Transfusion practices for patients with sickle cell disease at major academic medical centers participating in the Atlanta Sickle Cell Consortium

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The Atlanta Sickle Cell Consortium represents more than 2600 pediatric and adult patients with sickle cell disease (SCD) in the metropolitan Atlanta, Georgia, area receiving care at four major locations, each providing comprehensive care 24 hours a day, 7 days a week. Both transfusion services that support these sites use two levels of prospective phenotype matching to decrease the rates of alloimmunization. Although exact rates are unknown and are currently under investigation, alloimmunization occurs infrequently with the exception of chronically transfused SCD patients, who represent the minority of active SCD patients. With increasing availability, red blood cell genotyping will be used in the near future both for determination of predicted patient phenotypes and for provision of genotypically matched donor units. ***Immunohematology* 2012;28:24–6.**

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The Atlanta Sickle Cell Consortium represents more than 1000 adult and 1600 pediatric patients with sickle cell disease (SCD) in the metropolitan Atlanta area receiving care at four major locations. The Aflac Cancer Center and Blood Disorders Service of Children's Healthcare of Atlanta (CHOA) offers the largest comprehensive pediatric SCD program in the country, serving 1675 active patients with SCD at three sites in metropolitan Atlanta: Children's at Egleston (ECH), providing care for 573 active patients; Children's at Scottish Rite (SR), providing care for 648 active patients; and Children's at Hughes Spalding (HS), providing care for 454 active patients. With nearly a dozen pediatric hematology faculty members from either Emory University or Morehouse Schools of Medicine, the SCD program provides 24-hour acute care, health maintenance services, chronic transfusion services, patient counseling including follow-up from newborn screening, SCD education, and blood and marrow transplants for eligible patients. With outcomes exceeding the national average, the Aflac Cancer Center and Blood Disorders Service has performed more blood and marrow transplants for patients with SCD than any other program in the country. To date, more than 30 children with SCD have been cured through matched sibling bone marrow transplants with a 96 percent disease-free survival rate; the first successful unrelated cord blood transplant for SCD was also performed at CHOA. In fiscal year 2010, there were a total of 1402 inpatient hospitalizations (ECH, 605; SR, 500; HS, 297) and 7155 outpatient Aflac clinic visits (ECH, 2272, SR, 2622, HS, 2261) among all sites.

Once these patients reach adulthood (age 18 and older), their SCD care is most often transitioned to the Georgia Comprehensive Sickle Cell Center at Grady Health System (GHS), which was the first 24-hour comprehensive primary-care clinic for patients with SCD and has been focused on SCD management for more than 30 years. With 1035 active patients, the GHS Sickle Cell Center also provides complementary outpatient services including a clinic to ease the transition from pediatric to adult services, a multidisciplinary health maintenance clinic, leg ulcer and hydroxyurea clinics, chronic transfusion services, and other counseling and SCD management resources.

Transfusion support for patients with SCD at the previously referenced sites is provided by hospital transfusion services located at ECH, SR, and Grady Memorial Hospital under the medical direction of faculty from Emory University School of Medicine in collaboration with the American Red Cross (ARC) Blood Services, Southern Region, primary blood supplier of CHOA and GHS transfusion services. Although each blood bank has individual policies and procedures, the transfusion support of patients with SCD is similar across hospital systems.

SCD Transfusion Protocol

Children's Healthcare of Atlanta

On receipt of a blood sample from an identified SCD patient, routine serologic testing including ABO and D typing and antibody detection and identification, if necessary, is

performed, similar to that for any potential transfusion recipient. When an SCD patient is initially seen at ECH or SR, a complete red blood cell (RBC) phenotype is performed by the ARC, which includes Rh, Kell, Duffy, Kidd, and MNS systems; phenotype testing is only performed if the patient has not been transfused within the last 3 months. The reference laboratory cost associated with an 11-antigen phenotype for C, E, c, e, K, Fy^a, Fy^b, Jk^a, Jk^b, S, and s is approximately $26 per antigen for a total cost of $286 per phenotype, but prices will vary by institution and reference laboratory. The CHOA protocol for transfusion of RBCs for SCD patients consists of two levels of prospective phenotype matching. The first category of matching is reserved for children who have not produced a clinically significant antibody and consists of prospective antigen matching for Rh (D, C, E, c, e), and Kell (K, k) (category 1). Once a child has become sensitized and produced clinically significant RBC antibodies (category 2), RBCs for transfusion are Rh (D, C, E, c, e), Kell (K, k), Fy^a, and Jk^b specific and must also be negative for any other antigens to which the patient has produced alloantibodies, if clinically significant (e.g., S, s, Js^a). In patients with a history of a warm autoantibody that is no longer detected by serologic testing, extended phenotype-matched units are provided. When the patient needs to be transfused, units are either ordered from the ARC Reference Laboratory or selected from the current stock of antigen-negative RBCs. RBC units for transfusion are all prestorage leukocyte reduced, hemoglobin S (HbS) negative, and as fresh as possible, preferably less than 14 days old; there is no requirement for irradiation. The cost for a RBC unit that is negative for C, E, K, and HbS is approximately $526, with an additional charge of approximately $80 for each additional antigen negative. This protocol is the same for all patients with SCD whether they are inpatients or outpatients and scheduled or urgent/emergent transfusions.

Grady Health System

When a patient with SCD is initially seen at either HS or GHS, the Grady blood bank performs a phenotype for C, E, c, e, K, Fy^a, Fy^b, Jk^a, Jk^b, S, and s, in addition to ABO and D typing, and antibody screening and identification if necessary. When a patient has been recently transfused, other methods may be needed to determine the patient's RBC phenotype using either a hypotonic wash method or molecular studies; however, currently genotyping is typically reserved for patients who develop alloantibodies that do not seem physiologically plausible given previous phenotyping results or for patients who have developed uncommon alloantibodies for which no typing sera are available. When urgent RBC transfusion is necessary and a phenotype is unavailable at our institution, records from the ARC or referring facilities are often obtained. In the event the antigen profile is unknown, RBCs are emergently released that are negative for C, E, and K until a phenotype can be determined. Similar to CHOA, the GHS transfusion service has two levels of prospective phenotype matching. For patients with SCD who have not developed an alloantibody or autoantibody, prestorage, leukocyte-reduced, HbS-negative RBCs are provided that are matched for C/c, E/e, and K. As a cost-saving initiative, the Grady blood bank has developed a screening algorithm using automated RBC typing equipment to determine the C, E, and K status of donor units provided by the ARC, and we have successfully been able to limit costs and maintain an adequate inventory of units negative for C, E, and K. Once a patient has developed RBC alloantibodies or autoantibodies, RBC units are provided that are Rh (D, C, E, c, e), Kell (K, k), Fy^a, Jk^b, and S specific and negative for any other antigens to which the patient has produced clinically significant alloantibodies; S– units are only provided for patients older than 16 years of age. All RBC units are prestorage leukocyte reduced and HbS negative. There is no donor unit age or irradiation requirement.

Emergency Protocols

In cases of urgent/emergent transfusion needs, it may not be possible to complete antibody identification, especially for autoantibodies and complex serologic panels, or provide phenotype-matched RBCs; however, in these situations direct consultation of the blood bank medical director and clinical team is crucial. At times, it is possible to delay transfusion until serologic studies can be completed and partially or completely phenotype-matched units can be provided. At minimum, RBC units must be antigen negative for clinically significant alloantibody specificities. Of course there are exceptions to every rule, and it is most important to treat the patient before protecting the integrity of prophylactic measures; it may be necessary to emergently release RBCs before serologic studies or antigen matching can be completed for patients in life-threatening situations.

SCD Transfusion Protocol Outcomes

Outcomes in Chronically Transfused Patients at CHOA

Although alloimmunization rates of patients with SCD at CHOA have not been specifically measured, the occurrence of new antibodies is infrequent. Occasionally, patients are

transfused elsewhere without partial phenotype matching, and in this setting, patients have become alloimmunized. Alloimmunization data is available for the minority of patients with SCD who are chronically transfused at all three CHOA sites; however, it is currently being collected on all active SCD patients. Table 1 compares alloimmunization rates in the chronically transfused CHOA patients with SCD. Data for autoantibody formation is currently only available for the children at HS, and 6 (15%) patients have developed warm autoantibodies. Although less than 10 percent of patients are chronically transfused, even fewer undergo chronic erythrocytapheresis, which would be clinically beneficial. Given the current limitations of reimbursement for outpatient RBC exchange procedures in the state of Georgia, chronic RBC exchange transfusion is not a feasible option for most qualifying patients.

Table 1. Alloimmunization statistics of chronically transfused patients with sickle cell disease

Site	Number of active patients	Number chronically transfused (%)	Number alloimmunized (%)	Number of patients receiving chronic RBC exchange
Egleston	573	48 (8.4)	12 (25)	0
Hughes Spalding	454	39 (8.6)	10 (25.6)	1
Scottish Rite	648	45 (6.9)	19 (42.2)	5

Alloimmunization Rates of GHS Patients with SCD

Of the 554 SCD patients with active blood bank records, 139 (25%) are alloimmunized and 52 (9%) have developed autoantibodies, thus requiring extended phenotype-matched units. However, this most likely represents an overestimation of alloimmunization as data were obtained from active blood bank records and many of these SCD patients were likely transfused prior to the initiation of prospective phenotype-matching programs. In addition, 20 of these patients have tracking notes in the blood bank information system that require a medical director's consult before issuing any RBC units; these patients have either complex alloantibodies or a history of hemolytic or unexplained severe transfusion reactions. Under these circumstances, there is most often a conversation between the transfusion service medical director and hematology attending physician to weigh the risks and benefits of transfusion in this select group of SCD patients.

Conclusions

Two major academic medical centers in Atlanta, Georgia, CHOA and GHS, provide comprehensive care to more than 2600 pediatric and adult patients with SCD. The transfusion services that support these sickle cell centers of excellence use two levels of prospective phenotype matching to prevent alloimmunization. Although alloimmunization rates are currently under investigation, most patients are infrequently alloimmunized with the exception of chronically transfused patients with SCD. As genotyping becomes more widespread, increased adoption of genotyping patients with SCD and provision of genotypically matched RBC donor units will become a possibility; CHOA will embark on prospective genotype matching in 2012.

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