REGULAR ARTICLE

blood advances

Measures to reduce red cell use in patients with sickle cell disease requiring red cell exchange during a blood shortage

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Key Points

- Availability of pretransfusion HbS% values before red cell exchange facilitates calculation of precise donor unit numbers required.
- Raising the red cell exchange end hematocrit can reduce red cell units required as a short-term measure to conserve blood in a shortage.

The COVID-19 pandemic has created major disruptions in health care delivery, including a severe blood shortage. The inventory of Rh and K antigen–negative red cell units recommended for patients with hemoglobinopathies became alarmingly low and continues to be strained. Because patients with sickle cell disease requiring chronic red cell exchange (RCE) incur a large demand for red cell units, we hypothesized that implementation of 2 measures could reduce blood use. First, obtaining the pretransfusion hemoglobin S (HbS) results by procedure start time would facilitate calculation of exact red cell volume needed to achieve the desired post-RCE HbS. Second, as a short-term conservation method, we identified patients for whom increasing the targeted end procedure hematocrit up to 5 percentage points higher than the pretransfusion level (no higher than 36%) was not medically contraindicated. The goal was to enhance suppression of endogenous erythropoiesis and thereby reduce the red cell unit number needed to maintain the same target HbS%. These 2 measures resulted in an 18% reduction of red cell units transfused to 50 patients undergoing chronic RCE during the first 6 months of the COVID-19 pandemic. Despite reduction of blood use, pretransfusion HbS% target goals were maintained and net iron accumulation was low. Both strategies can help alleviate a shortage of Rh and K antigen–negative red cells, and, more generally, transfusing red cell units based on precise red cell volume required can optimize patient care and judicious use of blood resources.

Introduction

The COVID-19 pandemic has created critical blood shortages in the United States and globally.[1-4] Donations declined severely as the pandemic led to donor avoidance of public spaces and cancellation of community, corporate, and school blood drives. In a press release from the American Red Cross on 17 March, 2020, approximately 2700 of their blood drives had been canceled, losing donations that would normally contribute to more than 80% of their usual blood supply.[5] Initially, cancellation of elective surgeries and lower rates of hospitalization for non–COVID-19 illnesses alleviated some of the demand on blood. Now, as hospitals have proceeded with previously postponed surgery and medical care, demand for blood products has risen toward prepandemic levels, but blood collections have not rebounded to the same degree. Moreover, diversion of resources and donors to the production of COVID-19 convalescent plasma has impacted other blood product inventories.[6,7]

For patients with sickle cell disease (SCD) who require chronic transfusion therapy,[8] the need for Rh (C, E, or Cc, Ee)- and K-matched donor units has remained steady throughout the pandemic. Our center

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cares for a large cohort of patients with SCD who receive chronic red cell exchange (RCE) at 3- to 5-week intervals. Depending on patient size, baseline hematocrit, hemoglobin S% (HbS%) goal, and other patient characteristics, each exchange procedure typically requires 4 to 6 red cell units, but may require up to 10 units.[9,10] Because our program incurs a large demand for red cell units, we sought ways to reduce use in these patients as a response to the national blood shortage.

Starting in March 2020, we implemented 2 measures intended to decrease the number of red cell units required by patients with SCD who are chronically transfused by RCE without compromising their pretransfusion HbS% goals. First, we ensured accurate determination of the number of red cell units needed by obtaining pretransfusion HbS results before the start of the procedure. This was achieved by an enhanced turnaround time by the hematology laboratory (with the addition of a second Hb quantification run daily in the morning) and then using these results for precise calculation of units required to achieve the target fraction of cells remaining (FCR) after the procedure. The FCR reflects the percent of preprocedure cells remaining at the end of the exchange procedure; patients with a lower goal HbS generally require a lower FCR. Second, as a short-term method to conserve red cell units, we identified patients for whom increasing the targeted end hematocrit up to 5 percentage points higher than the pretransfusion level but not higher than 36% was neither medically contraindicated nor led to additional unit requirements. The intent of increasing the post-RCE hematocrit was to enhance suppression of endogenous erythropoiesis and use fewer units to maintain the target HbS%.

Because a major goal of RCE is to minimize transfusion iron overload, our standard protocol for patients with a pretransfusion hematocrit $\geq$ 27% is to program the procedure to leave the patient's post-RCE hematocrit the same as the pre-RCE value. For patients with a low baseline hematocrit, $<$27%, the post-RCE end hematocrit is programmed to 27%. With this practice, most patients have no net iron loading, whereas those patients with a baseline hematocrit $<$ 27% receive modest iron loads that are substantially lower than from simple transfusion. The blood conservation strategy during the COVID-19 pandemic was to raise the patient's hematocrit up to 5% higher but no higher than 36%; this was primarily considered for patients who consistently had a ferritin $<$ 1000 ng/mL. In consultation with each patient's primary hematologist, it was agreed that patients who were not heavily iron overloaded, had no neurologic events in the past year, and demonstrated maintenance of their goal HbS% could tolerate an increase in their postprocedure hematocrit. The STOP 1 trial, which compared transfusion with no transfusion in patients with SCD at high risk of stroke, provided the rationale for an upper limit of the hematocrit after transfusion of 36%.[11]

Here, we show these 2 blood conservation measures resulted in an 18% reduction of red cell units transfused to a cohort of 50 patients undergoing chronic RCE during the first 6 months of the COVID-19 pandemic. Despite reduction of blood use, the goal pretransfusion HbS% was maintained, and net iron accumulation was less than typically associated with 1 straight transfusion. The strategies are also applicable during blood shortages for reasons other than a pandemic. Notably, availability of the pretransfusion HbS levels before the start time of the procedure facilitated precise calculation of red cell units required per procedure, optimizing both patient care and use of blood resources.

Methods

The study was conducted in accordance with the Declaration of Helsinki. Under an institutional review board–approved protocol, we retrospectively and prospectively reviewed the transfusion history of all patients with SCD on a chronic RCE transfusion regimen at the Children's Hospital of Philadelphia. Inclusion criteria were patients with SCD on a regular schedule for chronic RCE and initiation of chronic RCE before November 2019. We excluded 3 patients who were not regularly transfused because of multiple missed appointments. We also excluded procedures that exceeded a 60-day transfusion interval because the unit number required would be adjusted for the higher HbS level and would not reflect a steady state blood requirement for that individual (n = 4 pre–COVID-19, n = 3 during COVID-19). All procedures and red cell volume calculations were performed on the Spectra Optia Apheresis System. The product hematocrits used for programming the Optia were 56% for AS-1, 55% for AS-3, and 71% for washed units based on institutional quality control measurements performed annually.

Clinical methods

Patient-specific ABO, Rh (D, C, E)- and K-matched red cell units for scheduled RCEs are preordered from our blood supplier 7 to 10 days before the date of need. Because pretransfusion Hb quantification results are not available at that time, preorders are guided by the patient's HbS levels and unit requirements from the prior 3 procedures and by the interval from the last RCE. Within 3 days of transfusion, each patient has a pretransfusion complete blood count, Hb quantification, blood type, and antibody screen. Per institutional policy, all red cell units are leukoreduced, γ-irradiated, and HbS negative.

Before the pandemic, a precise calculation of units required to achieve the target post-RCE HbS% was performed when a patient started the chronic RCE program but was not repeated for every procedure after a patient was established on a routine schedule. We aim for the FCR to result in a post-RCE HbS of 12% to 15% for patients with a goal to maintain a HbS% $<$ 30% and a post-RCE HbS of 20% to 25% for those with a goal HbS% $<$ 50%. The required FCR can be calculated (target post-HbS%/pre-HbS% $\times$ 100), and then the volume of donor red cells is determined. We typically use the Optia software to calculate the FCR with the patient's height, weight, and hematocrit, as well as the total volume and hematocrit of the available donor units. Previously, when the pretransfusion HbS% was not available by the day of RCE, we proceeded with the exchange using the number of units preordered based on values from the 3 prior visits (supplemental Figure 1). When both HbS% and hematocrit results were available, we often still used the same number of units preordered if the HbS% and hematocrit levels were not significantly different from the 3 prior visits, as assessed per provider. If there was a significant difference, RBC requirements would then be reassessed.

During the pandemic, the pre-RCE HbS% and hematocrit became consistently available before the start of the procedure, and we calculated the precise FCR and red cell volume needed to achieve the desired post-RCE HbS% using the Optia software. The clinical history and laboratory values were examined before each RCE, and

the programmed end hematocrit goal was determined at that time. After the procedure, a manual spun hematocrit was measured.

Research methods

To determine the number of units saved, we calculated the average unit use per RCE for each patient based on all their procedures performed in the 6 months before the pandemic. Units saved per procedure equaled the difference between the patient's average number of units per RCE used pre–COVID-19 and the number of units transfused for each RCE during the first 6 months the pandemic. We compared the most recent ferritin value before March 2020 to a level obtained 6 months after interventions were implemented.

Statistical analysis was done using GraphPad Prism version 9.0.0 for Mac (GraphPad Software, San Diego, CA). Paired *t* tests were used to evaluate associations between categorical variables. For patient-specific data, we calculated individual averages, and paired *t* tests were used to compare preintervention and postintervention measures. Welch's *t* test was used for categorical data with unequal variances. Simple linear regression was used to test correlation between continuous variables. $P < .05$ was considered to represent significant differences.

Results

Patient characteristics

Fifty patients with SCD-SS were on a regular, chronic RCE program and met eligibility requirements (Table 1). Patients ranged in age from 9 to 44 years, with a mean age of 23.5 years. The goal pretransfusion HbS is prescribed by the patient's primary hematologist and was <30% for 33 patients, <35% to 45% for 8, and <50% for 9. The most common indications for transfusion therapy were primary (n = 16) and secondary stroke prevention (n = 23), for which the typical goal HbS is <30%. Seven patients with a goal HbS of <50% were transfused for secondary stroke prevention and had their goal raised from <30% after a mean of 6 years of chronic transfusion with no additional neurologic events and review of neuro-imaging. Patients required RCE every 3 to 5 weeks with a red cell unit requirement that ranged from 2 to 10 units.

For 24 patients (47.1%), isovolemic hemodilution (IHD) was routinely performed (Table 1), in which immediately before the RCE, a red cell depletion with concurrent volume replacement with normal saline was performed with the intent of requiring one fewer unit for the RCE.[12,13] IHD was continued during the pandemic for these patients. Among the 26 patients who did not undergo IHD, 8 had a low preprocedure hematocrit (typically <27%), 7 had moyamoya documented by magnetic resonance imaging, 3 had a recurrent stroke, 3 had pulmonary hypertension, 2 had transient ischemic attacks and/or seizures, 1 had severe vasculopathy, 1 had a recent stroke, and 1 had recently started apheresis. Ten patients were prescribed chelation therapy for preexisting iron overload or to maintain iron homeostasis. Patient specific details are provided in supplemental Table 1.

RCE procedures during COVID-19 pandemic

From March 25, 2020 to September 11, 2020 (24 weeks), 318 exchange transfusions were performed. We completed 224, 51, and 43 procedures in patients with a goal HbS <30%, <35% to 45%, and <50%, respectively. In the 24 weeks before March 25, 2020, we performed 203, 52, and 41 procedures in this same cohort to maintain the HbS <30%, <35% to 45%, and <50% (Table 2), respectively. The mean FCR per patient increased from 43.4% pre–COVID-19% to 52.4% during the COVID-19 pandemic for patients with an HbS goal of <30% (paired *t* test, $P < .001$), from 48.7% to 54.7% for the <35% to 45% group (paired *t* test, $P = .022$), and from 54.8% to 60.6% for the <50% group (paired *t* test, $P = .013$; Table 2). There was individual variability, ranging from a 3.9% decrease to a 19.6% increase in average FCR during COVID-19 compared with pre–COVID-19 (supplemental Figure 2).

The apheresis device was programmed to raise the patient's hematocrit at the end of the procedure in 115 (51.3%), 14 (27.5%), and 9 (20.9%) procedures among patients with a goal HbS <30%, <35% to 45%, or <50%, respectively (Table 2). Among these 138 procedures (43%), the difference ranged from 1.0% to 5.6% above the patients' preprocedure hematocrit. The mean increment in the programmed target hematocrit was 2.8%, from a mean hematocrit of 30.3% before the procedure to 33.1% after the procedure. Per our usual practice, the hematocrit was raised to 27% because of a low baseline hematocrit in 38 procedures (12%). The patients' end hematocrit was not increased in 142 transfusions

Table 1. Demographics of SCD-SS patients on chronic red cell exchange

	Values or no. of patients
No. of patients	50
Mean age, y	23.5
Male	32
Female	18
Mean weight, kg	48.5
Mean height, cm	168.8
Mean total blood volume, mL	4699
Mean pretransfusion hematocrit, %	30.3
Mean ferritin, ng/mL	1064.6
Goal pretransfusion hemoglobin S %	
<30%	33
<35-45%	8
<50%	9
Transfusion indication	
Stroke/secondary stroke prevention	23
Abnormal transcranial Doppler/primary stroke prevention	16
Recurrent acute chest syndrome	5
Pulmonary hypertension	2
Cerebral vasculopathy/transient ischemic attacks	2
Priapism	1
Cardiac disease	1
Hemodilution	
Hemodiluted	24
Not hemodiluted	26
Chelation	
On chelation therapy	10
Not on chelation therapy	40

Table 2. Comparison of red cell exchange procedures pre– and during COVID-19 for patients with goal HbS of <30%, 35% to 45%, and <50%

	Goal HbS <30%			Goal HbS of 35% to 45%			Goal HbS <50%		
	Pre-	During	*P*	Pre-	During	*P*	Pre-	During	*P*
Procedures, no	203	224		52	51		41	43	
Mean FCR, %*	43.4	52.4	<.001	48.7	54.7	.022	54.8	60.6	.013
No. of procedures with intent to increase hct, %		115 (51.3)			14 (27.5)			9 (20.9)	
Total red cell units saved, n		262			54			35	
Mean unit no. transfused per RCE*	6.4	5.3	<.001	6.0	4.9	.011	4.9	4.1	.021
Mean pretransfusion HbS, %*	30.1	27.9	.002	36.6	32.5	.15	41.2	41.9	.65
Mean transfusion interval, d*	25.9	25.4	.37	30.2	28.1	.29	32.5	32.7	.84

*Mean of individual averages among 33 patients with a goal HbS < 30%, 8 with a goal HbS of 35% to 45%, and 9 with a goal HbS < 50%.

(45%) because of a ferritin level > 1000 ng/mL (n = 49), a baseline hematocrit > 33% to 35% (n = 69), or practitioner choice (n = 24).

In total, 1594 units were transfused, and 351 units (18.0%) were saved during the 6-month period, determined by the difference between the patient's mean number of units used per RCE pre–COVID-19 and the number of units transfused for each RCE during the first 6 months the pandemic. The units saved for patients with a HbS goal <30%, <35% to 45%, and <50%, were 262, 54, and 35 units, respectively (Table 2). On average, the number of RBC units transfused per procedure decreased from 6.1 to 5.0 units (paired *t* test, $P < .001$). For patients maintaining a HbS goal of <30%, <35% to 45%, and <50%, the average unit requirement per procedure decreased from 6.4 to 5.3 (paired *t* test, $P < .001$), 6.0 to 4.9 (paired *t* test, $P = .011$), and 4.9 to 4.1 units (paired *t* test, $P = .021$), respectively (Table 2). The percent of units saved per patient in the COVID-19 period correlated with the patient's average increase in FCR from their pre–COVID-19 to COVID-19 procedures (Figure 1A; simple linear regression, $R^2 = 0.64$, $P < .001$; supplemental Table 1).

Because the effect of increasing the hematocrit is expected to become fully evident over multiple procedures, we compared the unit requirement per RCE for patients whose hematocrit was consistently raised (n = 11) or not changed from our prepandemic practice (n = 20) in at least 75% of their procedures. Although there was unit savings for both groups (Figure 1B; paired *t* test, $P < .001$), a greater proportion of units was saved in patients whose hematocrits were increased. The average percent of units saved per RCE was 24.1% for the cohort whose hematocrit was raised at least 75% of the time compared with 15.8% in those whose hematocrit was not consistently changed (Figure 1C; Welch's *t* test, $P = .018$). Expectedly, the %FCR increase for COVID-19 period procedures was greater in those whose hematocrit was raised compared with those whose hematocrit was not changed (Figure 1D; Welch's *t* test, $P = .035$), consistent with less units transfused per RCE.

Given the red cell unit savings, we next compared the pre–COVID-19 and COVID-19 periods for the primary therapeutic goal of maintaining the patient-specific pre-transfusion HbS%. Overall, the pre-transfusion HbS% was maintained below each patient's goal. For the HbS <30% cohort, the mean pre–COVID-19 HbS% decreased from 30.1% to 27.9% (Table 2 paired *t* test, $P = .002$). For patients with a HbS goal <35% to 45%, the mean HbS% decreased from 36.6% pre–COVID-19 to 32.5% during COVID-19 (paired *t* test, $P = .15$). For those whose goal HbS was <50%, the mean HbS% remained approximately the same: 41.2% pre–COVID-19 and 41.9% during the COVID-19 period (paired *t* test, $P = .65$). Maintenance of the goal HbS% occurred without a significant change in the transfusion interval. For the groups with a HbS goal of <30%, <35% to 45%, and <50%, the mean transfusion interval remained similar: 25.9 vs 25.4 days pre– and during COVID-19 (paired *t* test, $P = .37$), 30.2 vs 28.1 days (paired *t* test, $P = .29$), and 32.5 vs 32.7 days (paired *t* test, $P = .84$), respectively (Table 2).

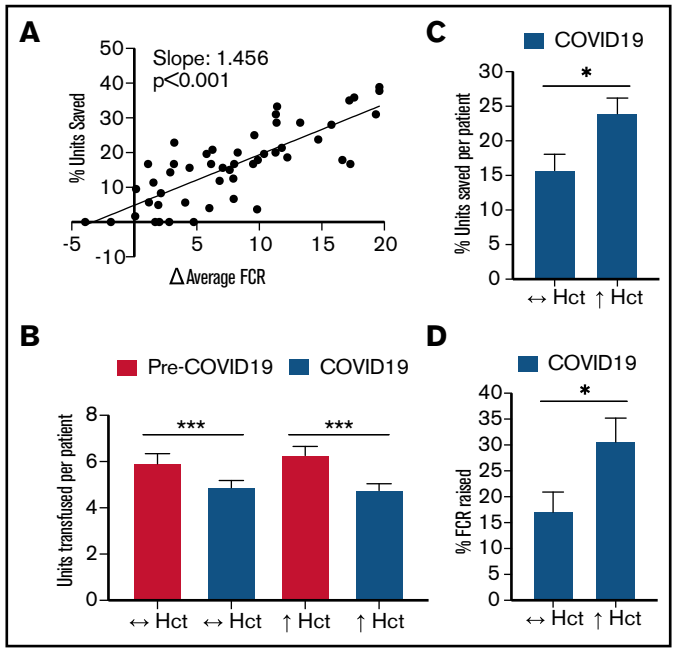

Figure 1. Red cell units saved during the COVID-19 pandemic. (A) The percent of units saved per patient during COVID-19 period compared with their individual average increase in FCR from pre–COVID-19 to COVID-19 procedures (• represents individual patients, n = 50). (B) Average red cell units transfused per RCE pre–COVID-19 and during COVID-19 for patients whose hematocrit was maintained at baseline (↔ Hct, n = 20) vs patients whose hematocrits were raised above baseline in ≥75% of procedures (↑ Hct, n = 11). (C) Percent of red cell units saved per patient and (D) average %FCR raised per RCE in COVID-19 procedures for patients whose programmed end hematocrit was not (↔ Hct, n = 20) or was increased (↑ Hct, n = 11) in ≥ 75% of procedures. *$P < .05$, ***$P < .001$.

A major benefit of RCE is achieving equal or negative red cell mass (RCM) balance to avoid iron loading. Pre–COVID-19, the mean RCM balance at the end of the procedure was 0.26 mL/kg (n = 50). For patients in whom the hematocrit was raised above the pretransfusion level in at least 75% of procedures during the COVID-19 period, the average RCM balance per RCE increased to 1.06 mL/kg. For patients whom the end hematocrit was not raised or raised to 27% (baseline practice) in at least 75% of procedures during COVID-19, the average RCM balance was 0.06 mL/kg (Figure 2A). Overall, the cumulative RBC mass gained over the first 6 months of the pandemic ranged from 4.00 to 11.50 RCM/kg for the 11 patients whose hematocrit were raised in ≥75% of their procedures (Figure 2B; simple linear regression, R^2 = 0.306, P = .078). The most recent ferritin values for the 11 patients in whom the hematocrit was raised above the pretransfusion level in >75% of procedures increased from a mean of 222.6 ng/mL (median, 103.0 ng/mL) to 522.4 ng/mL (median, 379.4 ng/mL; paired t test, P = .012; supplemental Figure 3).

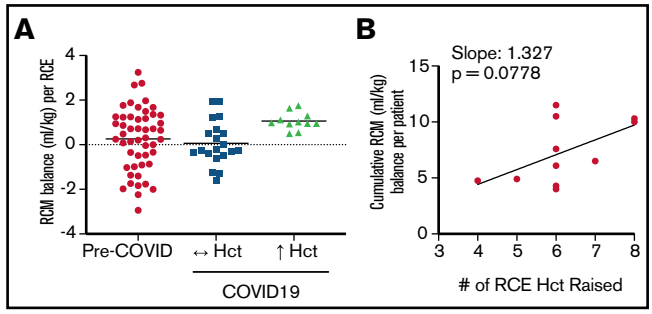

Figure 2. RCM balance in patients for whom the hematocrit was or was not consistently raised for RCE during COVID-19. (A) Average RCM balance (mL/kg) per RCE in patients pre–COVID-19 (n = 50) and for whom the hematocrit was consistently raised (↑ Hct, n = 11) or not (↔ Hct, n = 20) during COVID-19. (B) Cumulative RCM (mL/kg) balance and number of procedures per patient in which the hematocrit was raised consistently (● represents individual patients, n = 11).

Discussion

The COVID-19 pandemic has required health care systems to implement strategies for effective delivery of care while managing blood supply disruptions and shortages.[3,14-17] It is recommended that patients with hemoglobinopathies receive red cells prophylactically matched for Rh and K antigens,[8] but the COVID-19 pandemic disproportionately impacted this inventory, underscoring the need for blood saving practices. We report measures that resulted in a large reduction of red cell units transfused to patients with SCD undergoing chronic RCE. First, availability of pretransfusion HbS% results and precise calculation of the FCR and volume of red cells required led to significant unit savings. Second, we were able to increase the targeted end hematocrit modestly to enhance suppression of endogenous erythropoiesis in 43% of procedures and consistently for 11 patients. This short-term measure increased the FCR required to maintain the same target HbS%, further reducing the units transfused.

The Hematology laboratory facilitated the rapid turnaround of the Hb quantification that allowed for exact calculation of the required FCR and units needed by the time of the procedure. Collaboration with the primary hematologists was critical, particularly in determining whether raising the hematocrit at the end of the procedure was acceptable. Switching patients to straight transfusion was also considered, but all patients in our cohort had transitioned to apheresis because of severe iron overload, a high baseline hematocrit that precluded chronic simple transfusion, or an inability to maintain their goal HbS% on a straight transfusion program. For these reasons, none of our patients were transitioned to straight transfusion. Collaboration among the 8 apheresis nurses and 6 physicians (3 dual trained in hematology and apheresis) was key to rapid and coordinated implementation.

A primary concern for raising the hematocrit at the end of the RCE is a theoretical risk of increasing blood viscosity, particularly in those with severe vasculopathy or moyamoya. At the start of the pandemic, each patient's hematologist was contacted to determine whether increasing the hematocrit was safe and acceptable. Because the STOP 1 trial used a hematocrit limit of 36% in patients at risk of stroke,[11] we did not anticipate adverse side effects from this intervention. The programmed increase in hematocrit was modest, with an increase from a mean pretransfusion value of 30.3% to 33.1% after the procedure. There were 24 patients in whom the hematocrit was increased in more than half their procedures. In the 6-month period before the pandemic, 5 of these patients had a total of 9 emergency department (ED) visits or hospitalizations for vaso-occlusive episode (n = 7), headache (n = 1), or fever (n = 1). During the first 6 months of COVID-19, 5 of 24 patients also had a total of 9 ED visits or hospitalizations for vaso-occlusive episode (n = 4), headache (n = 2 in same patient), acute chest syndrome (n = 2), or fever (n = 1). Among the 11 patients whose hematocrits were raised >75% of procedures, there was only 1 ED visit for headache in the prepandemic period and 1 ED visit for fever during COVID. No strokes or transient ischemic attacks occurred in either of these periods. One case of acute chest syndrome and 1 fever were associated with COVID-19. Of note, 6 patients had confirmed COVID-19 during the study period, of which none required additional transfusion for their management.

The percent of units saved per patient in the COVID-19 period correlated with the average increase in FCR (Figure 1A). The average FCR difference per patient ranged from −3.9% to 19.6%, with 17 individuals having a mean FCR per procedure that was 10% to 20% greater during the pandemic period. The individual with the highest increase in average FCR of 19.6% had a 38.9% decrease in her blood use. She was transfused an average of 6.2 units with a mean pretransfusion HbS of 31.2% before the pandemic, which decreased to an average of 3.7 units without increasing her hematocrit and while maintaining her target HbS level. Similar to our prepandemic practices, many apheresis services order blood based on the number of units the patient historically receives rather than a precise calculation based on current pretransfusion HbS%, especially for patients who are consistently achieving their target pretransfusion HbS goal. Thus, there may be an opportunity for unit savings nationally. Combined with a modest rise in hematocrit when possible, we observed that 16 individuals averaged >20% unit savings and another 18 had 10% to 20% reduction in blood use. Only 6 patients demonstrated no unit savings during the COVID-19 period. Decreased donor exposure is an additional benefit of these measures, because alloimmunization is prevalent among chronically transfused patients with SCD.[8,18]

Because the programmed end hematocrit was typically raised no greater than 3% to 4% and many patients' hematocrits did not always allow for a raised value, the overall net iron accumulation was low for the 6-month period. Even in patients whose hematocrit was raised in at least 75% of their procedures during COVID-19, the average cumulative RCM for these patients was 5.9 mL/kg, which equates to less than the volume typically administered for 1 straight transfusion. Five patients had their hematocrits raised in 100% of their procedures during COVID-19. The cumulative RCM balance was 4.9, 6.5, 6.1, 10.3, and 10.5 mL/kg for these 5 individuals. Their mean ferritin value was 114 ng/mL pre–COVID-19 and 323.2 ng/mL after 6 months of implementing the raised hematocrit. Among these 5 patients, 144 units were used for a total of 32 RCE procedures, and 48 units were saved based on their pre–COVID-19 unit use (25% savings) without substantial iron loading. However, because a major benefit of RCE over simple transfusion is net iron neutrality, raising the hematocrit over an extended period is not ideal and should be reserved for severe blood shortages.

A limitation of this study is the relatively small cohort size of 50 patients that precluded detailed analysis of some variables such as IHD. Patients who routinely had RCE with IHD continued with this intervention throughout the pandemic. Among the 24 patients who had RCE with IHD, the average unit savings per patient was 17.5% compared with 15.4% in the 26 patients receiving RCE without IHD (unpaired t test, $P = .509$). No patients were initiated on IHD during the study period, precluding assessment of unit savings in individual patients who underwent RCE with and without IHD. Although our usual practice had been to order patient-specific blood from our blood supplier, a major change was to precisely determine unit requirements based on the patients' current pretransfusion HbS and hematocrit. The measures we implemented are not particularly novel but are simple and practical and resulted in a real-world reduction of blood used during a period of shortages.

The COVID-19 pandemic created major disruptions in the blood supply chain and severe shortages.[1,17] The Rh and K antigen negative red cell inventory that patients with hemoglobinopathies rely on was and continues to be disproportionately impacted. Our objective was to implement measures to decrease blood unit use without sacrificing patient care and safety. These relatively minor adjustments led to saving nearly 1 in 5 units of blood that would have been ordered and transfused before the pandemic. Maintenance of individual HbS% goals was not compromised, and, although net iron loading was modest over the 6-month period, increasing the end hematocrit will be considered a short-term measure only. Although COVID-19 vaccines have recently been approved, the time to reach herd immunity is estimated to be 6 to 9 months. In the interim, measures to reduce the large red cell unit requirements for patients undergoing chronic RCE can help ensure adequate blood for all individuals in need. More generally, the strategy of specific calculation of FCR and units required for each procedure by having the pretransfusion HbS level available could be recommended as a best practice that our Apheresis Service will adopt permanently.

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Authorship

Contribution: S.U., D.F.F., and S.T.C. designed the study, analyzed results, and wrote the manuscript; S.U. obtained informed consent and maintained all clinical data in a research database; and H.H.A., G.E.L., S.K., H.C.K., and D.S.-P. conducted research, analyzed results, and edited the manuscript.

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