

Transfusions: Is it Time to Order a Small Instead of a Grande?

By Margaret Ragni, MD, MPH

Both the Education and Scientific Committee Sessions on Transfusion Medicine focused on potential complications and immune reactions to transfusion component therapy. It is well known that up to 10 percent of the more than 14 million red cells and 1.6 million platelets transfused each year in the United States are associated with adverse events. These can range from transmissible infection, febrile reactions, bacterial contamination, allergic reactions, respiratory distress, and hemolytic reactions to metabolic and immune-related disorders. In trying to avoid these complications, there is a growing interest in optimal transfusion dosing and playing the innate immune response to the best advantage.

The controversial topic of platelet dosing was discussed by Sherrill Schlichter, MD, Puget Sound Blood Center, Seattle, WA, in the Education Session on Transfusion Medicine. She emphasized the increasing need for evidence-based, potentially cost-effective strategies for platelet transfusion. Ample evidence supports the need to evaluate reducing platelet dose per transfusion. Because platelets express the thrombopoietin receptor, it has been suggested that high-dose platelet transfusions may actually lengthen the duration of thrombocytopenia, as they decrease the circulating thrombopoietin level, which reduces the stimulus for marrow megakaryocyte proliferation. It is newsworthy that she is heading the Platelet Dose Trial (PLADO), which is evaluating the safety of three platelet dose levels in thrombocytopenia. Sponsored by the Transfusion Medicine Hemostasis Clinical Trials Network (TMH-CTN), this is the first prospective study to evaluate the optimal quantity of platelets per transfusion.

The impact of recipient immune response to transfusion was addressed in the Scientific Committee on Transfusion Medicine session, titled “The Scientific Basis of Innate Immunity in Transfusion and Bone Marrow Transplantation,” chaired by Christopher D. Hillyer, MD, Emory University Hospital. His colleague at Emory, James C. Zimring, MD, PhD, presented the first talk on “Overview of Innate Immunity and Its Role in Alloimmunization to RBC,” exploring how it is that sterile red-cell transfusion could be a “danger” signal to the immune system. While white cells, platelets, and infectious pathogens release activators of inflammation and are danger signals to the immune system, RBCs are sterile and would be expected to lack inflammatory or danger signals. Yet, RBC alloimmunization occurs in up to 6 percent of those transfused. Although the mechanism of RBC alloimmunization may involve genetics, HLA type, and toll receptors, the role of recipient immune response is gaining interest — for example, if RBC transfusion in a recipient with an underlying inflammatory disease may affect the development of alloimmunization to RBCs. Clearly, more research is needed to determine the mechanism of potential therapeutic targets, and to identify those at risk.

The second talk, titled “Platelets are Both Targets and Mediators of Innate Immunity,” by John W. Semple, PhD, St. Michael’s Hospital, Toronto, Canada, focused on the impact of recipient innate immunity and complications of platelet transfusion. Not only do platelets attract WBCs to sites of vessel injury, bind organisms, and secrete pro-inflammatory cytokines, they may be recognized by and/or stimulate the recipient’s innate immune response. Thus, host immune response to transfused platelets may determine development of thrombosis, atherosclerosis, and response to infectious pathogens. One example is Transfusion-Related Acute Lung Injury, or TRALI, in which platelets presenting lipopolysaccharide (LPS) to adherent white cells within the lungs induce life-threatening respiratory distress. This problem is a focus of ongoing research to define the pathophysiology of innate immune response to platelets, to avoid immunologic complications of transfusion in the future.

The final presentation given by Andrea Velardi, MD, University of Perugia, Italy, titled “Impact of Natural Killer Cell Alloreactivity on Allogeneic Hematopoietic Transplantation,” emphasized how donor NK cells affect the outcomes of transplantation. If bone marrow donors are NK reactive – that is, possess an inhibitory killer cell immunoglobulin-like receptor (KIR) not present in the recipient – the outcome of transplantation is greatly improved. There is a significantly lower rate of relapse and higher event-free survival than among donors without this response. In mouse models, this protective effect of NK-alloreactive cells has been shown to occur through NK-cell elimination of 1) leukemic cells, 2) T cells rejecting the graft, and 3) recipient-dendritic cells that cause graft-versus-host disease.