Triggers of Transfusion of RBCs

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Overview

- Definition of transfusion thresholds
- Mechanisms of adaptation to anaemia
- How RBC transfusion affect adaptation mechanisms to anaemia
- Triggers of RBC transfusion
  1. Blood loss
  2. Adult critical ill patients
  3. Neonates and children
  4. Chronic anaemia
Definition
**Transfusion Trigger:** is the Hb concentration at or below which packed red cells are usually ordered for transfusion.
How we can determine the ideal Hb Concentration for various groups or individual patients??

Transfusion threshold (trigger) is the lowest concentration of Hb that is not associated with symptoms of anaemia. BCSH 2001, guidelines
Mechanisms of adaptation to anaemia
Mechanisms of adaptation to anaemia

- Increased cardiac output
- Increased cardiac artery blood flow
- Increased oxygen extraction
- Increase of red blood cell 2,3 DPG (diphosphoglycerate)
- Increase production of EPO
- Increase erythropoiesis

Maintain tissue oxygenation
The tissue oxygenation depends on

- The concentration of Hb
- The $O_2$ saturation of Hb
- The oxygen tension in the tissues
- The affinity of Hb to $O_2$
- The $O_2$ requirements of tissues
Why we transfuse patients?

- To increase Hb  F/T
- To maintain blood low in microvascular circulation  F/T
- To maintain tissue oxygenation  F/T
Symptoms of anaemia = tissue hypoxia
How we determine the transfusion threshold that will prevent hypoxia in any individual patient

??
Parameters that affect the adaptation mechanisms to anaemia

- Acute/chronic anaemia
- Underlying conditions
- Transfusion of RBC??
Clinical parameters to evaluate when consider transfusion

- Age T/F
- Signs of anaemia T/F
- Speed of blood loss T/F
- Volume of blood loss T/F
- Cardiac function T/F
- Lung function T/F
- Ischemic heart disease T/F
- Pharmacological treatments T/F
How RBC transfusion affect adaptation mechanisms to anaemia
Red cells - Transfusion Triggers

TRICC Study, Hebert et al 1998

Prehistory

history
Red cells - Transfusion Triggers
TRICCC Transfusion Requirements in Critical Care

Hb 7-9g/dl vs Hb 10g/dl, 30 day mortality similar
Red cells - Transfusion Triggers
TRICC Transfusion Requirements in Critical Care

Hb 7-9g/dl vs Hb 10g/dl,

Patients with

- Acute Physiology and Chronic Health Evaluation II score of < or =20
  
mortality 8.7 vs 16.1, p=0.03

- <55 years of age
  
mortality 5.7 vs 13, p=0.02

Transfusion harmed the patients?
Why transfusion harmed the patients?
### Storage lesions

#### CPDA-1 days of storage

<table>
<thead>
<tr>
<th></th>
<th>DAY 0</th>
<th>DAY 35</th>
</tr>
</thead>
<tbody>
<tr>
<td>% viability</td>
<td>100</td>
<td>79</td>
</tr>
<tr>
<td>pH</td>
<td>7.6</td>
<td>6.98</td>
</tr>
<tr>
<td>ATP</td>
<td>100</td>
<td>56</td>
</tr>
<tr>
<td>2,3 DPG</td>
<td>100</td>
<td>&lt; 10</td>
</tr>
<tr>
<td>K+</td>
<td>4.2</td>
<td>26.3</td>
</tr>
</tbody>
</table>

![Bar chart showing percentage reduction in 2,3 DPG over storage days](chart.png)
Storage lesions

Loss of NO regulatory mechanisms

*vasoconstriction*

Formation of microparticles

*initiation of thrombotic process*

Activation of complement

*initiation of thrombotic process*

*Initiation of inflammatory process*

Changes in cell membrane

*autoimmune responses*
How RBC transfusion affect adaptation mechanisms to anaemia

Inflammation response

Initiation of thrombotic processes

2,3 DPG

vasoconstriction

Bone marrow

Lungs

Heart

Peripheral organs

Kidney

Respiratory rate ↑

Pulse rate ↑
Cardiac output ↑
Blood flow ↑

Tissue pH ↓  O₂ extraction ↑
Vasodilation
Blood shift

Erythropoietin release ↑

Erythropoiesis ↑
Red cells - Transfusion Triggers

To determine transfusion triggers good quality of clinical studies are needed to provide evidence
## Decision criteria to transfuse in acute anaemia (blood loss)

**BCSH guidelines for the clinical use of red blood cells, 2001**

<table>
<thead>
<tr>
<th>Class of haemorrhage</th>
<th>% reduction in blood volume</th>
<th>mL+</th>
<th>Indication for transfusion</th>
<th>GoR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class I</td>
<td>&lt;15%</td>
<td>&lt;750</td>
<td>No necessary*</td>
<td>2C</td>
</tr>
<tr>
<td>Class II</td>
<td>15-30%</td>
<td>750-1500</td>
<td>No necessary*</td>
<td>2C</td>
</tr>
<tr>
<td>Class III</td>
<td>30-40%</td>
<td>1500-2000</td>
<td>Probably necessary</td>
<td>2C</td>
</tr>
<tr>
<td>Class IV</td>
<td>&gt;40%</td>
<td>&gt;2000</td>
<td>necessary</td>
<td>2C</td>
</tr>
</tbody>
</table>
Guidelines on the management of anaemia and red cell transfusion in adult critically ill patients

Andrew Retter, Duncan Wyncoll, Rupert Pearse, Damien Carson, Stuart McKechnie, Simon Stanworth, Shubha Allard, Dafydd Thomas, Tim Walsh and British Committee for Standards in Haematology
Figure 1. A suggested approach to transfusion in critical care

Is the patient anaemic and haemodynamically stable?

- **Yes**
  - Is the Hb >90 g/l?
    - **Yes**
      - DO NOT TRANSFUSE
    - **No**
      - Does the patient have acute coronary syndrome, severe sepsis or a neurological injury?
        - **Yes**
          - SEVERE SEPSIS
            - Early (<6h from onset) and evidence of tissue hypoxia
              - Target Hb 90 – 100 g/l
            - Late (>6h from onset)
              - Target Hb >70 g/l
        - **No**
          - GENERAL CRITICAL CARE
            - Use a default Hb trigger of <70 g/l with a target range 70-90 g/l

Be LESS confident using an Hb trigger of 70 g/l (but target Hb should be between 70-90 g/l) IF:
- The patient is elderly with significant cardiorespiratory co-morbidities.
- The patient has evidence of inadequate oxygen supply to the tissues (high lactate or low ScvO₂).

Be confident using an Hb trigger of 70 g/l IF:
- The patient is younger than 55 years.
- The patient’s severity of illness is relatively low

ISCHAEMIC HEART DISEASE
- Acute coronary syndrome
  - Target Hb >80 – 90 g/l
- Patient with stable angina
  - Target Hb >70 g/l

NEURO CRITICAL CARE
- Traumatic brain injury and/or cerebral ischaemia
  - Target Hb 90 g/l
- Subarachnoid haemorrhage
  - Target Hb >80 -100 g/l
Case study I

A 56 years old male developed end stage renal disease drop the Hb from 123 g/L to 96 g/L (12.3 g/L to 9.6 g/dL) over the last 3 months and an MCV of 80 fL.

Serum iron 19 ug/dl
TIBC  25 ug/dl
Trasferrin saturation 18%
Ferritin 150 mcg/l
EPO 20 Units/l
Hypochromic cells 18%

Transfusion ??
## Decision criteria for transfusion in chronic anaemia

**BCSH guidelines for the clinical use of red blood cells, 2001**

<table>
<thead>
<tr>
<th>Hb value</th>
<th>GoR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb&lt;8g/dl</td>
<td>1A</td>
</tr>
<tr>
<td></td>
<td>After evaluation of aetiopathogenesis and consideration of alternatives to transfusion</td>
</tr>
<tr>
<td>Hb 8-10g/dl</td>
<td>2C</td>
</tr>
<tr>
<td></td>
<td>Transfuse when is a marked decrease in oxygenation (comorbidities eg heart disease)</td>
</tr>
<tr>
<td></td>
<td>Chemotherapy</td>
</tr>
<tr>
<td></td>
<td>Thrombocytopenia</td>
</tr>
<tr>
<td>Hb 9-9.5 g/dl</td>
<td>2C</td>
</tr>
<tr>
<td></td>
<td>Thalassaemia</td>
</tr>
</tbody>
</table>
Chronic anaemia

Patients undergoing chemo or radio

Threshold Hb 10g/dl

• to counteract the protective effect of hypoxia on the neoplasia
• to improve the pharmacokinetics of some chemotherapeutic agents
Chronic anaemia

Threshold Hb 8-10g/dl

Co-morbidities that affect cardiac, respiratory function

Hb 10 g/dl?

Take into consideration

- Iron overload
- Adaptation to anaemia

Research on quality of life parameters to tailor transfusions
Chronic anaemia
Thalassaemia major

Why these children should be transfused?
What should be the aim?
Chronic anaemia
Thalassaemia major

Why we do not over transfuse?
To reduce iron overload

Blood transfusions → 1–3.5 g of excess iron per year
Increased intestinal iron absorption

IRON OVERLOAD

Monitoring of iron levels required
Chronic anaemia subgroups

**Thalassaemia**
*Threshold 9-9.5*
To inhibit bone marrow erythropoiesis
To reduce iron overload

**Sickle cell disease**
*No Threshold*
Transfuse for anaemia and venocclusive crisis

to prevent or to stop intravascular sickling by diluting the pathological circulating RBC with normal RBCs.

HbS<30%
Surrogate markers of anaemia
- Respiratory irregularity
- Tachycardia
- Poor weight gaining
- Poor suck
- Lethargy
- Increased blood lactate levels

Tissue O₂ extraction >40% ?

It is impossible to produce clear evidence based criteria for the administration of red cells in the neonate period
## Neonates

Recommendations for the transfusion of red blood cells Blood Transf 2009;7:49-64

<table>
<thead>
<tr>
<th>Threshold</th>
<th>GoR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb 12-13g/dl</td>
<td>24 hours of life</td>
</tr>
<tr>
<td></td>
<td>In the presence of cardiac or respiratory failure</td>
</tr>
<tr>
<td>Hb 10 g/dl</td>
<td>&gt;24 hours</td>
</tr>
</tbody>
</table>
References

Guidelines on the management of anaemia and red cell transfusion in critical ill patients, BJH 2013; 160:445-464

Recommendations for the transfusion of red blood cells Blood Transf 2009;7:49-64

Transfusion guidelines for neonates and older children BJH 2004;124:433-453

The clinical use of red cell transfusions BJH 2001;113:24-31

Guidelines for the use of platelet transfusions BJH 2003;122:10-23
Cases study I
Chronic anaemia

Patient A
A 35 years old female patient visits her GP complaining for dizziness and tiredness

WBC 5.7x10⁹/L
RBC: 3.02 x10¹² /L
HGB: 8.1 g/dL
HCT: 25.2%
MCV: 83 fl
PLT: 450x10⁹/L

Patient B
A 70 year male patient visits his GP complaining for tiredness and breathlessness at rest

WBC 5.7x10⁹/L
RBC: 3.02 x10¹² /L
HGB: 8.1 g/dL
HCT: 25.2%
MCV: 83 fl
PLT: 450x10⁹/L

Should patients be transfused??
Chronic anaemia

Patient A

Ferritin 2 mcg/L (normal values >15mcg/L)
TIBC increased
Iron levels low
Transferrin saturation low

Patient B

Ferritin 2 mcg/L normal values >15mcg/L
TIBC increased
Iron levels low
Transferrin saturation low

Both iron deficient. Treat with iron supplements.
Investigate patient B for GI bleed.
Case study  III

An athletic 80 year old lady, on return from her vacation in Florida, complained she could not longer play tennis because of pain, soreness and weakness in her shoulders. She appeared healthy but had tenderness of the shoulder girdle musculature. A clinical diagnosis of polymyalgia rheumatica was entertained. The following laboratory results were consistent with the diagnosis:

- Hb 9.5 g/dl
- MCV 82 fl (normal 85-95)
- ESR 94 mm
- Serum iron 4 ug/dl (low)
- Trasferrin 40 ug/dl
- Ferritin 450 mg/L
- Saturation of trasferrin 10%

What is the diagnosis of anaemia? What are the therapeutic options?