Haemolytic Transfusion Reactions in patients with Haemoglobinopathies

Haemoglobinopathies are genetic conditions which affect haemoglobin, the oxygen carrying part of the blood. These changes in haemoglobin make-up can affect the function and structure of red blood cells and lead conditions such as sickle cell disease and Beta thalassaemia. Sickle cell disease, known as SCD, affects approximately 15,000 people in the UK and 1 in 76 babies born in the UK carry sickle cell trait. Beta thalassaemia affects approximately 1,000 people, with around 214,000 carriers.

Haemolytic transfusion reactions, known as HTR, occur when antibodies in the patient's plasma react with antigens on transfused red blood cells, causing haemolysis. This can have serious clinical impacts such as anaemia, kidney damage and death. People with haemoglobinopathies are at a higher risk of Haemolytic transfusion reactions due to the high volume of transfusions received and increased rates of alloimmunisation. Mismatches in ethnicity between the UK blood donor population and the majority of people with haemoglobinopathies also contributes to higher rates of alloimmunisation. Further complications also occur in pregnant patients with haemoglobinopathies.

There are other specific requirements to consider when selecting blood for patients with haemoglobinopathies, that may be overlooked when shared care is sub optimal: Both groups require blood which matches the patients Rh and Kell phenotype, and need to be transfused with blood which is negative for any corresponding alloantibodies the patient may have formed. Patients with sickle cell disease also require blood which is HbS negative and where possible less it should be than 10 days old. Testing for patients with haemoglobinopathies can be complicated as it is not always possible to detect all historical antibodies and there may be difficulties with phenotyping in chronically transfused patients.

Patients with SCD often have shared care and transfusion labs may not be informed that the patient:

- has sickle cell disease
- has been recently transfused
- has a record of antibodies
- has been phenotyped
- has been genotyped (nationally)

HTRs can also be overlooked as they often present as sickle cell crisis.

These combined factors mean that the patient doesn't always get the full laboratory testing required, or blood that is negative for the required antigens. In these cases, the patient is at increased risk of avoidable haemolytic transfusion reaction following an anamnestic response, or avoidable alloimmunisation.

Looking at data over the past 10 years, errors reported to SHOT mainly involve haemolytic transfusion reactions and specific requirements not met for patients with SCD, and febrile, allergic and hypotensive reactions and specific requirements not met for patients with thalassaemia.

- Preventing alloimmunisation must be a priority when managing patients with haemoglobin disorders.
- All transfusions should have a clear indication and be authorised by haematology team.
- And Any historical antibodies should be clearly documented in clinical notes and transfusion records including national databases such as Specialist Services electronic reporting using Sunquest's Integrated Clinical Environment, known as Sp-ICE, in England.

The following is a real case reported to SHOT involving care of a patient with SCD. A 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-Fya, anti-Fyb and anti-Fy3. She had been transfused with appropriate phenotype blood, and the antibodies were not detectable for several years. She underwent preoperative exchange transfusion at the specialist centre with eight units. Neither her base hospital transfusion laboratory records nor Sp-ICE data were 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-Fya and anti-Fy3 (which were identified in the eluate).
She made a full recovery.

Patients with haemoglobinopathies are also at increased risk of hyperhaemolysis. This is a severe, life threatening transfusion reaction with worsening haemolysis affecting transfused red cells and the patient's own red cells. It results in a reduction in the patient's haemoglobin to below pre-transfusion levels, which is often associated with a reticulocytopenia. There are two types of hyperhaemolysis (acute and delayed). Differentiating HH reactions and other haemolytic transfusion reactions can be difficult.

First line treatment of hyperhaemolysis is corticosteroids and intravenous immunoglobulin. Various second line treatments are emerging, and supportive therapy is often required. Despite these therapies, extreme anaemia and death may still occur, therefore close monitoring of the patients and access to specialist support is essential.

In patients with a history if hyperhaemolysis, prevention may be more effective than treatment – first line prevention is administration of corticosteroids and IVIG prior to transfusion, and in adults rituximab may also be used, if necessary, as a 2nd line approach.

SO what are the key take-home haemovigilance messages?

- Patients with haemoglobin disorders are vulnerable to transfusion complications
- Staff need to be aware about specific requirements, complications and management
- Timely and accurate communication between clinical and laboratory teams is essential
- Patient awareness and involvement are vital
- Initiatives to increase availability of better-matched donors are ongoing

Further information:

SHOT Bite No.14 - Transfusion Errors and Reactions in Patients with Haemoglobinopathies
SHOT Bite No.15 – Hyperhaemolysis
SHOT HTR and Haemoglobinopathies Webinar 2021

BSH Guidelines - Red blood cell specifications for patients with hemoglobinopathies: a systematic review and guideline (ICTM Collaboration)
Sickle Cell Society - Standards for the Clinical Care of Adults with Sickle Cell Disease in the UK
UK Thalassemia Society – Standards for the Clinical Care of Children and Adults with Thelassemia in the UK