23 Haemoglobin Disorders n=46

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Abbreviations used in this chapter

ADU	Avoidable, delayed and under/overtransfusion
AHTR	Acute haemolytic transfusion reaction
APPG	All-party parliamentary group
BSH	British Society for Haematology
CMV	Cytomegalovirus
CT	Computerised tomography
DAT	Direct antiglobulin test
DHTR	Delayed haemolytic transfusion reaction
Hb	Haemoglobin
HCC	Haemoglobinopathy Coordinating Centre
HPLC	High-performance liquid chromatography
HTR	Haemolytic transfusion reactions
LIMS	Laboratory information management system
NHS	National Health Service
NHSBT	NHS Blood & Transplant
SCD	Sickle cell disease
Sp-ICE	Specialist Services electronic reporting using Sunquest's Integrated Clinical Environment
SRNM	Specific requirements not met

Key SHOT messages

- Alloimmunisation is a significant problem in SCD and therefore each transfusion decision must take into consideration the intended benefits and potential risks
- Transfusion in SCD should have a clear indication in line with national guidance (BSH Davis et al. 2017)
- Robust processes must be in place to ensure haemoglobinopathy patients are highlighted on transfusion requests

Recommendations

- Haematology teams must be informed when sickle cell patients are admitted to secondary care
- All haemoglobinopathy patients should have an extended phenotype and receive extended Rh- and K-matched units
- Transfusion history should be sought including history of previous alloimmunisation and transfusion reactions. Antigen-negative blood should be given for any corresponding historic clinically significant alloantibodies
- Red cell genotyping can provide more accurate information and confirm any discrepancies identified on serological testing (NHSBT n.d.)

Action: All clinical staff involved in transfusion

Introduction

Patients with haemoglobinopathies are at increased risk of red cell alloimmunisation and therefore require extended Rh- and K-matched blood. Patients with SCD are at increased risk of HTR which can be severe and associated with significant morbidity. Transfusion decisions should be made with input from a specialist haemoglobinopathy team. NHS England has now commissioned the providers of specialised haemoglobinopathy services to support the provision of both specialist and non-specialist haemoglobinopathy services, expert opinion and management of complex patients (NHS England 2019).

Deaths related to transfusion n=2

There were 2 deaths reported. The first report was of a thalassaemia intermedia patient in her 70s with a history of previous transfusion reactions. The patient attended the haematology unit for a transfusion and received antigen-positive blood. During the transfusion the patient developed bronchospasm and had acute loss of consciousness requiring intubation and ventilation. A CT brain scan demonstrated extensive ischaemia secondary to carotid artery dissection. Acute haemolytic transfusion reaction was listed on the death certificate as a significant condition contributing to death.

A young male with SCD underwent an endoscopic procedure and was readmitted the following day with biliary sepsis. During the admission he developed an acute vaso-occlusive crisis and was transferred to critical care where he was transfused. He continued to deteriorate and developed multi-organ failure and died. The coroner report suggested earlier transfusion should have been considered. This case has been discussed in further detail in Chapter 11a. Delayed Transfusions (Case 11a.3).

Major morbidity n=10

There were 7 reports associated with major morbidity occurring in patients with SCD, and 3 in patients with thalassaemia, 3 of which required critical care admission. These included 6 cases of HTR, 3 cases of FAHR and 1 case in UCT.

Haemolytic transfusion reactions n=13

There were 13 cases of haemolytic transfusion reactions reported, 12 cases were in patients with SCD and 1 case in a thalassaemia patient. The reports included 1 case of AHTR, 7 DHTR and 5 with hyperhaemolysis. Further details can be found in Chapter 18, Haemolytic Transfusion Reactions (HTR).

Figure 23.1: HTR in haemoglobinopathy patients in 2021 (n=13)

HTR=haemolytic transfusion reactions

Case 23.1: Hyperhaemolysis in a patient with SCD

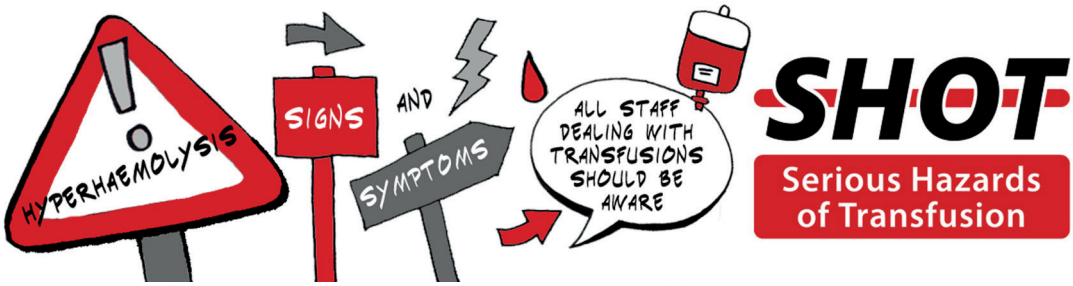
A young female with SCD received a two-unit top up transfusion. There was a history of alloimmunisation with anti-S and therefore she received S-negative units. The patient presented 5 days later with a Hb of 30g/L. Urine HPLC was reported as consistent with hyperhaemolysis. A new anti-Fy^a antibody was identified, and a decision was made to transfuse further red cells. The patient developed additional complications with transient encephalopathy and hypertensive crisis. She was treated with corticosteroids, intravenous immunoglobulin, eculizumab and rituximab.

Case 23.2: Delayed haemolysis in a patient with SCD

A young female with SCD and a history of alloimmunisation received a red cell exchange transfusion. She presented 8 days later with generalised body pains and fever. She was known to have anti-Fy^a and anti-Jk^b but had now developed an anti-Fy3.

Learning point

- Anti-Fy3 develops in individuals with a null Fy(^{a}-negative,^{b}-negative) phenotype and reacts strongly with Fy^a-positive and Fy^b-positive cells. This phenotype is rare in most of the UK population (<1%) but common in individuals from black African/Caribbean backgrounds and therefore this restricts the individual to predominantly black African/Caribbean blood donors for future transfusion (Daniels 2002)



Febrile, allergic and hypotensive reactions (FAHR) n=10

There were 5 febrile reactions and 5 allergic reactions. Most were following red cell transfusion with 1 anaphylactic reaction following platelets in a SCD patient post haemopoietic stem cell transplant.

Avoidable, delayed and under or overtransfusion (ADU) n=9

There were 3 reports of avoidable transfusion in SCD where transfusion was not indicated or intended. There were 3 reports of delayed transfusion, 1 of which resulted in death described in the section above. There were a further 3 transfusions reported as overtransfusion where an incorrect volume of red cells was administered however none of these resulted in adverse outcome.

Case 23.3: Unnecessary transfusion due to assumption by staff resulting in incorrect handover

A young male with SCD was admitted and a group and crossmatch was requested to have red cells on standby in case of clinical deterioration. The day nursing staff assumed that a transfusion was required and handed this over to the night nursing staff who then asked the junior night doctor to prescribe the blood which was then administered.

The treatment plan should be clearly communicated to all involved in the care of the patient and documented in the patient's notes. Handover must be accurate and all staff authorising transfusions must have sound understanding of the indication instead of just doing this based on a nursing handover. Shared decision-making involving patients is recommended.

Case 23.4: 20-hour delay in transfusion for a patient with acute chest syndrome

A female in her 20s with SCD was admitted with a vaso-occlusive pain crisis, increasing oxygen requirement and chest signs in keeping with acute chest syndrome. The haematologist requested for the patient to be transferred to the haematology ward and to receive an urgent two-unit top-up transfusion. Due to delays with bed availability the patient was not transferred until later that night, and the transfusion was not administered until 20 hours after the decision to transfuse. There had been a clinical deterioration in the patient which the haematologist thought was due to delay in transfusion and subsequently the patient required a further two-unit blood transfusion.

Specific requirements not met (SRNM) n=12

There were 8 SCD and 4 thalassaemia patients who did not receive blood components meeting their specific requirements. In 10 of these cases, extended Rh and K-matched units were not provided. There was 1 report where antigen-negative red cells were not provided for the corresponding antigen and 1 case where CMV-negative red cells were not provided in pregnancy.

Case 23.5: Alloimmunisation after not receiving extended Rh-matched red cells in thalassaemia

A young patient with thalassaemia attended for routine transfusion but was not provided with extended Rh and K-matched red cells and subsequently developed an anti-E antibody. The reason for the error noted was that no specific system flag was in place at the laboratory to provide extended phenotype-matched red cells.

Case 23.6: Ambiguous antibody investigation report on national database (Sp-ICE)

A SCD patient in his 40s received eight units of red cells during a red cell exchange procedure. The laboratory checked the Sp-ICE record which stated there was a previous positive DAT but insufficient sample for antibody investigation. It was reported that there were no further instructions on what blood to crossmatch. It was later confirmed after contacting the previous hospital the patient had visited that he had developed an alloantibody, but this had not been updated on Sp-ICE.

Sp-ICE is an important reference point for confirming a patient's antibody status particularly if the patient has attended more than one hospital. It is vital that this record is updated in real time to ensure the information is accurate.

Case 23.7: D-positive red cells transfused to female child with SCD

Transfusion was requested for a young female with SCD with a known D-variant who should have received D-negative red cells. The Blood Service supplied D-positive units following the 'over the telephone' request. The LIMS flagged up that there was a mismatch in relation to the specific transfusion requirement. The laboratory staff overrode the system and issued the units. Explanation provided by the laboratory staff for the error included low staffing levels and increased workload.

Case 23.8: Laboratory not informed of a diagnosis of SCD when requesting red cells

A male child with SCD was admitted to critical care and required a four-unit red cell transfusion. The transfusion was requested by a junior doctor who did not state on the request that the patient had SCD, and the transfusion laboratory staff were not aware of the diagnosis or need to provide extended Rh and K-matched and HbS-negative red cells.

Uncommon complications of transfusion n=1

Case 23.9: Seizures during transfusion

A pregnant patient in her 30s underwent an elective 10-unit red cell exchange for sickle cell disease. This was the patient's seventh red cell exchange in the last 18 months and all previous procedures had been well tolerated. The patient suffered a prolonged grand mal seizure during the 10th red cell exchange unit. There was no change in blood pressure or other observations. The patient received a calcium infusion, IV diazepam, but had recurrence of seizures after 10-15 minutes. The patient was intubated, ventilated and transferred for escalation of care. A head CT scan was normal and CT

venogram showed no abnormality either. The patient made a full recovery and was discharged 48 hours after admission. There was no evidence of a serological or haemolytic transfusion reaction. No biochemical abnormality was found. It was later discovered that the patient did have a history of seizures which had not previously been recorded. The seizure threshold could have been lowered due to pregnancy and other medication (cyclizine, opiates, venlafaxine) worsened by possible citrate with transient hypocalcaemia relating to the exchange transfusion.

Near miss n=1

Case 23.10: Surgical team arranging transfusion in SCD

A patient with SCD in his 50s was admitted for a renal transplant. Three units of red cells were requested however the transfusion laboratory was not informed of the diagnosis of SCD. Due to a grouping anomaly the laboratory contacted the patient's usual hospital and discovered the patient was known to have SCD. The haematology team were only informed following transfusion that the patient was admitted. The learning point highlighted by the reporter was that sickle cell patients requiring transfusion should be discussed with the haematology team.

'No One's Listening' APPG report

An APPG inquiry report 'No One's Listening: An inquiry into the avoidable deaths and failures of care for sickle cell patients in secondary care' was published in November 2021 (Sickle Cell Society 2021).

This report highlighted multiple failures in sickle cell care and has made 31 recommendations including the following which must be put in place to enhance patient safety and promote safe transfusion practice.

Improving joined-up sickle cell care:

All NHS Trusts/Health Boards to require that haematology teams are informed when sickle cell patients are admitted to hospital.

Improving education and training for healthcare professionals about sickle cell care:

Undergraduate training in sickle cell as part of curriculums for training healthcare professionals.

Health Education England to provide additional funding for sickle cell training programmes including for training in the delivery of blood transfusion for non-specialist doctors.

National Haemoglobinopathy Registry (NHR)

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The NHR is a register of people in the UK with all types of inherited red cell disorders. The register is held by NHS England and is intended to support direct clinical care, and for commissioning services within England.

The current system to find up-to-date transfusion records about the red cell antibody status of a patient requires hospital transfusion laboratories to opt-in to the NHSBT Sp-ICE system, and for patients to carry antibody cards if they have been transfused elsewhere.

As part of a national initiative to improve access to antibody results and enhance patient safety, a NHR-NHSBT linkage is being developed. This will allow NHSBT to upload antibody test results and eventually genotype and phenotype results from the Hematos system within NHSBT to the NHR based on NHS number and diagnosis. Transfusion laboratories will be able to upload antibody test results onto the NHR.

These changes will allow clinical teams to have an up-to-date record of antibody status on the NHR which will be a step further in improving patient safety, reduce risk of DHTR and development of alloimmunisation.

For further information please visit https://nhr.mdsas.com

Conclusion

HTR are a significant risk for haemoglobinopathy patients, in particular those with SCD. To minimise this risk, it is important that each transfusion decision is carefully considered, taking into account individual risk factors and potential benefits.

A detailed history should be obtained for all haemoglobinopathy patients requiring transfusion including any prior alloimmunisation or transfusion reactions. Clear communication between clinical and laboratory staff is essential to ensure specific transfusion requirements are provided. All hospitals should have protocols for the management of acute complications of SCD. Specialist haemoglobinopathy teams should be involved in the management of all these patients.

The APPG report has highlighted the inadequacies in healthcare for sickle cell patients. SHOT supports the recommendations set out in the report. Education and training for all healthcare professionals is essential to ensure safe transfusion practice, reducing the risk of morbidity and mortality.

To support safe transfusion in haemoglobinopathy patients, several new online resources have been developed by NHSBT and SHOT (listed below). These resources are intended for use within HCC and specialist hospital teams to support the development of training programmes for their haemoglobinopathy networks.

Recommended resources

SHOT Bite No. 14: Haemoglobinopathies
SHOT Bite No. 15: Hyperhaemolysis
https://www.shotuk.org/resources/current-resources/shot-bites/

SHOT Video: Haemolytic Transfusion Reactions in patients with Haemoglobinopathies
https://www.shotuk.org/resources/current-resources/videos/

Patient Blood Management England Video: Setting up and Performing a Manual Exchange Red Cell Exchange in Sickle Cell Disease (Under 40kg)
https://youtu.be/e2itKcfXQAE

Patient Blood Management England Video: Setting up and Performing a Manual Exchange Red Cell Exchange in Sickle Cell Disease (Over 40kg)
https://youtu.be/5QFiLziDxbc

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