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.*

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HOT TOPICS

Is your hospital blood utilization data being properly utilized?

William Crews, MD

Both AABB and CAP have standards that require monitoring of transfusion practice for all blood components. These standards state what to monitor, but do not specify how to monitor, and they do not provide benchmarking data to guide improvements, so knowing how your hospital compares to other hospitals regionally or nationally is difficult to determine. [1, 2]

With little ability for external benchmarking, hospitals can perform internal benchmarking against themselves. This involves reviewing current data to determine baseline transfusion practice. Current institutional policies should also be reviewed to determine whether they reflect the latest research and recommendations, including transfusion recommendations from specialty societies. [2] After completing the evaluation, the transfusion committee can recommend proposed changes, supported by results of the review and the data collected. While this does not provide external references, or the ability to learn from hospitals with more experience, it does provide an opportunity to create process improvement.

Once the current practice baseline has been determined, and goals have been established, it is important to generate awareness of any new guidelines by providing educational opportunities for staff and providers on appropriate use of resources, and encouraging the adoption and use of current capabilities of IT systems, such as clinical decision support and other communication resources.

In addition to internal benchmarking, choosing the right metrics to track, analyze, and report are all critical to achieving improvement. Metrics are quantifiable measures that track and assess progress toward improvements in patient care. Two important metrics are operational metrics and financial metrics. Operational metrics include performance of functions, such as number of products issued, number of transfusion reactions, or other similar measures. Financial metrics should always be considered in the goals of blood utilization.

Effective metrics must be specific, measurable, achievable, relevant, and time-specific. An example of this may be a goal to increase 1-unit transfusions to 75% over the next year. The data collected should be decided with input from the transfusion committee, and the different service lines with significant use of blood products, when possible.

Data collection is used to report the level of achievement. The data should be shared with service lines and hospital administration

Reports generated from the transfusion service should be cross-checked with data from other databases within the hospital, such as HIS, OR, outpatient, finance, etc. for a complete, more accurate picture. Reports should be communicated and distributed in a clear manner that allows providers to compare their individual results with their peers in addition to institutional goals.

Another key step is to monitor the progress toward compliance with policies that were initiated. Progress is measured by recording the same data points collected during the initial evaluation. Periodic and regular data collection will compare current practice to the standards to be achieved and track the changes achieved over time.

Benchmarking blood utilization is a valuable tool for process improvement in healthcare and should be used as part of a larger quality improvement tool to learn from others, identify performance gaps, implement best practices, improve patient care and reduce costs.

References:

1. Fredrich N, Gammon R, Richards CA, Tauer R. PBM Metrics. Bethesda, MD: AABB Press, 2019.
2. Combes JR, Arespacochaga E. Appropriate use of medical resources. American Hospital Association's Physician Leadership Forum, Chicago, IL, November 2013. Chicago, IL: AHA, 2013

COVID-19 Convalescent Plasma High Titer Only, what does that mean for my patients?

Geeta Paranjape, MD

On August 23, 2020, the Food and Drug Administration (FDA) granted Emergency Use Authorization (EUA) to use convalescent plasma as part of the treatment option for patients admitted to the hospital with COVID-19 infection.[1] Prior to the EUA, COVID-19 Convalescent Plasma (CCP) was being used as an Investigational New Drug (IND) and in Mayo Clinic's Expanded Access Program (EAP). These studies proved the safety of using CCP in COVID-19 patients. Clinical studies investigating use of CCP in different patient populations are ongoing and encouraged by the FDA; their use of CCP is governed by what the study protocol states.

Neutralizing antibody titers are labor-intensive and can be performed only in certain laboratories. In the August 23rd EUA authorization letter, the FDA specified that the EUA CCP units must be tested for titer by a specific test (Ortho SARS CoV 2 IgG assay), with the option left open to add more tests if manufacturers submitted relevant data to FDA. If the CCP units' titer results meet a certain threshold, they are to be labeled as "High titer," and, if below that, are to be labeled "Low titer." [1]

The FDA has been studying data presented by different test manufacturers and updated the EUA letter on March 9, 2021, to include a list of 11 SARS CoV 2 antibody tests that can be used to titer CCP by testing laboratories. The FDA lowered the titer requirement for Ortho SARS CoV 2 IgG assay (currently in use by Carter BloodCare to titer CCP) from signal to cutoff (S/C) ratio of 12.5 to 9.5 based on additional data analysis.

In the updated EUA letter, the FDA clearly stated that ONLY units labeled as high titer can be utilized for patient treatment. They did not put a time limit on the use of high titer CCP, but provided a general guideline that CCP should be utilized "early" in the course of illness (before any ventilator support is needed). Any patient infected with SARS CoV 2 and unable to mount humoral immune response is also eligible for CCP use at any time.

Along with the updated EUA letter, the guidance document was updated. The update occurred on January 12, 2021, and provided clarity regarding donors who had received the COVID-19 vaccine. Another update took place on February 11, 2021, to include the terms of the updated EUA, as well as the FDA's position about monoclonal antibody treatment in CCP donors.

For CCP donors who are vaccine recipients, the donor must have received the vaccine AFTER the illness. Illness must be proven by a diagnostic test result and the individual can only donate up to six months after recovery. Carter BloodCare currently does not verify diagnostic testing with CCP donors since we perform a screening with a different type of antibody test (this test is positive only if you get exposed to the virus and not positive if you only got the vaccine) and follow it up with the titer test if positive. We have chosen to defer CCP donors if they have been vaccinated and ask them to become a regular allogeneic donor.

For CCP donors who were treated by monoclonal antibody, the FDA has recommended that these donors wait for 90 days post receipt of treatment before they donate CCP.

To further complicate matters, the FDA has stated that blood collectors have until May 31, 2021, to perform titer testing, so some blood centers will still be collecting and labeling units as the Investigational New Drug (IND). The FDA is allowing the use of non-titered CCP for patient care acknowledging that at least half of the units may not be high titer.

Carter BloodCare is currently only collecting CCP from donors who have tested as "high titer" and releasing units for patient care that are high titer. Unfortunately, if we are not able to collect the units we need locally, we may end up importing and distributing CCP units that are labeled as "IND" and, therefore, without a titer test.

Carter BloodCare's data for the two weeks prior to the High Titer CCP requirement shows hospital shipments of 160 CCP units per day on average, while after the requirement went into effect (and the type of patients who could receive it was specified), the daily average shipment is about 60 CCP units.

Reference:

Food and Drug Administration. Investigational COVID-19 Convalescent Plasma: Guidance for Industry. Issued Feb. 11 ,2021.

Resource:

Convalescent Plasma EUA Letter of Authorization March 9, 2021

Platelet Refractoriness: Case Presentation
Frances Compton, MD

A patient has received 4 prophylactic platelet transfusions in the past 24 hours for a platelet count of <10,000/µl each time. Of note, each of the post-transfusion platelet counts were obtained within 1 hour of the previous platelet transfusion. The clinical team astutely asked for human leukocyte antigen (HLA) matched platelets as this appears to be a case of immune-mediated platelet refractoriness. This patient's HLA type is already known as she is in the hospital for a stem cell transplant.

The clinical team is correct in being concerned that this patient has been requiring frequent prophylactic platelet transfusions without an increase in the post-transfusion platelet count. A patient is generally considered to be platelet refractory if they have two 1-hour post-transfusion corrected count increments (CCIs) which are <7,500.[1,2] While nonimmune causes of platelet refractoriness (fever, DIC, splenomegaly, medications) are much more common than immune-mediated platelet refractoriness,[1] immune-mediated platelet refractoriness can sometimes be distinguished by low CCI within 1 hour after transfusion (vs. 24-hour poor increments).[2]

$$\text{CCI} = \text{Post transfusion increment} \times \text{Body surface area } (m^2) \div \text{Number of platelets transfused } (10^{11})$$

Platelet HLA matching is graded based on how closely the donor HLA type matches the recipient HLA type. Antibodies to Class I HLA-A and –B antigens are responsible for most immune-mediated platelet refractoriness, therefore matching is performed for these two HLA loci. When grading HLA matched platelets, an A match is the best match, as it is an identical HLA match (all 4 A and B antigens are the same).[3] B1U and B1X are also good matches, as they both have 3 identical antigen matches with only 1 imperfect match which is either unknown or in the same cross-reactive group, respectively. [3] C and D grade matches have 1 and 2 mismatched antigens, respectively.[3]

Based on the two 1-hour CCI < 7,500, an HLA matched platelet (B1X grade) is obtained and transfused. Unfortunately, the patient has a CCI of 2,000 after receiving the B1X grade HLA matched platelet. The clinical team is curious why this patient still did not have an appropriate platelet increment after transfusion.

While anti-HLA-A and –B antibodies are most frequently the cause of immune-mediated platelet refractoriness, they are not the only cause.[1,2] Immune-mediated platelet refractoriness can also be caused by anti-ABO antibodies and anti-human platelet antigen (HPA) antibodies.[1,2] It is important to distinguish between the different types of antibodies which may cause platelet refractoriness. Carter BloodCare can perform a platelet antibody screen which can identify the presence of both anti-HLA and anti-HPA antibodies. Therefore, if an HLA matched platelet does not give the expected post-transfusion platelet increment, it is important to confirm the presence of the correct type of platelet antibody, if any. Remember, there is always a chance that the patient is refractory due to other, nonimmune, causes as well.

Further investigation showed that the HLA matched platelet was ABO identical to the patient, and she was found to have no anti-HPA antibodies on the platelet antibody screen. However, the platelet antibody screen was positive for anti-HLA antibodies. HLA antibody identification test was ordered and revealed 90% panel-reactive antibodies (PRA), which included antibodies against antigens in her cross-reactive group which happened to be present in the HLA B1X grade unit that had been issued for transfusion. Knowing this, the next HLA matched platelet unit for this patient was selected to ensure it was antigen negative for the HLA antibody specificities identified in the patient. Subsequent platelet transfusion resulted in a CCI of well over 10,000.

HOT TOPICS Continued

It is important to understand all potential causes of platelet refractoriness, both immune and nonimmune, as this can significantly affect clinical outcomes and healthcare costs.[2] Early identification of platelet refractoriness can improve patient care and preserve limited platelet resources.

References:

1. Juskewitch, Norgan and De Goey et al. How do I . . . manage the platelet transfusion–refractory patient? Transfusion 2017; 57: 2828–2835.
2. Stanworth, Navarrete, Estcourt et al. Platelet refractoriness--practical approaches and ongoing dilemmas in patient management. Br J Haematol. 2015; 171 (3): 297-305.
3. AABB Technical Manual, 19th ed. 2017. Edited by Fung M, Eder AF, Spitalnik SL and Westhoff CM.

MEDICAL MINDS

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

Click **here** to submit your choice.

PHYSICIAN RESOURCES

Download updates

- Blood Bulletin Vol. 20, No. 4: The Case for Transfusion of Low Yield Platelets
- Investigational COVID-19 Convalescent Plasma Guidance for Industry