

Haemoglobin Disorders: Update

24

Author: Paula Bolton-Maggs

Key SHOT messages

The management of sickle cell disease could be improved by careful communication:

- Clinicians should inform the transfusion laboratory of the diagnosis so that appropriate units of red cells can be selected
- Where patients with sickle cell disease present to hospitals who rarely see such patients, advice should be sought from the local haematologist, and the national sickle cell disease network as necessary (West Midlands Quality Review Service 2016)
- Biomedical scientists (BMS) should ensure the red cell phenotype is recorded prior to transfusion
- BMS should pay particular attention to seeking out any historical antigen sensitisations in sickle cell patients in their own laboratory records, in national databases such as Sp-ICE (Specialist Services Electronic Reporting using Sunquest ICE) in England, and by contacting other hospitals where the patient has been transfused in order that appropriate antigen-negative units can be selected for transfusion

Sickle cell disease n=160

HTR	61
SRNM	59
ATR	21
ADU	9
IBCT	6
TACO	2
TAD	1
TTI	1

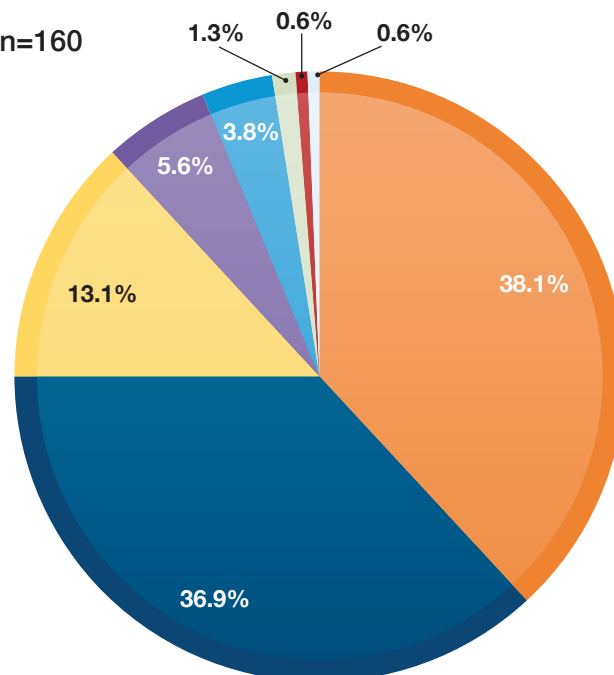
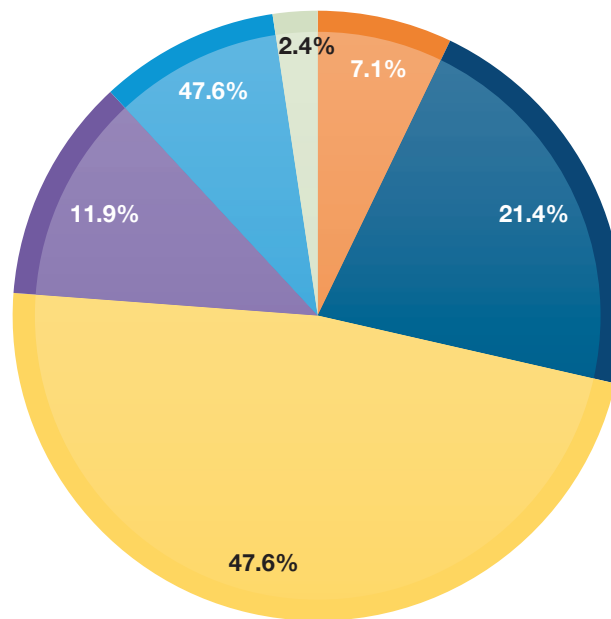


Figure 24.1:
Cumulative data
for adverse events
in haemoglobin
disorders 2010 to
2016

Thalassaemia n=42

HTR	3
SRNM	9
ATR	20
ADU	5
IBCT	4
TACO	1



ATR=acute transfusion reaction; ADU=avoidable, delayed or under or overtransfusion; IBCT=incorrect blood component transfused; SRNM=specific requirements not met; TACO=transfusion-associated circulatory overload; TAD=transfusion-associated dyspnoea; HTR=haemolytic transfusion reaction; TTI=transfusion-transmitted infection

As in previous years the majority of reported adverse incidents in patients with sickle cell disease (SCD) are haemolytic transfusion reactions and instances where specific requirements were not met, together 120/160 (75.0%) incidents, compared to 12/42 (28.6%) in patients with thalassaemia. Patient education may help reduce some of these incidents.

The median age of patients reported in 2016 was 32 years, range 2 to 73 (9/51 aged more than 40 years and one over 70).

Specific requirements not met

The most striking feature from this year of reporting is the increase in cases where specific requirements were not met (n=24 compared with n=10 in 2015), particularly in patients with SCD n=21. These 24 errors occurred both in clinical (n=9) and laboratory (n=15) areas. (In one case it was not clear whether the haemoglobin disorder was SCD or thalassaemia).

Clinical errors occurred mainly because the clinical staff failed to inform the laboratory that this was a patient with haemoglobinopathy (5/9). In three cases hepatitis E virus (HEV)-screened components were not requested for patients with SCD who had undergone renal transplants. One pregnant patient (thalassaemia) did not receive cytomegalovirus (CMV)-screened red cells and 5 patients with SCD did not receive appropriate phenotypes.

Laboratory staff failed to select an appropriate phenotype in 11/14 cases of SCD (failure to notice diagnosis on request form; failure to heed historical results e.g. Case 10.10). One of these patients had been transfused fourteen units over a 2-year period with red cell units issued by four different members of staff. One 15-year old developed anti-e following transfusion when admitted in sickle crisis. Her Rh genotype had not been determined and she did not receive phenotype-selected units. The report noted staffing issues: 'Staffing levels plus new staff meant that covering night shifts was difficult'.

A thalassaemia patient who was supposed to receive R1R1 (CDe/CDe) red cells was supplied from the Blood Centre with rr (cde/cde) which was then not noticed in the transfusion laboratory prior to transfusion risking sensitisation to the c antigen.

Case 24.1: An elderly patient develops alloantibodies

This 73-year-old man with SCD had not been seen since 2009 and was not transfusion dependent. He attended the emergency department (ED) in late 2015 requiring transfusion. The BMS followed historic crossmatch instructions on his record, which only stated to give Rh-compatible red cells with no additional comment indicating that genotype/Rh phenotype should be performed. All haemoglobinopathy patients since 2012 have had either a Rh/K phenotype or genotype tested as minimum prior to issuing red cells for these patients. This patient developed anti-E in response to transfusion of two units of red cells during this admission. One of these units was E-positive. His genotype showed that he should have been receiving C-negative, E-negative units. An in-house Rh/K phenotype performed on his pre-transfusion sample demonstrated a mixed field reaction with both C and E antigens implying that the patient had been transfused elsewhere within the past three months.

Avoidable transfusion**Case 24.2: Inappropriate transfusion due to poor knowledge**

A pregnant woman with known SCD, who normally has a low haemoglobin (Hb), was taken to theatre. She was not actively bleeding. The doctor wanted two units of O D-negative blood for the patient, and did not want to wait for crossmatched units. Transfusion of the first unit started but was rapidly stopped by the haematology registrar after 20mL was transfused.

This was an avoidable transfusion as the patient's Hb was normal for her and she was not actively bleeding. The use of O D-negative units for a known sickle cell patient is not optimal and could result in the development of antibodies. The patient did not require any blood following the surgery. 'Expert haematology advice must be sought before a decision is made to transfuse, unless in an emergency' (Davis et al. 2017b).

Incorrect blood component transfused

Three patients received wrong red cell transfusions.

A 17-year-old D-negative woman required exchange transfusion. She received six units of D-positive red cells following an error in ordering from the Blood Service which was not detected either in the laboratory or at the bedside. Fortunately testing several months later has not detected anti-D formation.

A 5-year-old child newly diagnosed with SCD was noted to be D-positive and transfused with D-positive cells, however this was a D-variant and she should have received D-negative cells.

A young man with SCD received a transfusion of a unit which was incompatible by crossmatch. This was related to mislabelling but fortunately he suffered no ill effects.

Haemolytic transfusion reactions

Eight were recorded, all in patients with SCD. Six were classified as hyperhaemolysis (details in Table 19.2 in Chapter 19, Haemolytic Transfusion Reactions (HTR)) of whom 2 died, one probably related to the transfusion (Chapter 19, Case 19.1) and in the other death was unrelated (Case 24.3 below). All 8 patients suffered major morbidity; two other patients had classical delayed HTR.

Case 24.3: Death from complications of SCD in a woman who also had hyperhaemolysis

A pregnant woman with known sickle cell disease and alloantibodies was transfused with appropriate antigen-matched units. One week later she presented with a painful episode, fever and probable chest infection. She also had signs and symptoms of intravascular haemolysis with a low reticulocyte count but very high lactate dehydrogenase (LDH). The direct antiglobulin test (DAT) was negative throughout admission and no new alloantibodies were identified. A diagnosis of hyperhaemolysis was made and she was treated with intravenous (IV) antibiotics, IV methyl prednisolone and intravenous immunoglobulin (IVIg). The Hb continued to fall and she was transferred to the intensive therapy unit (ITU) and emergency caesarean section performed. Post section there was initial improvement and Hb stabilised at 55g/L but lactate rose. Therefore a decision was made to transfuse one unit of blood

with further steroids and give erythropoietin, B12 and a multivitamin injection. The Hb increased to 65g/L and then remained stable. She continued to deteriorate and had cardiac arrest - three further units were transfused but unfortunately the patient died. The coroner concluded she died from complications of SCD and that the transfusion reaction did not play a role in her death as there was evidence that the haemolysis was already under control.

Case 24.4: Failure to consult available historical records in SCD prior to exchange transfusion

A 43-year-old woman was under shared care between two different hospitals. She required specialist surgery at another centre which was not her usual base. She had a history of anti-S, anti-E, anti-Fy^a, anti-Fy^b and anti-Fy3. She had been transfused with appropriate phenotype, and the antibodies were not detectable from 2013. She underwent preoperative exchange transfusion at the specialist centre with eight units. Her base hospital transfusion laboratory records and Sp-ICE data were not accessed for her antibody history. Four days later she presented to her own hospital unwell with haemoglobinuria and was initially thought to be in sickle crisis. However this was a delayed haemolytic transfusion reaction associated with anti-Fy^a and anti-Fy3 (identified in the eluate). She made a full recovery.

This was an avoidable complication had the historical data been sought as is recommended in guidelines (Davis et al. 2017a). (Case 19.9 in Chapter 19, Haemolytic Transfusion Reactions (HTR)).

Literature update

New transfusion guidelines have been published for SCD and should be consulted and adhered to in order to avoid complications (Davis et al. 2017a; Davis et al. 2017b). In particular 'a transfusion history should be obtained in all sickle cell disease patients requiring transfusion, whether elective or emergency. Close communication is essential between clinical and laboratory teams so that appropriate blood is given' (Davis et al. 2017a). There is also a series of Cochrane reviews of transfusion in SCD (Estcourt et al. 2016a; Estcourt et al. 2016b; Estcourt et al. 2016c), and a series of review articles in Lancet (Editorial 2016; Gladwin 2016; Lettre and Bauer 2016).

References

- Davis BA, Allard S et al. (2017a) **Guidelines on red cell transfusion in sickle cell disease. Part I: principles and laboratory aspects.** Br J Haematol 176(2), 179-191
- Davis BA, Allard S et al. (2017b) **Guidelines on red cell transfusion in sickle cell disease Part II: indications for transfusion.** Br J Haematol 176(2), 192-209
- Editorial (2016) **Sickle-cell disease: managing comorbidities.** Lancet 387(10037), 2480
- Estcourt LJ, Fortin PM et al. (2016a) **Red blood cell transfusion to treat or prevent complications in sickle cell disease: an overview of Cochrane reviews.** Cochrane Database Syst Rev 2016(2)
- Estcourt LJ, Fortin PM et al. (2016b) **Regular long-term red blood cell transfusions for managing chronic chest complications in sickle cell disease.** Cochrane Database Syst Rev(5): CD008360
- Estcourt LJ, Fortin PM et al. (2016c) **Preoperative blood transfusions for sickle cell disease.** Cochrane Database Syst Rev 4: CD003149
- Gladwin MT (2016) **Cardiovascular complications and risk of death in sickle-cell disease.** Lancet 387(10037), 2565-2574
- Lettre G and Bauer DE (2016) **Fetal haemoglobin in sickle-cell disease: from genetic epidemiology to new therapeutic strategies.** Lancet 387(10037), 2554-2564
- West Midlands Quality Review Service (2016) **Services for People with Haemoglobin Disorders, Peer Review Programme 2014-16 Overview Report.** http://www.haemoglobin.org.uk/wp-content/uploads/2017/04/HD-Overview-Report-V2-20161123_1479987444.pdf [accessed 15 March 2017]