HOW DO I MAINTAIN AN ADEQUATE INVENTORY AND AVOID WASTAGE DURING NORMAL TIMES AND IN A PANDEMIC?

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The COVID-19 pandemic has tested the resilience of the United States blood supply. The blood community experienced major fluctuations in blood donations following closure of community donation venues and postponement of elective admissions at hospitals. Shortages of supplies, reagents and personal protective equipment further impacted blood centers at a time when they were also being called on to initiate collection of an unproven, novel therapy: COVID-19 convalescent plasma. These problems were unparalleled, but not unforeseen; most hospitals and blood centers had decades-old pandemic plans, originally designed for influenza.[1] In this light, the COVID-19 pandemic offers an opportunity to consolidate lessons learned and plan for future disasters.

The US blood supply is dependent on a complex supply chain that converges on blood centers as the ultimate providers of blood components.[2] Donor recruitment, phlebotomy, testing, manufacturing and distribution must operate synchronously to ensure that the right blood is available for the right patient at the right time. Disruptions impact all stages of the process. Most disruptions are local and some predictable, including inclement weather, holidays, fires, floods and earthquakes.

Throughout the COVID-19 pandemic, agencies such as the AABB Interorganizational Task Force on Domestic Disasters and Acts of Terrorism (which was originally founded following the September 11, 2001 terrorist attacks) marshalled a coordinated local and federal response. Ultimately, while the details of pandemic influenza plans of a decade ago were not as well suited to the epidemiology of COVID-19, the planning was indispensable.[3]

Fortunately, large scale disruptions of the blood supply in the US have been rare. However, events such as the September 11 terrorist attacks, Hurricane Katrina, West Nile virus, severe acute respiratory syndrome, the 2009 H1N1 pandemic, and the Ebola and Zika epidemics served as a prologue to the ongoing COVID-19 pandemic.

Assuming the next pandemic is different, unpredictable in timing and scope, we seek lessons learned from the current pandemic to inform preparations for the next. What if it has the fatality rate of MERS-CoV (~36%) or SARS-CoV-1 (10%)[4], predominantly impacts young people, or is transfusion-transmitted? Redesigned operations, communications and messaging, regulatory imperatives, data availability, blood center infrastructure and supply chain redundancy are anticipated.

DEFINITIONS OF SHORTAGES

Shortage in the blood supply causes a reduction in inventory so that an adequate number of components are not available.[5] Any duration of a long-term shortage is projected to have an interval of greater than two weeks.[5]

Shortages can be mild, moderate or severe.[5] In a mild shortage, the blood supplier's inventory is 25% lower than expected and the hospital's blood supply may be impacted by this degree.[5] In a moderate shortage, the blood supplier's inventory is 50% lower than expected and the hospital's blood supply may be impacted by this degree.[5] In a severe shortage, the blood supplier's inventory is 75% lower than expected and the hospital's blood supply may be impacted by this degree.[5] Finally, shortages can be limited to certain types of blood products or widespread, involving multiple components.[5]

MAINTAINING INVENTORY

Every hospital should develop a phased plan that responds to the degree of shortage (Table 1). Therefore, understanding the degree of shortage is critical to success.[5] One can compare the current inventory level to the previous week's rolling utilization to get a sense of whether the inventory is appropriate to meet the expected level of need.[5] Once a shortage is recognized, communication between the blood center and the hospital transfusion service, as well as with physicians in the hospital, is essential.[5]

Blood collection centers may be able to provide a daily dashboard showing blood inventory levels and larger suppliers with centers across the US can send a daily email showing the local and national inventory levels.[5]

Other methods to reduce bleeding or manage anemia should be implemented in hospitals.[5] These include, but are not limited to, use of intraoperative cell salvage in surgical cases with blood loss anticipated at greater than 500 mL, use of antifibrinolytic medications to enhance clot stability, use of acute normovolemic hemodilution (ANH) when appropriate, and identifying and treating iron deficiency anemia in patients with severe anemia due to iron deficiency.[5] Patient blood management (PBM) guidelines, and the most recent evidence for transfusion thresholds, should be reviewed and implemented. RBC orders should be limited to one unit for non-hemorrhaging patients.[6] Orders for more than one unit should either be prospectively reviewed or filled with one unit along with an alert to the clinical team that a second unit is available if needed.[5] Hospitals should cancel all routine blood draws and, when possible, use "pedi-tubes" to reduce the volume of necessary blood draws.[5]

Outpatient blood needs may be different and changes to them should be approached with caution.[5] Outpatients are often "topped-off" or "tanked-up" with an extra unit of RBC or platelets to lengthen the interval between visits.[5] Since health care facilities may have been associated with high risk for COVID-19 transmission during the pandemic, it may be better in some cases to continue larger, less frequent transfusions.[5] Anemia management by micronutrient replenishment can help reduce blood transfusions in patients with iron deficiency anemia.[5]

TABLE 1

Different phases of blood shortages require different levels of response. Suggested responses are shown below.

ACTIONS TO REDUCE BLOOD USE	SHORTAGE SEVERITY		
	Mild	Moderate	Severe
Preventing transfusion	Review and update guidelines; Use pharmacologic options to enhance coagulation; Correct iron-deficiency, B12, or folate	Cancel elective surgeries; Prospective audits for blood orders	Cancel non-essential high blood use surgeries; Place an upper-limit on blood use for procedures and MTPS
Expanding Inventory	Identify and correct limiting factors for collections in hospital-based donor centers	Split RBC and platelet units; Extend platelet shelf-life from 5 to 7 d; Apply for a variance for deferral limits; train additional staff	Consider emergent release of platelets from pedigreed donors
Preventing waste	Minimize temperature-related waste; minimize outdating by shifting inventory before expiration	Return to RBCs to inventory if slightly above 10°C; return platelets to inventory if placed on ice; Consider finishing transfusion of unit implicated in mild reactions	Continue measures for moderate shortage; Consider loosening restrictions further
General medical transfusions	For non-bleeding patients, restrict orders to one unit and apply evidence-based guidelines: high 7.0 g/dL for RBC transfusion threshold; Pit count 10 000/μL for prophylactic platelet transfusion	Continue with measures for mild shortage	Consider restricting prophylactic platelet transfusions; Reevaluate thresholds for ECMO; Consider lowering RBC and platelet transfusion thresholds
Surgical transfusions	Encourage ANH and cell salvage; Give IV iron for anemic patients scheduled for surgery; Encourage pharmacologic options to enhance coagulation	Continue measures for mild shortage	Continue measures for mild shortage; Place an upper-limit on blood use for procedures; communicate with surgeons before high-blood-use surgeries such as liver transplant
RBC exchanges and TPE	Reevaluate maintenance exchanges for SCD: Consider simple transfusions, reevaluate target HbS% for each patient. Use 1:1 ratio plasma/albumin for TPE when plasma is indicated	Consider transitioning some SCD patients to simple transfusions or partial exchanges. Adjust procedural parameters for higher FCR	Continue with measures for moderate shortage, allowing even higher FCR
Massive transfusions	Communicate shortage information to MTP teams early	Consider limiting number of units based on hospital inventory	Determine and enforce MTP limit

Adapted from: Cohn CS, Pagano MB, Allen ES, et al. How do I manage long-term blood component shortages in a hospital transfusion service? *Transfusion*. 2020;60:1897–1904.

If the shortage falls into the moderate category, additional options should be considered.[5] For example, the platelet inventory can be stretched by using point-of-release testing to extend a unit's shelf life from five to seven days.[5] Facilities can also consider simply extending the outdate by 12 hours to avoid wastage.[5] When a measure like this is taken in an emergency, it must be approved by the blood bank medical director (MD) and clearly documented.[5] If the MD chooses to apply this outdate extension more broadly then a Food and Drug Administration variance should be sought.[5] At this stage, consideration of postponement of all elective surgeries that involve blood use should be considered with continued implementation of ANH and/or intraoperative cell salvage during surgery.[5]

When the shortage becomes severe, some institutions may consider lowering the threshold for RBC transfusions from 7.0 to 6.5 g/dL or lower in stable, asymptomatic patients.[5] This is outside of evidence-based practice and should be done only in consultation with other specialties (e.g., hematology, cardiology) on a patient-by-patient basis.[5] Similarly, platelet transfusion thresholds may need to be lowered below 10,000/ μL in non-bleeding patients, a practice that is already recommended in certain populations,[7] although in other groups it may increase the risk for a spontaneous hemorrhage.[5]

Massive transfusion protocols (MTPs) in this phase of a shortage are a difficult but critical area to address.[5] When a single patient uses a disproportionate amount of a dwindling resource, consideration must be given for the good of the larger community.[5] Ideally, hospital leadership should establish an ethics board, which should meet with surgeons, emergency room physicians and intensivists to develop thoughtful and realistic guidelines that can help with blood conservation efforts.[5] Plans that limit MTPs and other high blood use procedures are necessary.[5] Consideration of laboratory markers that could be used as futility indicators in massively transfused patients should be considered.[8] A recent study suggested that peak lactate ≥10.0 mmol/L, nadir pH <7.00, and age ≥65 years were significantly associated with higher rates of in-hospital mortality among massively transfused patients.[8] The study authors suggested that incorporating these clinical parameters into a futility index for massive transfusions will be useful in situations where blood products are scarce and/or mortality may be unavoidable.[8]

USE OF DATA SCIENCE TO OPTIMIZE INVENTORY

When COVID-19 became a pandemic, BC and hospitals implemented business continuity plans (BCP).[9] The pandemic resulted in decreased blood demand.[9] Blood centers had the challenge of having adequate collections and inventory to meet hospital's orders during changing demands.[9] The blood center used its data science methodologies to develop a demand model (DM) that consisted of a time series-forecasting algorithm to predict future values on previously observed data.[9]

To adjust for impact of COVID-19, the model was optimized by a change point detection informed manual step function to reflect future decreases and increases in demand relative to the new environment.[9] Once the supply and demand ratios became imbalanced, collection goals were adjusted to bring inventory levels comfortably into equilibrium with the predicted demand.[9] In this particular scenario, the DM allowed collections at one blood center to be adjusted to bring inventory

levels into equilibrium with predicted demand reducing inventory by 11,244 units in 21 days and helped to ensure adequate supply when elective surgeries resumed.[9] DM at this blood center minimized RBC wastage to an average of 0.48% during 2020.[9] The authors concluded that the blood center nimbly adapted to rapidly changing donor conditions and transfusions though BCP and use of DM to ensure collections met orders while minimizing wastage.[9]

REDUCING WASTAGE

Finally, preventing blood wastage can conserve the blood supply without directly impacting a patient's care.[5] For RBCs and plasma, optimal usage of coolers, mobile refrigerators, and remote refrigerators can keep products within appropriate temperature ranges.[5] Following the precept of issuing one unit of RBCs at a time to nonbleeding patients minimizes the number of units that are returned out of temperature range.[5] For platelets and RBCs, shifting inventory that is near expiration from low volume to high-volume transfusion centers, when possible, where it is most likely to be used, increases efficiency.[5] This might be done within a hospital system or between hospital systems as facilitated by a blood supplier.[5] Liquid plasma may also be considered for MTP especially in non-trauma hospitals since it has a much longer expiration (26 days with CPD anticoagulant) vs. thawed plasma (5 days).

ADDITIONAL STRATEGIES

To reduce unnecessary usage during the COVID-19 pandemic, a provincial infographic in British Columbia, Canada, emphasizing evidence-based restrictive practices for transfusion and guidance regarding consequences and avoidance of iatrogenic anemia was developed and distributed to clinical departments and personnel involved in transfusion.[10] The Emergency Operations Center provided a valuable method to disseminate essential communications to clinical stakeholders.[10] Practices intended to directly limit unnecessary transfusions were developed, including best practice alerts in the electronic order entry systems for RBC transfusion orders and laboratory screening guidelines for prospective review of plasma or platelet orders falling outside of usual ordering practices for stable inpatients.[10]

Another option is to split platelet units. This should only occur during times of extreme platelet shortage, usually well below critical level, and when there is also an acute demand for platelet transfusion. This procedure requires MD approval. While the physicians treating patients may question why they are being offered a split platelet, when it is made clear that this is because of the available blood supply, the product in most cases is accepted. If there is an option of choosing which patients receive a split unit, the aim should be for more stable patients, inpatients (if possible), and patients who are very close to their stated platelet goal (Personal communication- J. Karp – 02/17/2022). An important point is that in the US the minimum apheresis dose of $3x10^{11}$ platelets is higher than in most other nations, so that even if the product is split, the dose may be comparable to those administered in other countries.[11]

CONCLUSION

The COVID-19 pandemic has created a unique scenario for the blood community, and creative – and sometimes unorthodox – solutions may be needed.[5] While the shortage is still mild, the response should include strict application of evidence-based guidelines and PBM to stretch the blood inventory.[5] If the blood shortage becomes severe, however, then efforts must be made to extend the supply so that as many patients as possible receive the transfusions they need.[5] In the context of a critical shortage, the rules and regulations that stress safety above all for donors and patients may contribute to blood wastage.[5] A sensible balance must be struck when considering the safety of transfusing a possibly compromised blood component (e.g., due to mildly elevated storage temperature) versus the risk of anemia or bleeding due to a lack of sufficient blood.[5] As with all difficult medical decisions, sound medical judgment is critical, and documentation is essential.[5] Resourcefulness, ingenuity, and a practical approach can stretch the limited blood supply.[5] Success was found with governmental collaborative efforts that facilitated the development of initiatives focused on minimizing potential COVID-19–related disruptions in transfusion services.[10] It is hoped that the framework developed early in the pandemic will facilitate timely responses to possible disruptions in future waves of infection or pandemics.[10]

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