Carter BloodCare
SPECIALTY SERVICES

Blood Matters

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News for Blood Bank Medical Directors, Physicians and the Lab

Blood Matters is a quarterly news *outlet with important medical information for you, our customers and colleagues, from Carter BloodCare. We hope you will share it with others interested in the work we do together.*

IN THIS ISSUE

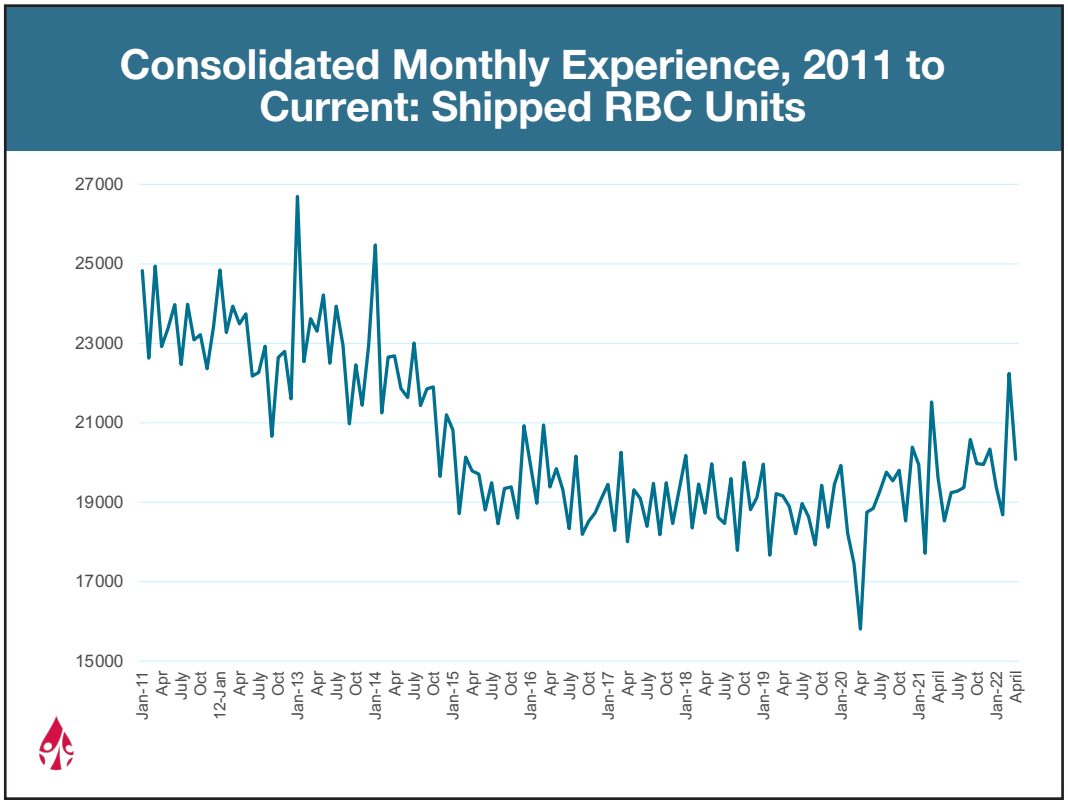
HOT TOPICS

Trends in Red Blood Cell Distribution

Merlyn Sayers, MBBCh, PhD

Most blood programs keep daily records of distributions of blood and components to hospitals to help planning recruitment and blood drives. Changes in demands, over time, are often revealing, as is shown in the accompanying graph. The time covered is from January 2011 to April 2022 and monthly shipments of red cell units are plotted for this period time. No major changes in the number or size of client hospitals occurred during this period of time.

The effect of patient blood management and the recognition by physicians that a lower threshold for transfusion could be invoked for certain categories of patients, can be seen in the declining distributions of red blood cells in the four-year period between January 2011 and January 2015. For the next five years, relative stability in the numbers of red cell shipments suggested that there was no further reduction in red cell demand imposed by patient blood management and what benefits were to be achieved by more conservative transfusion practices had been realized.



The onset of the COVID-19 pandemic in the first quarter of 2020 can be seen in the profound decrease in shipments during that period. What has happened subsequently, over the next two years, has been a gradual increase in red cell demand for transfusion dependent patients with distributions to hospitals, on many occasions, exceeding the demands that had all but plateaued out once the patient blood management conservatism had been realized. There are a number of reasons why red cell demand should be increasing, including transfusion support for an aging population undergoing treatment for malignancy and an increasing number of hospitals providing massive transfusion protocols. Supportive evidence for increasing demands from oncology patients comes from Carter BloodCare's experience with hospital requirements for apheresis platelet inventories, which showed a steady increase in requirement despite any patient blood management efforts made.

The Use of Cold Stored Platelets for Surgical Patients

Frances Compton, MD

We have seen great success since the implementation of cold stored platelets (CSPs) on January 17, 2022. This new blood component has been a valuable product for bleeding patients; allowed for a longer shelf-life of a limited resource and provided inventory relief during the local winter storms.

While many hospitals have benefitted by being able to keep a CSP on their refrigerator shelf without needing to utilize a platelet rotator, other larger trauma hospitals have been able to provide this pre-activated product, which is primed for hemostasis, to their bleeding patients. Our CSP FDA variance is approved for use in "actively bleeding patients," allowing many of these products to be ultimately transfused in a massive transfusion protocol (MTP) shipment or out of a trauma ED refrigerator. This is certainly a useful and productive way to take advantage of the benefits of this product, as preliminary studies suggest that CSP products are superior at bleeding control.[1]

A local, non-trauma hospital has also been able to utilize the advantages of this product in the operating room (OR). This surgical hospital has transfused 46 CSPs to cardiovascular surgical patients. The use of CSPs in surgical patients is of great interest in the medical community. In fact, there is an ongoing clinical trial called CHIPS (CHIlled Platelet Study), funded in part by the US Department of Defense, which plans to evaluate the non-inferiority/superiority of CSP transfusion at multiple storage durations (up to 21 days) in complex cardiac surgery cases.[2] Two of the key outcomes being investigated are perioperative bleeding score and chest tube output. The study, still in the recruitment phase, is a phase 3 randomized partially blind study which will include 1,000 study participants.

Is your hospital interested in transfusing CSPs in the OR? The clinical and logistical benefits of CSPs are likely equally beneficial for both trauma and OR situations (as well as other bleeding scenarios). Furthermore, the local surgical hospital that has successfully implemented the use of these products has not wasted a single CSP product due to improper OR cooler packing to date. CSPs are, in fact, easier and simpler to handle for OR staff as they can be packed with RBCs and thawed plasma in a chilled cooler. To ensure your hospital has access to this life-saving product, contact hospitalrelations@carterbloodcare.org.

References:

1. Reddoch-Cardenas KM, Bynum JA, Meledeo MA et al. Cold-stored platelets: A product with function optimized for hemorrhage control. *Transfusion and Apheresis Science.* 2019; 58: 16-22.

2. ClinicalTrials.gov; CHIlled Platelet Study "CHIPS" (CHIPS) https://www.clinicaltrials.gov/ct2/show/NCT04834414

MEDICAL MINDS

What topics would you like to see in a future issue of Blood Matters?

Click **here** to submit your choice.

PHYSICIAN RESOURCES

Review Updates

- December 2021 Circular of Information (COI) - Updated
- Blood Bulletin Vol. 22, No. 2: Obstetric Hemorrhage — Are You Prepared?

HOT TOPICS Continued

Updates in the Treatment of Acquire Thrombotic Thrombocytopenic Purpura

Nicole De Simone, MD, MPH

Thrombotic thrombocytopenic purpura (TTP) is a life-threatening disease in which disseminated microthrombi lead to ischemic organ injury/failure and potentially to death. Platelet-rich microthrombi form due to a lack of ADAMTS-13, an enzyme responsible for cleaving ultra-large von Willebrand (UL-VWF) multimers into smaller multimers. These UL-VWF multimers that persist are inherently stickier and avidly bind platelets, which leads to the thrombocytopenia seen in TTP. In addition, these platelet-rich microthrombi cause shearing of circulating RBCs, which leads to a microangiopathic hemolytic anemia. Other entities, such as atypical hemolytic uremic syndrome or disseminated intravascular coagulation, have very similar clinical presentations. Thus, an ADAMTS-13 activity <10% is used to confirm a diagnosis of TTP. The distinction between TTP and the other thrombotic microangiopathies is essential since more tailored therapies, such as eculizumab and caplacizumab, have become available.

Plasma exchange (PLEX) acts to replace ADAMTS-13 and remove autoantibodies, and along with corticosteroids, has been the mainstay in the treatment of acquired TTP (aTTP). More recently, use of other immunosuppressants to eradicate autoantibodies, such as rituximab, have led to improvement in the clinical course of patients with aTTP. In February 2019, the FDA approved caplacizumab-yhdp (CABLIVI, Sanofi) for treatment of adults with acquired TTP, in combination with PLEX and immunosuppressive therapy.

Caplacizumab is a nanobody that binds the A1 domain of von Willebrand factor (vWF) and blocks the binding of platelets via GPIb to this domain, which ultimately leads to a reduction in microvascular thrombosis. HERCULES, a phase 3 double-blind randomized controlled trial, demonstrated significantly shorter time to platelet count normalization and decrease in duration of PLEX and hospital stay compared to placebo. The trials and package insert doses on the first day of plasma exchange and once daily for 30 days following the last plasma exchange. The most common adverse event was bleeding, with the majority of cases being mild-moderate mucocutaneous bleeding. Bleeding was seen in both treatment and placebo groups, 65% and 48%, respectively.

HOT TOPICS Continued

Real-world use of caplacizumab has confirmed similar efficacy findings but increased rates of bleeding, and in particular, cases of severe bleeds, such as intracranial hemorrhage, have been reported.[1] Questions regarding caplacizumab's cost-effectiveness have also been debated. A single dose is $7,700; an average course of therapy would be ~$275,000. A study using ADAMTS-13 monitoring to guide duration of caplacizumab use found that 58.3% of patients did not require treatment for the full 30 days, which resulted in a cost savings of $3.4 million.[2] In addition, the United Kingdom TTP forum has recommended discontinuation of caplacizumab with an ADAMTS-13 activity >30%, which could limit drug exposure and additional drug costs.

Additional studies are ongoing that will hopefully lead to better information as to how to best treat patients with aTTP.

References:

1. Dutt T. Shaw R. Scully M. et al. *Real-World Experience with Caplacizumab in the Management of Acute TTP. Blood* (2021) 137(13):1731-1740.

2. Dutt T. Shaw R. Scully M. et al. *Real-World Experience with Caplacizumab in the Management of Acute TTP. Blood* (2021) 137(13):1731-1740.