBC associated with infections
Keller et al. [20]	Retro single	86	Trauma patients with 1 to 4 units of PRBC	13	23 ± 1 days	>14 days old PRBC associated with increasing hospital stay
Murrell et al. [19]	Retro single	275	Trauma patients receiving ≥ 1 unit PRBC	18	NA	Older PRBC associated with longer ICU stay.
Weinberg et al. [15]	Retro single	1,813	Trauma patients receiving ≥ 1 unit PRBC	26	≥ 14 vs.<14 days	Older PRBC associated with mortality in subgroup with ≥ 6 units received.
Leal-Noval et al. [22]	Retro single	1,624	ISS <25, no PRBC in first 48 hours	14	>14 days	Older PRBC associated with higher mortality, renal failure and pneumonia.
Leal-Noval et al. [22]	Pros single	66	Brain injured	~30	<10, 10-14, 15-19, >19 days.	Increased cerebral oxygenation, except in >19 days old PRBC.
Vandromme et al. [16]	Retro single	1,615	Trauma patients receiving ≥ 1 unit PRBC	27	≥ 14 vs.<14 days	Older PRBC associated with increase pneumonia.
Spinella et al. [5]	Retro single	202	Trauma patients receiving ≥ 5 units PRBC	24	≥ 28 vs. <28 days	Older PRBC associated with increased venous thrombosis and mortality
Kiraly et al. [21]	Pros single	32	Trauma patients with anemia	~25	≥ 21 vs. <21 days	Thenar tissue oximetry decreased with receipt of older PRBC.
Cohn et al. [25]	Pros single	63	Trauma patients	22	<10 vs.>20 days	It is feasible to conduct a study using ABO blood type to differentiate between young and old blood

Retro=Retrospective Study; Pros=Prospective Study; RCT=Randomized Control Trial; PRBC=Packed Red Blood Cells; Single=Single Institution Study; ISS=Injury Severity Score.

Table 1: Literature Review of Age of Blood and Trauma.

"old" type A, B and A/B blood (median age 18 days) when used in trauma patients during resuscitation after injury [25]. We were able to establish the feasibility of utilizing this scheme to develop a wide gap in the age of blood (12 days) for the trauma population. While this pilot study was not designed to identify statistically significant differences in clinical outcomes, we did note some interesting inequalities between groups (bacteremia incidence was 0 in "young" blood, versus 5 (11%) in "old" blood, p=0.31).

In conclusion, it appears feasible to conduct an age of RBC trial using ABO blood type to differentiate patients transfused either "young" or "old" blood, and it may be more efficient than alternative prospective cohort designs. Future multicenter trials could employ this methodology to assess the impact of the age of transfused blood in severely bleeding trauma patients where a classic randomized controlled trial may not be possible due to the inability to maintain an adequate inventory of all ABO types.

References

1. Weinberg JA, McGwin G Jr, Griffin RL, Huynh VQ, Cherry SA 3rd, et al. (2008) Age of transfused blood: an independent predictor of mortality despite universal leukoreduction. J Trauma 65: 279-282.
2. Weinberg JA, McGwin G Jr, Vandromme MJ, Marques MB, Melton SM, et al. (2010) Duration of red cell storage influences mortality after trauma. J Trauma 69: 1427-1431.
3. Moore FA, Moore EE, Sauaia A (1997) Blood transfusion. An independent risk factor for postinjury multiple organ failure. Arch Surg 132: 620-624.
4. Malone DL, Dunne J, Tracy JK, Putnam AT, Scalea TM, et al. (2003) Blood transfusion, independent of shock severity, is associated with worse outcome in trauma. J Trauma 54: 898-905.
5. Spinella PC, Carroll CL, Staff I, Gross R, Mc Quay J, et al. (2009) Duration of red blood cell storage is associated with increased incidence of deep vein thrombosis and in hospital mortality in patients with traumatic injuries. Crit Care 13: R151.
6. Koch CG, Li L, Sessler DI, Figueroa P, Hoeltge GA, et al. (2008) Duration of red-cell storage and complications after cardiac surgery. N Engl J Med 358: 1229-1239.
7. Eikelboom JW, Cook RJ, Liu Y, Heddle NM (2010) Duration of red cell storage before transfusion and in-hospital mortality. Am Heart J 159: 737-743.
8. Hébert PC, Wells G, Blajchman MA, Marshall J, Martin C, et al. (1999) A multicenter, randomized, controlled clinical trial of transfusion requirements in critical care. Transfusion Requirements in Critical Care Investigators, Canadian Critical Care Trials Group. N Engl J Med 340: 409-417.
9. Ho J, Sibbald WJ, Chin-Yee IH (2003) Effects of storage on efficacy of red cell transfusion: when is it not safe? Crit Care Med 31: S687-697.
10. Tinmouth A, Fergusson D, Yee IC, Hébert PC; ABLE Investigators; Canadian Critical Care Trials Group (2006) Clinical consequences of red cell storage in the critically ill. Transfusion 46: 2014-2027.
11. Steiner ME, Stowell C (2009) Does red blood cell storage affect clinical outcome? When in doubt, do the experiment. Transfusion 49: 1286-1290.
12. Weiskopf RB, Feiner J, Hopf H (2006) Fresh blood and aged stored blood are equally efficacious in immediately reversing anemia-induced brain oxygenation deficits in humans. Anesthesiology 104:911-920.
13. Walsh TS, McArdle F, McLellan SA, Maciver C, Maginnis M, et al. (2004) Does the storage time of transfused red blood cells influence regional or global indexes of tissue oxygenation in anemic critically ill patients? Crit Care Med 32: 364-371.
14. Hébert PC, Chin-Yee I, Fergusson D, Blajchman M, Martineau R, et al. (2005) A pilot trial evaluating the clinical effects of prolonged storage of red cells. AnesthAnalg 100: 1433-1438, table of contents.
15. Weinberg JA, McGwin G Jr, Marques MB, Cherry SA 3rd, Reiff DA, et al. (2008) Transfusions in the less severely injured: does age of transfused blood affect outcomes? J Trauma 65: 794-798.
16. Vandromme MJ, McGwin G Jr, Marques MB, Kerby JD, Rue LW 3rd, et al. (2009) Transfusion and pneumonia in the trauma intensive care unit: an examination of the temporal relationship. J Trauma 67: 97-101.
17. Offner PJ, Moore EE, Biffl WL, Johnson JL, Silliman CC (2002) Increased rate of infection associated with transfusion of old blood after severe injury. Arch Surg 137: 711-716.
18. Zallen G, Offner PJ, Moore EE, Blackwell J, Ciesla DJ, et al. (1999) Age of

transfused blood is an independent risk factor for postinjury multiple organ failure. Am J Surg 178: 570-572.

19. Murrell Z, Haukoos JS, Putnam B, Klein SR (2005) The effect of older blood on mortality, need for ICU care, and the length of ICU stay after major trauma. Am Surg 71: 781-785.

20. Keller ME, Jean R, LaMorte WW, Millham F, Hirsch E (2002) Effects of age of transfused blood on length of stay in trauma patients: a preliminary report. J Trauma 53: 1023-1025.

21. Kiraly LN, Underwood S, Differding JA, Schreiber MA (2009) Transfusion of aged packed red blood cells results in decreased tissue oxygenation in critically injured trauma patients. J Trauma 67: 29-32.

22. Leal-Noval SR, Muñoz-Gómez M, Arellano-Orden V, Marín-Caballos A, Amaya-Villar R, et al. (2008) Impact of age of transfused blood on cerebral oxygenation in male patients with severe traumatic brain injury. Crit Care Med 36: 1290-1296.

23. Glynn SA (2010) The red blood cell storage lesion: a method to the madness. Transfusion 50: 1164-1169.

24. Schulman CI, Nathe K, Brown M, Cohn SM (2002) Impact of age of transfused blood in the trauma patient. J Trauma 52: 1224-1225.

25. Cohn SM, Derosa M, Kumar A, Harrison C, Dent D, et al. (2014) Impact of the age of transfused red blood cells in the trauma population: A feasibility study. Injury 45: 605-611.