Sikkelcelziekte en transfusiebeleid

Wanneer (niet)?

Jean-Louis Kerkhoffs
Transfusie specialist Sanquin
Internist-Hematoloog HagaZiekenhuis
INTRODUCTION

- SCD in brief
- Acute indications for transfusion of RBCx in SCD
- Chronic indications for transfusion of RBCx in SCD
- Risks of transfusions in SCD
- Exchange versus simple RBC transfusions
- General remarks with regard to type and dose of RBCs
- Summary of indications
SICKLE CELL DISEASE (SCD)

- Caused by a glu-val substitution at the 6th codon of the beta-globine gene
- One of the most prevalent inherited disorders worldwide
- HbS polymerizes at deoxygenation causing hemolysis and “stiff” red cells
- Leading to several acute and chronic complications and a reduced life expectancy

TRANSIT TIME!
COMPLICATIONS

Cerebral Vascular Bleeding (Stroke)
- Cerebrovascular accident

Auditory Impairment
- Inner ear dysfunction

Hepatomegaly
- (Choleliathiasis, jaundice)

Growth Impairment
- (Endocrine dysfunction)

Renal Pathology
- (e.g. Haematuria, Enuresis)
- (Papillary necrosis)
- (Sequestration)

Micro-Vascular Occlusions
- (e.g. Mesenteric)

Hand Foot Syndrome
- (Dactylitis)

Priapism
- (Involuntary erection of penis)

Physical Disability
- (Bony deformity)

Diploe Expansion
- (Skull bone expansion)

Retinopathy

Cardiomegaly

Chest Syndrome
- (Pulmonary)

Splenomegaly

Delayed Puberty

Reduced Fertility

Skeleto-pathology
- (Aplastic crisis)
- (Osteonecrosis)
- (Leg ulcers)

Obstetric Complications

Immunosuppression
- Chronic haemolytic anaemia
- Psychosocial implications
INDICATIONS (GENERAL)

- Anemia related
- Related to vasculopathy
- Related to vaso-obstruction
- Specific circumstances

- Triggers are usually: Hb/Ht and HbS%
ACUTE INDICATIONS

1. Hb triggered
   a) Splenic sequestration
   b) Aplastic crisis
   c) Hemolytic crisis

2. HbS triggered
   a) ACS
   b) CVA
   c) MOF
SPECIAL CONDITIONS

- Surgery
- Pregnancy
A COMPARISON OF CONSERVATIVE AND AGGRESSIVE TRANSFUSION REGIMENS IN THE PERIOPERATIVE MANAGEMENT OF SICKLE CELL DISEASE

Elliot P. Vichinsky, M.D., Charles M. Haberkern, M.D., Lynne Neumayr, M.D., Ann Noonan Earles, R.N., P.N.P., Dennis Black, Ph.D., Mabel Koshy, M.D., Charles Pegelow, M.D.,

\[ T_k = C_k \]

B_k

A_k

TAPS ??
72 pregnant females were randomized; 36 received prophylactic RBCx and 36 received RBCx on demand.

Perinatal outcome: n.s. different.

The occurrence of a perinatal death in a previous pregnancy and the presence of twins in the present pregnancy were two major risk factors for an unfavorable outcome.

Prophylactic transfusion significantly reduced the incidence of painful crises of sickle cell disease (P<0.01) and substantially reduced the cumulative incidence of other complications of this disorder (P = 0.07).

Increases in costs, the number of hospitalizations, and the risk of alloimmunization were disadvantages of prophylactic transfusion.
CHRONIC INDICATIONS

1. Hb triggered: none

2. HbS triggered:
   a) CVA secondary prevention
   b) Abnormale TCD
   c) Recurrent ACS
   d) Recurrent vaso-occlusion
STOP TRIAL

- n = 130 children, age 8.3 ± 3.3 years with increased blood-flow velocity measured using TCD (velocity > 200 cm/sec) were randomized to receive chronic transfusions to reduce HbS below 30% (n = 63) versus standard care (n = 67).

- Outcome measure: the incidence of stroke

- Trial was terminated early

12 strokes in the standard care group versus 1 in the chronic transfusion group
STOP - 2

- **n = 79** children with a normalised TCD were randomized to either continue (**n = 38**) or stop chronic transfusion therapy (**n = 41**).

- **Outcome measure**: stroke or conversion to abnormal TCD.

- **Trial was stopped early.**

Impact of chronic transfusion on incidence of pain and acute chest syndrome during the Stroke Prevention Trial (STOP) in sickle-cell anemia

Scott T. Miller, MD, Elizabeth Wright, PhD, Miguel Abboud, MD, Brian Berman, MD, Bea Files, MD, Charles D. Scher, MD, Lori Styles, MD, and Robert J. Adams, MD, for the STOP Investigators

<table>
<thead>
<tr>
<th>Intent to treat</th>
<th>Transfusion</th>
<th>Standard care</th>
<th>Poisson R</th>
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<tbody>
<tr>
<td>N</td>
<td>63</td>
<td>66</td>
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<tr>
<td>Patient-years</td>
<td>104.96</td>
<td>97.88</td>
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<tr>
<td>No. patients with ACS</td>
<td>4</td>
<td>14</td>
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<tr>
<td>Total ACS events</td>
<td>5</td>
<td>15</td>
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<tr>
<td>ACS events/100 patient-years</td>
<td>4.8</td>
<td>15.3</td>
<td>0.0027</td>
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<tr>
<td>No. patients with pain</td>
<td>11</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>Total pain events</td>
<td>17</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>Pain events/100 patient-years</td>
<td>16.2</td>
<td>27.6</td>
<td>0.13</td>
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Compliant patients

<table>
<thead>
<tr>
<th>Intent to treat</th>
<th>Transfusion</th>
<th>Standard care</th>
<th>Poisson R</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>59</td>
<td>65</td>
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<tr>
<td>Patient-years</td>
<td>92.78</td>
<td>95.84</td>
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<tr>
<td>No. patients with ACS</td>
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<td>14</td>
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<tr>
<td>Total ACS events</td>
<td>2</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>ACS events/100 patient-years</td>
<td>2.2</td>
<td>15.7</td>
<td>0.0001</td>
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<tr>
<td>No. patients with pain events</td>
<td>6</td>
<td>12</td>
<td></td>
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<tr>
<td>Total pain events</td>
<td>9</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>Pain events/100 patient-years</td>
<td>9.7</td>
<td>27.1</td>
<td>0.014</td>
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</table>

ACS, Acute chest syndrome.

(J Pediatr 2001;139:785–9)
RISKS OF TRANSFUSION

1. The formation of red cell allo-antibodies
2. Hyperhemolysis
3. Hyperviscosity
4. Iron overload
<table>
<thead>
<tr>
<th>studie</th>
<th>n pat</th>
<th>Allo ab (% pt)</th>
<th>Auto ab</th>
<th>Match strategy</th>
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<tr>
<td></td>
<td></td>
<td>tot</td>
<td>1</td>
<td>&gt; 1</td>
</tr>
<tr>
<td>Ameen (2003)</td>
<td>190 (thal)</td>
<td>30</td>
<td>13</td>
<td>17</td>
</tr>
<tr>
<td>Moreira (1996)</td>
<td>85</td>
<td>13</td>
<td>8</td>
<td>5</td>
</tr>
<tr>
<td>Vichinsky (1990)</td>
<td>107</td>
<td>30</td>
<td>14</td>
<td>16</td>
</tr>
<tr>
<td>Murao (2005)</td>
<td>828</td>
<td>10</td>
<td>6</td>
<td>4</td>
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<tr>
<td>Aygun (2002)</td>
<td>140</td>
<td>37</td>
<td>10</td>
<td>27</td>
</tr>
<tr>
<td>Castro (2002)</td>
<td>351</td>
<td>29</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Singer (2000)</td>
<td>64 (thal)</td>
<td>22</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rosse (1990)</td>
<td>1814</td>
<td>19</td>
<td>9</td>
<td>10</td>
</tr>
<tr>
<td>Overall</td>
<td></td>
<td>24</td>
<td>10</td>
<td>14</td>
</tr>
</tbody>
</table>
(Hyper)hemolysis

Definition: hemolysis 6-10 days 1 week after RBC transfusion, associated with pain and profound anemia. Incidence: 1-4%.

Signs: Pain, fever and hemoglobininuria most prominent.

Lab: ↓↓HbA and HbS; DAT+ 30%; new allo-Ab 30%; reticulopenia 60%!

Complications/associations: ACS, CHF, ARF, pancreatitis; Mortality: 10-20% (?).

Therapy: corticosteroids, IVIG, epo
Longitudinal Changes in Ferritin During Chronic Transfusion: A Report From the Stroke Prevention Trial in Sickle Cell Anemia (STOP)

Beatrice Files, M.D., Don Brambilla, Ph.D., Abdullah Kutlar, M.D., Scott Miller, M.D., Elliott Vichinsky, M.D., Winfred Wang, M.D., Suzanne Granger, M.S., and Robert J. Adams, M.S., M.D.

**FIG. 2.** Each point represents the median of serum ferritin at cumulative transfusion volume per kg for the 10 patients who reached the highest total transfusion volume. Plots occur at 50-ml/kg intervals.
Fig. 3. Blood viscosity-shear rate relations for deoxygenated 100 percent SS RBCs suspended in autologous plasma at 0.20 (□), 0.25 (○), 0.30 (●), and 0.40 Hct (■). Data are mean ± SD; \(n = 7\).
EXCHANGE VS “TOP-UP”

**TOP-UP**

- Easy
- Rarely necessary
- Risk of hyperviscosity
- Risk of Iron overload

**RBC EXCHANGE**

- Less easy
- Adequate for isocritic decreasing HbS%
- No of reduced risk of hyperviscosity or iron overload
GENERAL REMARKS

✓ Goals for RBC(x): Ht 30% and HbS < 30%
✓ RBCs should be matched for: ABO-D-CEK
✓ In case of parvo B19 IgG negativity: “Parvo-safe”
### Samenvatting indicaties voor transfusie bij SCD

#### Acute indicaties

<table>
<thead>
<tr>
<th>Indicatie</th>
<th>Transfusieformaat</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milt sequestratie als Hb &lt; 3.3 en/of circulatoir falen</td>
<td>Enkelvoudige transfusie</td>
<td>D</td>
</tr>
<tr>
<td>Acute chest syndroom met (dreigend) respiratoir falen</td>
<td>Wisseltransfusie</td>
<td>C</td>
</tr>
<tr>
<td>Acuut CVA</td>
<td>Wisseltransfusie</td>
<td>D</td>
</tr>
<tr>
<td>Multiorgaafalen</td>
<td>Wisseltransfusie</td>
<td>D</td>
</tr>
<tr>
<td>Priapisme</td>
<td>Geen indicatie</td>
<td>D</td>
</tr>
<tr>
<td>Vaso-occlusieve crisis</td>
<td>Geen indicatie</td>
<td>D</td>
</tr>
<tr>
<td>Preoperatieve voorbereiding</td>
<td>(Wissel)transfusie</td>
<td>C</td>
</tr>
<tr>
<td>Zwangerschap; meerlingzwangerschap of belaste VG</td>
<td>(Wissel)transfusie</td>
<td>A2</td>
</tr>
</tbody>
</table>

#### Chronische indicaties

<table>
<thead>
<tr>
<th>Indicatie</th>
<th>Transfusieformaat</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preventie recidief CVA</td>
<td>(Wissel)transfusie</td>
<td>C</td>
</tr>
<tr>
<td>Primaire CVA preventie, afwijkend TCD onderzoek</td>
<td>(Wissel)transfusie</td>
<td>A2</td>
</tr>
<tr>
<td>Stille herseninfarcten</td>
<td>Geen indicatie</td>
<td>D</td>
</tr>
<tr>
<td>Recidiverende vaso-occlusieve crisis niet reagerend op HU</td>
<td>(Wissel)transfusie</td>
<td>C</td>
</tr>
<tr>
<td>Recidiverend ACS</td>
<td>(Wissel)transfusie</td>
<td>C</td>
</tr>
</tbody>
</table>