The severity of illness and inflammatory markers cannot predict red blood cell alloimmunization in cancer patients

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Red Blood Cell (RBC) alloimmunization remains a major complication for transfusion-dependent patients but factors governing risk for alloimmunization are little known. Antibody production is a serious complication in patients on long-term transfusion therapy; it may cause potentially life-threatening delayed hemolytic transfusion reactions (DHTRs), autoantibody formation as well as logistic problems, for example, to obtain timely and properly matched transfusion blood for patients in which new alloantibodies are detected. Even non-chronically transfused patients who become alloimmunized are 20 times more likely to form additional antibodies after one or more repeat transfusion events[1-3]. This is not an ideal scenario for a patient population in which the benefit is proportional to the longevity of transfused RBCs and this may result in an extensive laboratory workup that consumes significant time and resources.

In an effort to reduce alloimmunization, some programs have been designed and implemented to provide Rh and K antigen-matched RBC transfusions to patients who are in need of chronic transfusion support but some patients still become alloimmunized despite this antigen matching[4,5]. In contrast to prophylactic antigen matching, some institutions argue that the data supporting a reduction in DHTRs are insufficient to offset the cost of labor and resources required to perform extended matching for polytransfused patients. Characterization of patients and clinical conditions with high alloimmunization risk could help in the selection of patients who need to be extensively matched. By identifying such risks, it may be possible to predict responders and non-responders, thereby avoiding the use of costly antigen-matched units for non-responders, and only selecting phenotyped/genotyped-matched units for responders to reduce alloimmunization-associated morbidity and mortality.

Several factors are predicted to influence the reaction of the recipient`s immune system to alloantigens including the dose and the immunogenicity of the antigen as well as genetic, and acquired patient-related factors and clinical conditions[6,7]. It has also been shown that the number of transfusions plays an important role in RBC alloimmunization and that immune-compromised patients have a lower risk to develop red cell antibodies. However, other patient-related risks are little known. Although unexpected risk factors were found, such as solid tumors because of their chronic inflammatory state, there are few and limited studies showing that the inflammatory status of human transfusion recipients may regulate the immunogenicity of transfused RBCs[8].

In this issue of the *Revista Brasileira de Hematologia e Hemoterapia*, there is an important retrospective case-control study on a small group of alloimmunized and non-alloimmunized patients with solid cancer, regarding the risk of RBC alloimmunization[9]. The authors evaluated clinical factors related to the severity of the disease (ECOG performance scale, Karnofsky scale, presence of metastasis and body mass index) and inflammatory background (C-reactive protein) and concluded that these factors cannot be used to predict the risk of RBC alloimmunization in such patients. Although the relatively small number of patients is a limitation of the study, this paper represents an additional contribution in the field of RBC alloimmunization in patients with solid tumors.

The results of the studies of Dinardo et al. do not ratify the thesis that the inflammatory status regulates the immunogenicity of transfused RBCs[9]. This finding supports the concept that there are combinations of factors influencing the immune response to RBC antigens.

We will have to look to future studies by this group and others to better understand the risk factors of RBC alloimmunization in cancer patients in order to provide or not antigen-matched RBC transfusions.

References

1. Cox JV, Steane E, Cunningham G, Frenkel EP. Risk of alloimmunization and delayed hemolytic transfusion reactions in patients with sickle cell disease. Arch Intern Med. 1988;148(11):2485-9.
2. Schonewille H, Haak HL, van Zijl AM. Alloimmunization after blood transfusion in patients with hematologic and oncologic diseases. Transfusion. 1999;39(7):763-71.

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3. Schonewille H, van de Watering LM, Brand A. Additional red blood cell alloantibodies after blood transfusions in a nonhematologic patient cohort: Is it time to take precautionary measures? Transfusion. 2006;46(4):630-5.
4. Tahhan HR, Holbrook CT, Braddy LR, Brewer LD, Christie JD. Antigen-matched donor blood in the transfusion management of patients with sickle cell disease. Transfusion. 1994;34(7):562-9. Comment in: Transfusion. 1994;34(7):558-60.
5. Lasalle-Williams M, Nuss R, Le T, Cole L, Hassel K, Murphy JR, et al. Extended red blood cell antigen matching for transfusions in sickle cell disease: a review of a 14-year experience from a single center. Transfusion. 2011;51(8):1732-9.
6. Bao W, Yu J, Heck S, Yazdanbakhsh K. Regulatory T-cell status in red cell alloimmunized responder and nonresponder mice. Blood. 2009;113(22):5624-7
7. Bao W, Zhong H, Li X, Lee MT, Schwartz J, Sheth S, Yazdanbakhsh K. Immune regulation in chronically transfused allo-antibody responder and nonresponder patients with sickle cell disease and β-thalassemia major. Am J Hematol. 2011;86(12):1001-6.
8. Bauer MP, Wiersum-Osselton J, Schipperus M, Vandenbroucke JP, Briët E. Clinical predictors of alloimmunization after red blood cell transfusion. Transfusion. 2007;47(11):2066-71.
9. Dinardo CL, Ito GM, Sampaio LR, Mendrone Jr A. Study of possible clinical and laboratory predictors of alloimmunization against red blood cell antigens in cancer patients. Rev Bras Hematol Hemoter. 2013;35(6):414-6.

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