King's College Hospital NHS
NHS Foundation Trust

Transfusion In the Haemoglobinopathies

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Transfusion History

- Transfusion in sickle cell being used for many years – sub-Saharan, unknown exactly how long.
- Evidence based practice – 1990 STOP trial looking at transfusion in paediatrics with stroke – first documented clinical indication for transfusion in sickle
- Thalassaemia – evidence of the use of transfusion in 1925
- Improved methods – unit selection, automated exchange

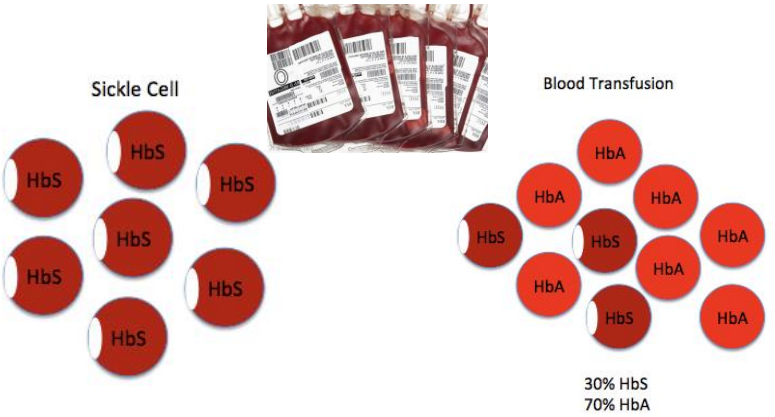
Indications for Transfusion

- Reduction of HbS% (Sickle/Sickle Beta-Thal)
- Increase oxygen carrying capacity (sickle/thal)
- Increase in healthy circulating red cells (sickle/thal)
  - Prevent/ stop recurrence of adverse sickle related events: risk of/ strokes, ACS, priapism, sickle related emergencies e.g. splenic/hepatic sequestration
  - Treat symptomatic anaemia
  - In surgery – pre –surgery to reduce S%
- Suppression of ineffective erythropoiesis

Transfusion in Thalassaemia

- Main stay treatment of Thal major and some intermedia
- Main purpose –
  - Improve the symptoms of anaemia
    - Poor growth
    - Organ dysfunction
    - Cardiac disease
    - Dysmorphic bone changes
  - Suppress ineffective erythropoiesis

Mechanism



Sickle Cell patient prior to transfusion (almost all blood has the potential to sickle)

Sickle Cell patient post transfusion (in this case 30% sickle blood remaining and HbA (healthy blood)

Methods of Transfusion

Simple 'top up transfusion'

- Used when there is 'room' to top up –
  - Falling Hb
  - Paediatrics
  - Patients who can not have exchanges
- Based on how much room to 'top up'

e.g. current Hb 60g/L steady state Hb 10g/L space to top up 40g/L packed red cells (3-4 units)

- Can be used as part of a chronic top up transfusion regime or in sickle related emergency.
- Main outcome – to increase Hb –will also dilute HbS – to a degree
- Used as a main 'management' for Beta thalassaemia

Methods of Transfusion

- Positives of simple 'top up' transfusions
  - Can be carried out quickly on the ward by most nursing staff
  - No specialist equipment required
  - Inexpensive
  - Reduced donor exposure/ low blood use
- Negatives
  - Can not be used where there is 'no space' to top up
  - Can lead to antibody production
  - When used frequently – will lead to iron overload
  - Could lead to hyper viscosity in sequestration

Methods of Transfusion

Manual Exchange

- Manual removal of whole blood from the patient – using syringes, replaced with packed red cells
- Often used in a emergency when automated exchange machines and staff are not available
- Carried out the bed side by a doctor or trained nurse

Methods of Transfusion

- Positives of Manual Exchange
  - No specialist equipment required
  - Inexpensive
  - Can be carried out quickly in an emergency
  - Can be completed at the bedside
  - Would result in less circulating serum iron
- Negatives
  - Very 'crude' method – whole blood out – packed cells in
  - Can lead to antibody production
  - When used, can lead to deficiencies in electrolytes, clotting factors, platelets etc.
  - Very few people trained to safely carry out the procedure

Methods of Transfusion

Automated exchange

- Automated removal of red cells via gravitational filtration from the patient – using apheresis machinery , replaced with packed red cells
- Used as part of automated exchange programs for approved indications and sickle related emergencies
- Volume of the transfusion calculated on the basis of desired HbS% body weight – total blood volume
- Requires trained staff to carry out the procedure

Methods of Transfusion

- Positives of Automated Exchange
  - Can maintain steady haemoglobin (can be done within the steady state)
  - Automated – less room for human error (**less**)
  - Removes mainly packed red cells – so less likely to cause coagulation/electrolyte imbalance
  - Most effective method of reducing sickling red cells/HbS%
- Negatives
  - Expensive (kits, staff, slots in apheresis)
  - Requires anywhere between four-ten units of blood
  - Requires trained staff and specialist equipment
  - May not be readily available
  - Requires good IV access

SHOT

Serious Hazards of Transfusion

Serious Hazards Of Transfusion SHOT

'An independent Professionally led Haemovigilance scheme'

Identify issues and risks and form recommendations

Hospitals reports all adverse incidents relating to blood products and transfusion

Risks of Transfusion

Viral

HIV 1&2	1 : 7 million
Hep C	1 : 26 million
Hep B	1 : 1.6 million
Hep E	

Bacterial

RBC 1:500,000

Platelets 1:12,000

4 near misses in 2016 (3x S.Aureus)

Other

Acute Haemolytic Reaction	1:250,000
Delayed Haemolytic Reaction	1:1000
TACO	1:300
TRALI	1:5,000-200,000
TA-GVHD	1:1,000,000
Antibody sensitisation/ Allo - Auto	

Other things to worry about:

- Migration related risks
  - Unknown risk

Unknown Risk Ratio with variant and non variant CJD

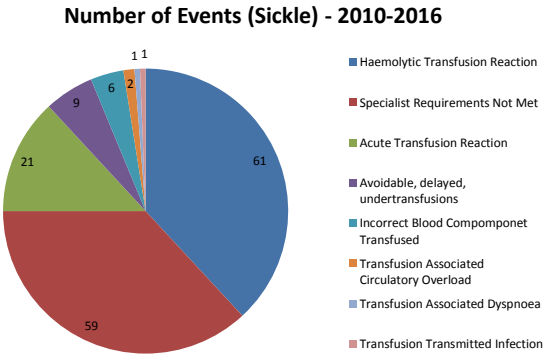
Human Error 1:300

Handbook of Transfusion Medicine, 2014

Adverse Events

Serious Hazards Of Transfusion **SHOT**

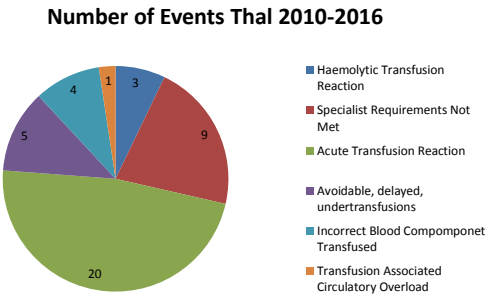
Sickle Cell
n=160



Adverse Events

Thalassaemia
n=42

SHOT



Adverse effects of Transfusion

- Alloimmunisation – antibody production
  - Matching for ABO, CDE K typing
  - As many as 500 not typed for
  - Sickle patients likely to become 'responders'
  - Many make multiple antibodies
- Auto antibodies (against own blood)
- Iron overload (systemic/ organ) manage with chelation

Iron Overload

- Occurs mainly in top up transfusions
- The body does not readily excrete iron and will store it
- One unit of blood = 250mg iron (person needs approx. 1 mg iron to replenish iron stores)

- Can cause:
  - Increased serum iron
  - Iron deposits in the organs – liver, heart, endocrine glands
  - Cirrhosis of the liver – zonal iron deposits to fibrosis
  - Diabetes – caused by selective iron deposit in the pancreatic islet beta cells
  - Cardiomyopathy
  - Arthritis – calcium pyrophosphate
  - Tanned skin (bronze diabetes)
  - Testicular failure

Treatments for IO

- Venesection/ blood letting/ erythocytopheresis
- Iron chelation –
  - Deferasirox
  - Deferoxamine
  - Deferiprone
- Combined therapy
  - Chelation and exchange

The Provision of Blood

- Blood comes from voluntary donations
  - Majority of blood donations (almost 95% will come from ethnic majority groups)
  - 5% will be from BAME backgrounds
  - Some antigens only exist in some ethnic groups (U in the white population)
  - U negative exists only in the black population
  - U negative units often needed for sickle patients
- Most units are 'wet'
- Some 'specialist units' are frozen (liverpool)
- Sickle requirement- less than 7-10 days old HbS neg CDE and K matched
- High requirement for r^0 subtype units (Dce) – only 2% donors

Case Study

B RhD positive

DAT

IgG	IgA	IgM	C3c	C3d	Control
1+	0	0	0	0	0

Red Cell Antibody Results

Type	Specificity	Technique	Sample Type
Auto	Pan-reactive antibody	IAT and enzyme IAT	Plasma
Allo	Anti-E	Previously reported; not detected on this occasion	Plasma
Allo	Anti-S	Previously reported; not detected on this occasion	Plasma
Allo	Anti-Fy3	Previously reported; not detected on this occasion	Plasma
Allo	Anti-Jkb	Previously reported; not detected on this occasion	Plasma
Allo	Anti-McCa	Previously reported; not detected on this occasion	Plasma
Not specified	Anti-HI	Previously reported; not detected on this occasion	Plasma

Virtually impossible to get suitable units for transfusion

Could never have an automated exchange

Clinical Setting

- Necessity of transfusion –
  - donor exposure
  - Risks of Transfusion
- Frequency
  - Top ups
  - Automated
  - Long term (indications)
- Feasibility
  - Access
  - Blood availability
- Special Requirements
  - HbS Neg
  - Exchange units – paediatric
  - Antigen matched
  - Transfusion history
- Advice for patients
  - Risks in transfusion
  - Education
  - Symptoms of reactions (DHTR)
  - Importance of compliance

Alternatives

- Bone marrow transplantation –
  - Not suitable for all
  - Rely on the condition of the patient
- Hydroxyurea
  - Breakthrough treatment in sickle
  - refractory patients, poor compliance due to side effects

Nothing quite like a bag of blood, its easy and it works

King's

BLOOD DOESN'T GROW ON TREES