

Blood Component Therapy

*S Karim¹, E Hoque², MM Hoque³, SM Rahman⁴, K Islam⁵

ABSTRACT

Transfusion medicine has undergone advancements since its initiation in the early 20th century. One of these was the discovery that blood can be divided into individual components and delivered separately. Today, blood transfusions nearly always consist of the administration of 1 or more components of blood. Whole blood transfusion is now limited to situations involving massive resuscitation (trauma). The most familiar cellular components include packed red blood cells (PRBC), washed PRBC, leukoreduced PRBC and pooled or aphaeresis platelets. Plasma products such as FFP or cryoprecipitate, ant hemophilic factor (CRYO). The transfusion of red blood cells (RBCs), platelets, fresh-frozen plasma (FFP), and cryoprecipitate has the potential of improving clinical outcomes in perioperative and peripartum settings. These benefits include improved tissue oxygenation and decreased bleeding. However, transfusions are not without risks or costs. With the advent of blood component therapy, each unit of whole blood collected serves the specific needs of several, rather than a single patient.

Key Words: component therapy, blood banking, transfusion medicine, packed RBCs, plasma, platelets, cryoprecipitate.

Introduction

The first documented animal-to-animal (dog) blood transfusion was performed at Oxford in 1665 by Richard Lower, followed by the first animal-to-human blood transfusion in 1667 by Jean Denis. The first human-to-human blood transfusion was performed by James Blundell in 1818. In the year 1900, the ABO blood grouping system was classified by Landsteiner and, based on this, the first pretransfusion cross-match was done by Ottenberg in 1907. The system of Rh typing was invented by Landsteiner and Wiener in the year 1940. After this, there have been major inventions in the 20th century and that made component therapy possible, e.g. invention of anticoagulant and preservative solutions, refrigeration, plastic blood

bags, component administration, infectious disease testing, high-risk donor screening, etc.

Packed RBCs

Blood transfusion can be a lifesaving procedure, but it has risks, including infectious and noninfectious complications. There is debate in the medical literature concerning the appropriate use of blood and blood products. Clinical trials investigating their use suggest that waiting to transfuse at lower hemoglobin levels is beneficial.^{1,2} Red blood cell transfusions are used to treat hemorrhage and to improve oxygen delivery to tissues. Transfusion of red blood cells should be based on the patient's clinical condition. Indications for transfusion include

¹*Dr. Shanaz Karim, Associate Professor, Department of Transfusion Medicine, Dhaka Medical College Hospital

²Prof. Dr. Ehteshamul Hoque, Professor, Department of Oncology, Anwer Khan Modern Medical College Hospital

³Prof. Dr. Md. Mazharul Hoque, Professor, Department of Transfusion Medicine, Dhaka Medical College Hospital

⁴Dr. Syeda Masooma Rahman, Associate Professor, Department of Transfusion Medicine, Dhaka Medical College Hospital

⁵Dr. Kashfia Islam, Registrar, Department of Transfusion Medicine, Dhaka Medical College Hospital

*Corresponding Author

Date of submission: 20.01.2018, Date of acceptance: 24.05.2018

symptomatic anemia (causing shortness of breath, dizziness, congestive heart failure, and decreased exercise tolerance), acute sickle cell crisis, and acute blood loss of more than 30 percent of blood volume. Packed red blood cells (RBCs) are prepared from whole blood by removing approximately 250 mL of plasma. 1 unit = 220 mL. Each unit contains approximately 42.5-80 g of hemoglobin or 128-240 mL of pure red cells, 50 mL of donor plasma, in addition to preservative and anticoagulant solutions.

Indications for transfusion of pRBCs include symptomatic anemia, which manifests as high pulse rate, increased respiratory rate, dizziness, and weakness. While there is no standard hemoglobin or hematocrit used to define a need for transfusion, most institutions set one. Hemoglobin of less than 7 g/dL or 8 g/dL are commonly used cutoffs. Packed RBC transfusions should not be used to treat nutritional deficiencies or to expand blood volume.³

Several institutions are adopting measures to ensure physicians are ordering pRBCs and other blood components appropriately. One way of doing this is to encourage the physician to determine and state the indication on the order form.

One unit of pRBCs should increase the hemoglobin by 1 g/dL to 1.5 g/dL and the hematocrit by 3%-5%.⁴ One unit should typically be transfused in less than 4 hours. As with all blood components, only normal saline should be administered in conjunction with pRBCs to protect the cells against osmolarity disruption.^{5,6}

Start infusion slowly at 2 mL per minute. If no sign of reaction after the first 15 minutes then increase rate to 150-300 mL/hour nonemergency setting. Adjust flow rate according to the volume that the patient's circulatory system can tolerate. Red Blood Cells are capable of transmitting cytomegalovirus, mediating graft-versus-host disease and causing febrile, nonhemolytic reactions. For recipients at particular risk from these transfusion related complications, use of CMV reduced-risk (i.e. CMV seronegative or LR-RBC), gamma-irradiated and leukoreduced preparations should be considered.

Plasma

Plasma contains all of the coagulation factors. Fresh frozen plasma infusion can be used for reversal of anticoagulant effects. Thawed plasma has lower levels of factors V and VIII and is not indicated in patients with consumption coagulopathy (diffuse intravascular coagulation).⁷ Plasma transfusion is recommended in patients with active bleeding and an International Normalized Ratio (INR) greater than 1.6, or before an invasive procedure or surgery if a patient has been anticoagulated.^{8,9} Fresh Frozen Plasma is prepared from whole blood or apheresis donations and is frozen within 8 hours of collection.¹⁰ Once thawed, plasma contains all clotting factors at physiological levels although there is considerable variability between donors in their level of individual clotting factors.¹¹ However, since anti-HLA antibodies are often implicated in causing transfusion related acute lung injury (TRALI),¹² and because multiparous females are often sensitized to HLA antigens,¹³ many donor centers are diverting the plasma component of female donations to fractionation. To make up the shortfall in plasma supply, there are several other plasma products that can be prepared. Plasma frozen within 24 hours of phlebotomy (FP24) is an AABB/FDA approved plasma product, which as its name suggests, represents plasma that is frozen between 8-24 hours after collection. Several studies have demonstrated that most clotting factor levels are well maintained in FP24 such that it is often used interchangeably with FFP.^{14,15,16,17} Once thawed, both FFP and FP24 can be maintained in the liquid state for up to 24 hours at refrigerator temperatures. Plasma should not be transfused prophylactically in patients undergoing cardiopulmonary bypass in the absence of diffuse microvascular bleeding¹⁸, nor should it be used as a volume expander or as a source of nutrition. When plasma is indicated, it should be administered in a dose of at least 10-15 mL/kg.^{19,20} Although a dose of 5-8 mL/kg has previously been recommended for warfarin reversal²¹, more recent guidelines suggest 10-15 mL/kg should be used.²² It is important to remember that hypothermia and acidosis should be corrected prior to plasma administration.

Platelet

Allogeneic platelet transfusions play a major role in the management of thrombocytopenic patients. The ready availability of platelet concentrates has made a major contribution to support the development of intensive treatment regimens for the treatment of patients with hematological and other malignancies. Although considerable advances have been made in many aspects of platelet transfusions in the last 30 years, several areas of controversy continue to exist with regard to the optimal approach to the use of platelet transfusions to further reduce the risk of clinically significant thrombocytopenic hemorrhage in patients with a hypoproliferative bone marrow and to minimize the frequency and severity of adverse events. Platelets for transfusion can be prepared by three different methods: (a) the platelet-rich plasma (PRP) method; (b) the buffy coat (BC) method; and (c) the apheresis method.^{23,24} The PRP method, which is used almost exclusively in the United States, and the BC method, which is used predominantly in Western Europe and Canada, derive platelets from units of whole blood collected from volunteer whole blood donors.²³ Studies comparing PRP and BC platelets have shown no difference in the *in vitro* quality of such platelet concentrates when they are stored for up to 5 days; however, few studies of direct *in vivo* head-to-head comparisons of these two methods of preparing platelet concentrates have been done.²⁵ The third method for preparing platelets is by the process of apheresis.²⁶ One of the major advantages of using apheresis platelets is that enough apheresis platelets can be derived from a single donor to provide a single clinically relevant platelet transfusion dose to an adult thrombocytopenic patient. In contrast, to obtain the equivalent number of transfused platelets required using either the PRP or BC methodology requires the pooling of platelet concentrates from 4 to 6 different donors. A number of Clinical Practice Guidelines have been published in both Europe and North America that provide "evidence-based" recommendations for the clinical use of platelet transfusions. In general, they recommend prophylactic platelet transfusions at a transfusion trigger of $10 \times 10^9/L$ ^{26,27,28,29} The use of therapeutic platelets is only recommended when there is significant bleeding or when an invasive intervention is anticipated.

PCs from Whole Blood. Often referred to as random-donor platelets, PCs are prepared by centrifugation of standard units of whole blood. There are two methods for doing this: (1) the platelet-rich plasma (PRP) method, and 2) the buffy coat (BC) method.³⁰ The PRP method is used in the United States, whereas the BC method is in common use in Europe. In the PRP method, an initial low G force (soft) spin produces PRP, which is separated from the red cells. The PRP is then centrifuged at a higher G force (hard) spin, and most of the platelet-poor plasma is removed.^{31,32,33,34} The residual PCs contain approximately 0.5 to 0.75×10^{11} platelets/unit or approximately 60% to 75% of the platelets from the original unit of whole blood. Because some blood centers now supply units with higher numbers of platelets, clinicians should be aware of the average dose provided by their particular center. One drawback to this method is that the resulting PCs also contain 10^8 to 10^9 WBCs or approximately 50% or more of the leukocytes from the original unit of whole blood.

This combination of storage container, agitation, preservative solution, temperature, and the use of approximately 50 mL of plasma permits satisfactory preservation of platelets for up to 7 days^{35,36} However, several instances of bacterial contamination of PCs stored for this period have been reported^{37,38} and the storage time from collection to transfusion is now limited to 5 days.³⁹

Single-Donor Platelets Produced by Apheresis. Although the Food and Drug Administration term for this component is "platelets, apheresis," the component is usually called single-donor platelets. Donors usually undergo two venipunctures. Blood pumped from one vein passes through a blood-cell separator centrifugation system with removal of the platelets or other cellular components and return of the plasma and RBCs to the donor's other arm. Current standards require that a bag of apheresis platelets must contain at least 3×10^{11} platelets in at least 75% of the products tested.⁴⁰

Platelets obtained by plateletpheresis are processed, tested, and labeled similar to whole blood. This includes ABO and Rh typing and testing for all required transfusion-transmitted diseases. The plateletpheresis product is stored for up to 5 days at $20^\circ C$ to $24^\circ C$.^{41,42,43,44} in the same manner as

platelets prepared from whole blood. The number of platelets contained in each bag is determined, although this information may not be recorded on the label. Each apheresis product has a volume of approximately 200 mL and contains few red cells. The WBC content varies, depending on the instrument and technique used for collection, but most plateletpheresis products now contain less than 5×10^6 leukocytes and can be considered to be leukocyte reduced.

Cryoprecipitate

Cryoprecipitated antihemophilic factor, known as cryoprecipitate or cryo, is extracted from frozen plasma (FFP or FP24) by slowly thawing a unit at 1°C - 6°C .⁴⁵ (When being prepared for transfusion, FFP or FP²⁴ are thawed more rapidly at 37°C .) This process produces a slushy-like substance, which is centrifuged to separate the insoluble component. Once removed, the cryo unit must be refrozen within 1 hour and expires 1 year later.

One unit of Cryoprecipitated contains at least 150 mg of fibrinogen and at least 80 IU of factor VIII. These represent 20%-40% of the fibrinogen and 50% of the factor VIII of the original unit of plasma. Von Willebrand factor is another important component of cryo.⁴⁶ Cryoprecipitate may be indicated for the treatment of hemophilia A, Von Willebrand's disease, congenital or acquired fibrinogen deficiency, Factor XIII deficiency and obstetric complications or other situations associated with consumption of fibrinogen, e.g., DIC. Start infusion slowly at 2 mL per minute. If no sign of reaction after the first 15 minutes then may infuse as rapidly as the patient's circulatory system can tolerate.⁴⁷ The usual dose in adults is 10 units of pooled cryoprecipitate.⁴⁸ Recommendations for dosing regimens in neonates vary, ranging from 2 mL of cryoprecipitate per kg to 1 unit of cryoprecipitate (15 to 20 mL) per 7 kg.⁴⁹

Conclusion

It is very essential that blood and its components should be used appropriately to reduce unnecessary and unsafe transfusions and to improve patient outcomes and safety. A single blood unit can provide treatment for two or more patients and correct specific deficiency. So it is desirable that educational programs be arranged for doctors

regarding appropriate use of blood to minimize existing ill practices. Adherence to proper indications for blood component therapy is essential because of its potential adverse effects and costs of transfusion.

Conflict of interest: non

References

1. Hébert PC, Wells G, Blajchman MA, *et al.* A multicenter, randomized, controlled clinical trial of transfusion requirements in critical care. Transfusion Requirements in Critical Care Investigators, Canadian Critical Care Trials Group [published correction appears in *N Engl J Med.* 1999; 340(13): 1056]. *N Engl J Med.* 1999; 340(6): 409-417.
2. Lacroix J, Hébert PC, Hutchison JS, *et al.*; TRIPICU Investigators; Canadian Critical Care Trials Group; Pediatric Acute Lung Injury and Sepsis Investigators Network. Transfusion strategies for patients in pediatric intensive care units. *N Engl J Med.* 2007; 356(16): 1609-1619.
3. Practice guidelines for blood transfusions: A compilation from recent peer-reviewed literature. American Red Cross; 2007
4. Hughes VC, Wright PA. Donor Screening and Component Preparation. In: Harmening DM. *Modern Blood Banking and Transfusion Practice.* Philadelphia, PA: FA Davis Company; 2005.
5. Standards for blood banks and transfusion services. Bethesda, MD: American Association of Blood Banks; 2006.
6. Circular of Information for the Use of Human Blood and Blood Components. Bethesda, MD: AABB; 2009.
7. King KE, Bandarenko N. *Blood Transfusion Therapy: A Physician's Handbook.* 9th ed. Bethesda, Md.: American Association of Blood Banks; 2008: 236.
8. Practice parameter for the use of fresh-frozen plasma, cryoprecipitate, and platelets. Fresh-Frozen Plasma, Cryoprecipitate, and Platelets Administration Practice Guidelines Development Task Force of the College of American Pathologists. *JAMA.* 1994; 271(10): 777-781.

9. Holland LL, Brooks JP. Toward rational fresh frozen plasma transfusion: the effect of plasma transfusion on coagulation test results. *Am J Clin Pathol.* 2006; 126(1): 133-139.
10. Brecher ME. *Technical Manual.* 16th ed. Bethesda, MD: AABB, 2008.
11. Holland LL, Foster TM, Marlar RA, Brooks JP. Fresh frozen plasma is ineffective for correcting minimally elevated international normalized ratios. *Transfusion* 2005; 45: 1234-5.
12. Triulzi DJ. Transfusion-related acute lung injury: an update. *Hematology Am Soc Hematol Educ Program* 2006: 497-501.
13. Kakaiya RM, Triulzi DJ, Wright DJ, Steele WR, Kleinman SH, Busch MP, Norris PJ, Hillyer CD, Gottschall JL, Rios JA, Carey P, Glynn SA. Prevalence of HLA antibodies in remotely transfused or alloexposed volunteer blood donors. *Transfusion* 2010; 50: 1328-34.
14. Kakaiya RM, Morse EE, Panek S. Labile coagulation factors in thawed fresh frozen plasma prepared by two methods. *Vox Sang* 1984; 46: 44-6.
15. O'Neill EM, Rowley J, Hansson-Wicher M, McCarter S, Ragno G, Valeri CR. Effect of 24-hour whole-blood storage on plasma clotting factors. *Transfusion* 1999; 39: 488-91.
16. Smith JF, Ness PM, Moroff G, Luban NL. Retention of coagulation factors in plasma frozen after extended holding at 1-6 degrees C. *Vox Sang* 2000; 78: 28-30.
17. Cardigan R, Lawrie AS, Mackie IJ, Williamson LM. The quality of fresh-frozen plasma produced from whole blood stored at 4 degrees C overnight. *Transfusion* 2005; 45: 1342-8.
18. Cross-sectional guidelines for therapy with blood components and plasma derivatives (edited by the Bundesärztekammer) *Transfus Med Hemother* 2009; 36: 419-36
19. Rossaint R, Bouillon B, Cerny V, Coats TJ, Duranteau J, Fernandez-Mondejar E, Hunt BJ, Komadina R, Nardi G, Neugebauer E, Ozier Y, RIddez L, Schultz A, Stahel PF, Vincent JL, Spahn DR. Managemnt of bleeding following major trauma: an updated European guideline. *Critical Care* 2010; 14: R52-R81.
20. Chowdhury P, *Br J Haematol* 2004;125:69-73
21. Questions and answers about transfusion practices. 3rd Ed. American Society of Anesthesiologists Committee on Transfusion Medicine. Pg 14. 1997
22. O'Shaughnessy DF, Atterbury C, Bolton Maggs P, Murphy M, Thomas D, Yates S, Williamson LM: Guidelines for the use of fresh-frozen plasma, cryoprecipitate and cryosupernatant. *Br J Haematol* 2004; 126: 11-28
23. Vassallo RR, Murphy S. A critical comparison of platelet preparation methods. *Curr Opin Hematol.* 2006; 13: 323-330.
24. Murphy S, Heaton WA, Rebutla P. Platelet production in the Old World - and the New. *Transfusion.* 1996; 36: 751-754.
25. Cardigan R, Williamson LM. The quality of platelets after storage for 7 days. *Transfusion Medicine.* 2003; 13: 173-187.
26. Slichter SJ. Evidence-based platelet transfusion guidelines. *Hematology (Am Soc Hematol Educ Program).* 2007: 172-178.
27. Schiffer CA, Anderson KC, Bennett CL, *et al.* Platelet transfusions for patients with cancer: clinical practice guidelines of the American Society of Clinical Oncology. *J Clin Oncol.* 2001; 19: 1510-1538.
28. Stanworth SJ, Hyde C, Heddle N, Rebutla P, Brunskill S, Murphy MF. Prophylactic platelet transfusion for haemorrhage after chemotherapy and stem cell transplantation (Review). *Cochrane Database Syst Rev.* 2004; 4: CD004269.
29. Stanworth SJ, Hyde C, Brunskill S, *et al.* Platelet transfusion prophylaxis for patients with haematological malignancies: where to now? *Br J Haematol.* 2005; 131: 588-595.
30. Murphy S, Heaton WA, Rebutla P: Platelet production in the Old World-and the New. *Transfusion* 36: 751-754, 1996
31. Slichter SJ, Harker LA: Preparation and storage of platelet concentrates. II. Storage and variables influence platelet viability and function. *Br J Haematol* 34: 403-419, 1976

32. Kahn RA, Cossette I, Friedman LI: Optimum centrifugation conditions for the preparation of platelet and plasma products. *Transfusion* 16: 162-165, 1976
33. Reiss RF, Katz AJ: Optimizing recovery of platelets in platelet rich plasma by the simplex strategy. *Transfusion* 16: 370-374, 1976
34. Slichter SJ, Harker LA: Preparation and storage of platelet concentrates. I. Factors influencing the harvest of viable platelets from whole blood. *Br J Haematol* 34: 395-402, 1976
35. Murphy S, Kahn RA, Holme S, *et al*: Improved storage of platelets for transfusion in a new container. *Blood* 60: 194-200, 1982
36. Hogge DE, Thompson BW, Schiffer CA: Platelet storage for seven days in second generation CLXTM blood bags. *Transfusion* 26: 131-135, 1986
37. Heal JM, Singal S, Sardisco E, *et al*: Bacterial proliferation in platelet concentrates. *Transfusion* 26: 388-390, 1986
38. Braine HG, Kickler TS, Charache P, *et al*: Bacterial sepsis secondary to platelet transfusion: An adverse effect of extended storage at room temperature. *Transfusion* 26: 391-393, 1986
39. Schiffer CA, Lee EJ, Ness PM, *et al*: Clinical evaluation of platelet concentrates stored for one to five days. *Blood* 67: 1591-1594, 1986
40. American Association of Blood Banks: Standards for Blood Banks and Transfusion Services (ed 16). Bethesda MD, American Association of Blood Banks, 1994
41. Slichter SJ: Efficacy of platelets collected by semi-continuous flow centrifugation (Haemonetics Model 30). *Br J Haematol* 38: 131-140, 1978
42. Patel IP, Ambinder E, Holland JF, *et al*: In vitro and in vivo comparison of single-donor platelets and multiple-donor pooled platelets transfusions in leukemic patients. *Transfusion* 18: 116-119, 1978
43. Turner VS, Hawker RJ, Mitchell SG, *et al*: Paired in vivo and in vitro comparison of apheresis and "recovered" platelet concentrates stored for five days. *J Clin Apheresis* 9: 189-194, 1994
44. Rock GA, Blanchette VS, Wong SC: Storage of platelets collected by apheresis. *Transfusion* 23: 99-105, 1983
45. Hughes VC, Wright PA. Donor Screening and Component Preparation. In: Harmening DM. *Modern Blood Banking and Transfusion Practice*. Philadelphia, PA: FA Davis Company; 2005.
46. Davenport RD, Mintz PD. Transfusion medicine. In: McPherson R, Pincus M. *Henry's Clinical Diagnosis and Management by Laboratory Methods*. Philadelphia, PA: Saunders Elsevier; 2006.
47. Sink BLS. Administration of Blood Components. In Roback JD *et al* eds. *American Association of Blood Banks (AABB) Technical Manual*; 16th edition (July 8, 2008)p 620
48. King KE, Bandarenko N. *Blood Transfusion Therapy: A Physician's Handbook*. 9th ed. Bethesda, Md.: American Association of Blood Banks; 2008: 236.
49. Poterjoy BS, Josephson CD. Platelets, frozen plasma, and cryoprecipitate: what is the clinical evidence for their use in the neonatal intensive care unit? *Semin Perinatol*. 2009; 33(1): 66-74.