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BLOOD BULLETIN

To Wash Blood Components or Not — Indications and Alternatives

Nancy Van Buren, MD, Medical Director at Innovative Blood Resources and Community Blood Center of Kansas City, divisions of New York Blood Center; Nanci Fredrich, RN, BSN, MM, Transfusion Safety Officer at Versiti; Richard Gammon, MD, Medical Director at OneBlood; Debra Smith, MD, PhD, Medical Director at Carter BloodCare; Ruchika Goel, MD, MPH, Medical Director at ImpactLife; Louis Katz, MD, Chief Medical Officer Emeritus at ImpactLife; Claudia S. Cohn, MD, PhD, Professor of Laboratory Medicine and Pathology at the University of Minnesota.

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KEY POINTS

- Washed blood components should be reserved for patients with documented clinical need.
- Washing blood components results in shortened shelf life, loss of red blood cells and/or platelets, and reduction in platelet function.
- Thorough investigation of all probable causes of anaphylactic transfusion reactions by clinicians is advised, including possible immunoglobulin A deficiency, to ensure safety of future transfusions.
- Screening of all orders for washed blood components and use of alternative strategies can help mitigate the nationwide shortage of processing kits.

DESCRIPTION

It is sometimes necessary to wash cellular components to remove unwanted plasma proteins or glycerol from previously frozen units.[1] Washing requires the use of 0.9 percent sodium chloride with or without dextrose. It results in some loss of red blood cells (RBCs) and platelets, as well as reduction in platelet function.[1] Since washing increases the risk of bacterial contamination, the shelf life is limited to 24 hours at 1 to 6° C for RBCs or four hours at 20 to 24°C for platelets.

BACKGROUND OF CURRENT SITUATION

During 2022, supply chain issues created a national shortage of the COBE 2991 cell washer processing kits. This caused an urgent need for blood centers and hospitals to implement an alternative solution so that the demand for washed components could be met. In the meantime, all orders for washed components should be being carefully screened. The recommendation for hospital transfusion services is to review all orders, work with physicians to determine if washing is clinically necessary, and consider the use of alternative options.

INDICATIONS FOR WASHING BLOOD COMPONENTS

1. Patients with recurrent or severe allergic reactions caused by plasma proteins is the main indication for washed components, including RBC exchange transfusions in sickle cell disease.[1-3]
2. Immunoglobulin A (IgA) deficient patients who have documented anti-IgA antibodies and a history of transfusion-associated anaphylaxis. IgA deficient blood components may be considered, if available.[1, 4]
3. Patients with congenital haptoglobin deficiency and antibodies to haptoglobin.[5, 6]
4. RBC units which have been frozen to prolong their shelf life require washing to remove the preservative (e.g. glycerol). This indication is particularly important when antigen-negative RBC units must be used for patients with rare RBC phenotypes, including those requiring chronic transfusion therapy for conditions such as sickle cell disease.
5. Reduction of free potassium for large-volume RBC transfusions in pediatric patients susceptible to hyperkalemia when fresher RBC units are not available.[7-9]
6. Intrauterine or fetal transfusions may be an indication for removal of supernatant containing high potassium in older (>7 days) or previously irradiated units.[10]
7. RBC or platelet components of maternal origin for fetuses or neonates who have hemolytic disease of the fetus and newborn or neonatal alloimmune thrombocytopenia due to antibodies directed against paternal antigens when antigen-negative units are not available.[10, 11]

USE IN IgA DEFICIENCY

The most common form of immune deficiency is isolated IgA deficiency (serum IgA less than 0.05 mg/dL).[12] The frequency of IgA deficiency varies by ethnic background; 1:143 in the Arabian Peninsula to 1:185,000 in Japan.[13] In addition, IgA deficiency may result from drug exposure, alcohol, chemicals such as benzene, or infectious agents such as toxoplasmosis, measles, or rubella. It has been estimated that up to 40 percent of IgA-deficient individuals develop antibodies to IgA, putting them at risk for severe allergic or anaphylactic reactions when exposed to IgA-containing blood components.[14] If antibodies to IgA are considered the likely cause of an allergic reaction, a pre-transfusion specimen should be tested for IgA levels and the presence of antibodies to IgA. It should be noted that many IgA assays cannot quantify IgA levels below 0.5 mg/dL, and therefore it may be necessary to send specimens to a reference laboratory to identify at-risk recipients using assays that have a lower limit of detection to ≤0.05 mg/dL.

Patients with allergic/anaphylactic reactions due to anti-IgA in the setting of IgA deficiency were first identified in 1968 using a serologic test rather than clinical criteria. More recently, authors of a commentary article, who evaluated various case reports, hemovigilance databases, and unpublished reports from diagnostic laboratories, concluded that IgA-related anaphylactic transfusion reactions are not an evidence-based entity.[15] Transfusion-related anaphylactic reactions occur in approximately one in 50,000 transfusions.[16] Not all patients experiencing anaphylactic transfusion reactions undergo testing for IgA status. Of those that experience anaphylactic reactions, the symptoms resolve promptly and often the patient is transfused at a later date without any allergic reactions. Because no alternative strategy or diagnostic laboratory test exists, a bias exists for IgA deficiency diagnosis based on existing assumptions. Clinicians are encouraged to investigate all possible causes of an anaphylactic transfusion reaction and consider other transfusion practice strategies, as may be indicated.

EFFECT OF WASHING CELLULAR BLOOD COMPONENTS

The early outdate of washed cellular components is due to the risk of bacterial contamination as the component is processed in an open system. Thus, transfusion must occur as soon as possible after washed components are issued. This requires significant coordination if washing occurs at a blood center and must be transported to the hospital. In addition, washing is associated with loss of approximately 20 percent of RBCs and 33 percent of platelets.[17] For RBC units, washing may result in increased free hemoglobin due to cellular damage from centrifugation, which is impacted by the age of RBCs prior to washing, length of storage after washing, and the method used.[18] It should also be noted that washing is not an acceptable method of leukocyte reduction, nor will it eliminate the risk of transfusion-associated graft-versus-host disease due to the residual number of viable leukocytes. Patients with a history of anaphylactic reactions may also need additional monitoring and surveillance for severe adverse reactions requiring in-hospital admission for their transfusion as a precaution.

ALTERNATIVES TO AUTOMATED WASHING

Manual washing may be an option when processing kits for automated washing are unavailable.[19] Volume reduction can be an alternative to washing and is conventionally performed by centrifugation of a blood component and the subsequent removal of the supernatant. A reduction in volume may be required for neonates and infants when the recipient is unable to tolerate large volume transfusions or has co-morbidities increasing their risk for transfusion-associated hyperkalemia.[7-9]. Another less optimal alternative to washing is use of platelet additive solution (PAS), a crystalloid nutrient media used in place of plasma for platelet storage. PAS replaces about 70 percent of plasma in platelet components, and as the total amount of storage plasma decreases, risk of allergic reactions is significantly decreased.[20, 21] Since washing isn't an option for plasma transfusion, solvent detergent treated pooled plasma may reduce the risk of refractory allergic transfusion reactions.[22]

CONCLUSION

The current shortage of kits for washing cellular components requires close communication and collaboration between hospitals, physicians, and blood centers. Alternatives to washing should be considered when possible, and dubious indications for washing should be rejected. Data on the clinical benefits of washed cellular components, other than reducing allergic reactions, are mixed and it is difficult to draw any firm conclusions.[18] Transfusion-related anaphylaxis induced by antibodies to IgA is a potentially serious, but rare event that must be differentiated from other causes of allergic reactions. It is important to recognize and confirm IgA deficiency with the presence of anti-IgA in recipients, because these patients require lifelong support with washed or IgA-deficient blood components. Most cases of allergic reactions are related to a specific unit and not the result of selective protein deficiency in the patient. Thus, washed blood components should be reserved for patients with an absolute need for this requirement.

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