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Transfusion support in patients with hematologic disease: Transfusions in special clinical circumstances

In the first of this 2-part review series, we presented advances in the field of transfusion medicine highlighting some of the new and novel transfusion modalities. These techniques have helped improve product quality and have thus impacted clinical outcomes in patients with hematologic diseases. Red cell genotyping, platelet product manipulations, and pathogen reduction initiatives have enhanced transfusion safety. Improvements in apheresis collections for cell and gene therapies have facilitated better understanding of product quality and potency. Less studied transfusible agents including granulocytes and Hemoglobin Based Oxygen Carriers were also reviewed.[1]

In the current (second) issue, we review evolving therapeutic indications for transfusion support in patients with hematologic conditions.

Sickle cell disease represents a common indication for transfusion support with an estimated global birth prevalence of 112 per 100,000 live births.[2] More than 60% of individuals with sickle cell disease receive at least 1 blood transfusion in their lifetime. The earliest studies confirming the clinical benefit of transfusion support in this hematologic disease were performed in the mid-1970s.[3] However, transfusion therapy is not without risk and indications for its judicious use are continuously evolving. Further, an increasing number of sickle cell disease patients are candidates for curative therapies such as stem cell transplantation and gene therapy.[4] It is necessary to consider the role of transfusion support and its potential effects in the context of these newer therapies. Sharma and colleagues review current evidence for transfusion approaches, indications, and challenges encountered with acute as well as chronic transfusions in this vulnerable disease population.

Patients with benign as well as malignant hematologic conditions undergo hematopoietic stem cell transplantation (HSCT). Since 1957, approximately 1.5 million transplants have been performed worldwide.[5] Recipients of HSCT develop cytopenias in the peri-transplant period requiring transfusion support. Using clinical vignettes, Brian Adkins, Garrett Booth, and Sumithira Vasu present standard indications for red cell and platelet transfusions in patients undergoing HSCT. In their review, they address issues unique to this vulnerable group including passenger lymphocyte syndrome, pure red cell aplasia, HLA allo-immunization, and platelet transfusion refractoriness.

Among individuals undergoing HSCT, pediatric patients are at particular risk for hemorrhage and its sequelae. There is also a dearth of prospective studies in pediatric transfusion medicine. In addition to HSCT, in 2016, 5 other areas were identified for prioritization in pediatric transfusion medicine by an NHLBI/DHHS/FDA-sponsored scientific meeting.[6] Meghan McCormick and Meghan Delaney summarize indications for blood product transfusion, thresholds for transfusion, and indications for blood product modifications in pediatric patients providing an updated evidence-base.

Transfusion of blood components other than red blood cells and platelets, that is, plasma and its derivatives (cryoprecipitate, immunoglobulins, clotting factor concentrates) have specific indications in hematologic disorders. Prajeeda Nair and team address the use of these agents in conditions such as DIC, liver disease, trauma, and immune deficiency states. With the successful use of newer agents such as caplacizumab, an anti–von Willebrand factor immunoglobulin fragment in lieu of plasma in the management of TTP, the team anticipates an increase in the development of recombinant products or engineered proteins.[7] Consequently, they predict an eventual replacement of plasma concentrates by these more specific alternatives.

In contrast, in his review evaluating the current indications for therapeutic plasma exchange in this issue, Zbigniew Szczepiorkowski speculates that newer age therapeutics including caplacizumab may not be widely used in the near future owing to high costs and limited safety and efficacy data thus far. In his review, he also provides ASFA guideline-based systematic evidence for therapeutic plasma exchange, erythrocytapheresis, leukapheresis as well as extracorporeal photopheresis in hematologic disorders.

CAR T-cells have demonstrated great potential in recent times for the treatment of hematologic malignancies. Clinical indications for their use are advancing rapidly and have been reviewed in detail by several groups.[8-11] The manufacturing aspects of these “living drugs” are complex and transfusion medicine specialists have applied apheresis and other blood banking principles for the safe and effective development of these novel immunotherapies for clinical use. Opal Reddy, David Stroncek and Sandhya Panch discuss current methodologies to improve these therapies by optimizing their critical quality attributes.

Opal Reddy, Bipin Savani, David Stroncek, and Sandhya Panch also address a broader question—the impact of cell and gene therapies on transfusion medicine. Specifically they outline the various treatment modalities available, and assess the impact of these curative therapies on blood product utilization. They also present data on harnessing novel technologies including gene editing and induced pluripotent stem cells for blood product synthesis and testing. Finally, they highlight the potential for blood collection centers to serve as ancillary facilities in cell and gene therapy manufacturing.

Transfusion support remains a critical part of the therapeutic armamentarium for hematologic diseases. Blood and its components are used to treat a variety of disorders such as

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sickle cell disease, chemotherapy/radiation/HSCT-induced cytopenias, hemophilia, DIC, and other coagulation abnormalities. Guidelines for their judicious use are constantly evolving. Apheresis procedures also continue to offer critical therapeutic support in conditions such as TTP despite the development of newer recombinant proteins and engineered products. Further, along with the science, the role of transfusion medicine specialists in hematology is also evolving. While gene therapies to treat hemophilia and other conditions may demonstrate some decrease in blood product utilization, blood banking principles are now being applied to the safe, consistent, and effective manufacture of newer cell and gene therapies such as CAR T-cells to treat hematologic disease. The future holds promise for further synergistic approaches to optimize patient care.

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