Adverse events in people with haemoglobin disorders

Paula Bolton-Maggs
Clare Milkins
Why?

• Sickle cell disease –
  – High rate of alloimmunisation (18-36% and 57% after >200 transfusions)
  – Increasing indications for transfusion particularly for management or prevention of stroke
  – Mobile population
• Beta thalassaemia major – regular transfusions for life unless HSCT
• Recognition of high proportion of events related to failure of communication between clinical teams and laboratory
• High rate of shared care
High risk patients

- ATRs are largely unpredictable and not preventable.
- HTRs may be preventable, are often serious and may cause death.
- Avoid unnecessary transfusion.
- Transfuse cautiously and with careful observation, and advice to patients to report back if any untoward events in subsequent days.

43% deaths and major morbidity in HTR was associated with SCD.
Cumulative data for SHOT categories 1996/7-2011

n=9925

- CS: Cell salvage and autologous transfusion
- TTI: Transfusion-transmitted infection
- PTP: Post-transfusion purpura
- PUCT: Previously uncategorised complication of transfusion
- ATR: Acute transfusion reaction
- TAD: Transfusion-associated dyspnoea
- HTR: Haemolytic transfusion reaction
- TA-GvHD: Transfusion-associated graft vs host disease
- TRALI: Transfusion-related acute lung injury
- TACO: Transfusion-associated circulatory overload
- Anti-D: Anti-D errors
- HSE: Handling & storage errors
- I&U: Inappropriate & unnecessary
- IBCT: Incorrect blood component transfused

Pathological reactions which may not be preventable

Probably or possibly preventable by improved practice and monitoring

Adverse events caused by error

Number of reports

5 July 2012
SHOT Symposium
Adverse events in patients with sickle cell disease

<table>
<thead>
<tr>
<th>Category</th>
<th>2010</th>
<th>2011</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute Transfusion Reactions</td>
<td>4</td>
<td>3</td>
<td>Minor morbidity</td>
</tr>
<tr>
<td>Haemolytic Transfusion Reactions</td>
<td>4</td>
<td>5</td>
<td>1 death 2010, 5 major morbidity 2011</td>
</tr>
<tr>
<td>Transfusion-associated circulatory overload</td>
<td>0</td>
<td>1</td>
<td>ITU for ventilation and recovered</td>
</tr>
<tr>
<td>Transfusion-associated dyspnoea</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Inappropriate and unnecessary</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Special requirements not met</td>
<td>3</td>
<td>6</td>
<td>Alloimmunisation in 1</td>
</tr>
<tr>
<td>Near miss</td>
<td>2</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>13</strong></td>
<td><strong>19</strong></td>
<td></td>
</tr>
</tbody>
</table>

The median age of haemoglobinopathy patients reported to SHOT was 28 yr compared to 61 yr overall; **SCD = 20% of all DHT**
Adverse events in patients with thalassaemia

<table>
<thead>
<tr>
<th>Category</th>
<th>2010</th>
<th>2011</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute Transfusion Reactions</td>
<td>6</td>
<td>3</td>
<td>Minor morbidity</td>
</tr>
<tr>
<td>Special requirements not met</td>
<td>0</td>
<td>2</td>
<td>Not given appropriate phenotype</td>
</tr>
<tr>
<td>Handling and storage errors</td>
<td>1</td>
<td>2</td>
<td>Ward refrigerator</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Long transfusion time</td>
</tr>
<tr>
<td>TOTAL</td>
<td>7</td>
<td>7</td>
<td></td>
</tr>
</tbody>
</table>

ATR includes severe urticaria, rash, swollen lips

One other adult with HbH disease was admitted 10 days after transfusion with signs of delayed haemolysis in whom 2 new antibodies were identified, anti-E and anti-Lu\(^b\).
Delayed transfusion reactions

- Complicated and should be considered in any patient who presents about 7-21d after transfusion
- May simulate sickle cell crisis
- May be complicated by hyperhaemolysis
  - A poorly understood syndrome
  - Can be exacerbated by further transfusion
  - Treated with IVIg and steroids
  - May be related to macrophage activity
Interval in days between administration of the implicated transfusion and signs or symptoms of a DHTR

![Bar Chart](image-url)
HTRs

• Severe immune haemolysis
  – Range of antibody specificities
  – Often multiple antibodies
  – Often complicated or masked by SCC
  – Sometimes avoidable

• Hyperhaemolytic transfusion reactions
  – With or without alloantibodies
HTRs

- Severe immune haemolysis
  - Range of antibody specificities
  - Often multiple antibodies
  - Often complicated or masked by SCC
  - Sometimes avoidable

- Hyperhaemolytic transfusion reactions
  - With or without alloantibodies
Special Requirements Not Met

• Shared care
  – Transfusion or antibody history not shared

• Presentation at different hospital
  – Fact that patient has SCD not conveyed to the laboratory

Avoidable HTR following anamnestic response

Avoidable alloimmunisation
Case 1: Immune haemolysis in a shared care patient with sickle cell disease

- A patient with known SCD was admitted with a minor stroke, and an exchange transfusion was arranged for the next morning at the nearest specialist centre.
- A crossmatch sample was taken at the first hospital using the NHS number and dispatched urgently for testing and crossmatching at the second hospital, the specialist centre.
- The first hospital had a record of anti-E, which was confirmed by the second centre on testing.
The patient was discharged 3 days later, but was admitted to a third hospital 9 days after the transfusion with falling Hb from 11.0g/dL to 3.8g/dL and increased bilirubin.

The historical record at the 3rd site confirmed the anti-E but also listed an anti-Jk^b and anti-S.

The reference laboratory confirmed anti-Jk^b and anti-S in the eluate confirming the clinical picture of a delayed transfusion reaction.
Case 2: Death due to hyperhaemolysis (2010)

- A child with SCD with Hb 8.1g/dL received a one-unit transfusion prior to tonsillectomy.
- 13 days later, Hb 5.4g/dL, transfused 2 units, deteriorated with Hb 4.8g/dL.
- Transferred to paediatric ITU, exacerbated haemolysis with further transfusion despite IVIg and steroids. No antibodies detected.
- Developed multi-organ failure and died
Case 3: Transfusion reaction

- A SCD patient presented with shortness of breath, tachycardia, back pain, hypotension and vomiting, and haemoglobinuria, 7 days after an 8-unit exchange transfusion.
- The bilirubin 216 micromol/L, creatinine 181 micromol/L.
- RC reference lab found auto anti-D, plus weak allo anti-C and anti-Fy\(^a\).
- All transfused units were RhC-, Fy\(^a\)-, and although the DAT was positive, the eluate was non-reactive.
- The cause of this reaction is unclear, but the patient subsequently suffered another similar episode following transfusion and this may be hyperhaemolysis.
Failure to provide appropriate red cells

- Diagnosis not transmitted to laboratory staff
- Patient presents to another hospital
- Historical antibodies may be undetectable
Case 4: Failure to provide phenotyped red cells results in haemolytic transfusion reaction

- A patient with SCD was admitted 7 days after transfusion with symptoms suggestive of HTR.
- The antibody screen showed 5 different alloantibodies (anti-D, -E, -C\textsuperscript{w}, JK\textsuperscript{b}, Lu\textsuperscript{a}).
- Transfused at a different hospital where the laboratory was not informed of the diagnosis of SCD.
Case 5: Preventable alloimmunisation:

- A young woman was transfused with two units in January on the basis of a verbal request.
- She was usually seen at another hospital for her SCD which was not communicated to the laboratory.
- In May she required further transfusion and this time the diagnosis was included on the request form.
- She had developed anti-E.
- Retrospective assessment confirmed that one of the units transfused in January was RhE positive.
Case 6: Transfusion associated circulatory overload

- A 50 year old woman with sickle cell disease was admitted in sickle crisis with Hb 2.8 g/dL.
- She was transfused at a rate of 140 mL/hr.
- During the 2nd unit she developed chest pain and respiratory distress with $\text{SaO}_2$ of 56% in air with gross pulmonary oedema on the chest X ray.
- She was transferred from a haematology ward to the intensive therapy unit (ITU) and ventilated, and made a full recovery.
- There was no history of cardiac disease.
Preventable risk of alloimmunisation

- Avoid unnecessary transfusion
- Inform laboratory of the diagnosis
Case 7: Inappropriate and unnecessary transfusion

- An 18 year old man with SCD was admitted with a sickling crisis and was unnecessarily transfused a unit of red cells.
- The A&E clinicians and the BMS were not aware of the guidance that all potential transfusions in SCD should be referred to a haematologist.
UK Sickle Cell Disease Standards

• Perform full phenotype at first opportunity
• Red cells should be matched for D,C,E,c,e and Kell, and be HbS negative, and ideally <2 wks old.
• Transfusion laboratories must keep an accurate and detailed transfusion history of every SCD patient who has contact with the hospital
How far to match the red cells?

- Rh and K is relatively simple for any transfusion laboratory and prevents more than 50% of alloimmunisations.
- Increased recognition of RhC and RhE molecular variants in people of African origin.
- Ro (cDe) is common and require E and C neg red cells (rr or Ro).
- More extended matching can be reserved for those who develop antibodies.
- Many SCD patients are Fy$^a$ and Fy$^b$ negative (68% Africans) but very rare in Caucasians.
Problems

• Common for SCD patients to present to several hospitals
• Confusion about names and name changes
• Although cards are encouraged, SCD patients may have 3
  – Disease details
  – Red cell phenotype
  – Irregular red cell antibodies
• Many health care workers do not know what they mean, and verbal messages may be wrong
SHOT Recommendations

- Clinicians must tell the laboratory about the diagnosis – mandatory field on transfusion request
- Patients need a single source of information to show clinical staff and should be educated to present it at every hospital contact
- Core curricula should ensure adequate education about haemoglobin disorders and transfusion needs
The Future

- National register?
- New guidelines in preparation