Patient Blood Management in the Netherlands: Between practice and evidence

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The Netherlands
Outline

• Introduction
• Blood use in the Netherlands
• What is patient blood management (PBM)?
• Practical implementation of PBM
• Evidence of PBM
• More opportunities for PBM?
• Conclusions
Introduction
Inhabitants
Estonia: 1,3 million
Netherlands: 16,9 million
Sanquin Blood Supply Foundation

- The only organization in the NL authorized to supply blood (products)
- Not-for-profit
- Approximately 3,000 employees; 5 divisions:
  - Blood Bank
  - Plasma Products
  - Diagnostic Services
  - Research – Sanquin staff working with / partly employed at academic centers
  - Reagents
Organization

Executive Board

Corporate staff

Blood Bank
Plasma Products
Diagnostic Services
Research
Reagents
Pharmaceutical Services

Donor affairs
Production
Dept Transf. Med
QRA
Sanquin

national hospitals and other healthcare institutes

Public sector

Privat sector

national and international organizations

red blood cells
platelets
fresh frozen plasma

pharmaceuticals derived from plasma, including Omniplasma®

3000 employees; 400,000 donors
Hospitals

• 90 hospitals
  • 8 university hospitals
• Each hospital has its own transfusion laboratory and performs compatibility tests
• Sanquin: reference laboratory

2 Sanquin production sites

7 issuing depts.

hospital transfusion laboratory
Blood use in the Netherlands
Number of blood transfusions in the Netherlands

**Blood products (2014)**

- 433,500 red blood cells (↓ 26%)
- 56,000 platelets (↑10%)
- 67,600 plasma (↓ 27%)
Benchmark Europe EDQM 2012

whole blood/ 1000 inhabitants

- Netherlands
- Ireland
- United Kingdom
- France
- Estonia
- Belgium
- Germany

Survey 2012 European Directorate for the Quality of Medicines and Health Care
Possible reasons for declined (red) blood use


• Quality Act for Health Care institutes and national hemovigilance office “TRIP” (Transfusion and Transplantation Reactions In Patients; founded 2001)

• Benchmark blood use between Dutch Hospitals organized by Sanquin

• Reimbursement system for blood products in the Netherlands

• Cost reduction health care -> hospitals have to economize (6%) and quality indicators Dutch Society of Surgeons -> concentration of care
What is Patient Blood Management (PBM)?
*Patient Blood Management* (PBM) is an evidence-based, multidisciplinary approach to optimising the care of patients who might or do need blood transfusion.
Three pillars of Patient Blood Management
(http://www.health.wa.gov.au/bloodmanagement/)

1. optimising the patient’s own blood

2. minimising surgical blood loss and bleeding

3. harnessing and optimising the patient-specific physiological reserve of anaemia (including restrictive transfusion thresholds)
1st Pillar
Optimize erythropoiesis
- Detect anemia
- Identify underlying disorder(s) causing anemia
- Manage disorder(s)
- Refer for further evaluation if necessary
- Treat suboptimal iron stores/iron deficiency/anemia of chronic disease/iron-restricted erythropoiesis
- Treat other hematologic deficiencies
- Note: Anemia is a contraindication for elective surgery

2nd Pillar
Minimize blood loss & bleeding
- Identify and manage bleeding risk
- Minimizing iatrogenic blood loss
- Procedure planning and rehearsal
- Preoperative autologous blood donation (in selected cases or when patient choice)
- Other

3rd Pillar
Harness & optimize physiological reserve of anemia
- Assess/optimize patient’s physiological reserve and risk factors
- Compare estimated blood loss with patient-specific tolerable blood loss
- Formulate patient-specific management plan using appropriate blood conservation modalities to minimize blood loss, optimize red cell mass, and manage anemia
- Restrictive transfusion thresholds

Preoperative
- Meticulous hemostasis and surgical techniques
- Blood-sparing surgical techniques
- Anesthetic blood conserving strategies
- Autologous blood options
- Pharmacological/hemostatic agents

Intraoperative
- Timing surgery with hematological optimization
- Vigilant monitoring and management of post-operative bleeding
- Avoid secondary hemorrhage
- Rapid warming/maintain normothermia (unless hypothermia specifically indicated)
- Autologous blood salvage
- Minimizing iatrogenic blood loss
- Hemostasis/anticoagulation management
- Prophylaxis of upper gastrointestinal hemorrhage
- Avoid/treat infections promptly
- Be aware of adverse effects of medication

Postoperative
- Stimulate erythropoiesis
- Be aware of drug interactions that can increase anemia
- Optimize cardiac output
- Optimize ventilation and oxygenation
- Restrictive transfusion thresholds
- Optimize anemia reserve
- Maximize oxygen delivery
- Minimize oxygen consumption
- Avoid/treat infections promptly
- Restrictive transfusion thresholds
Practical implementation of PBM in the Netherlands
National Guideline “Blood Transfusion”

- Effective use of blood products
  - so-called 4-5-6 rule
    (depending on the presence of co-morbidity, the threshold for RBC transfusion varies between 4.0 mmol/L (6.4 g/dL) and 6.0 mmol/L (9.7 g/dL)
  - alternatives for red blood cell transfusion
    pharmaceuticals, cell savers
  - improvement of operation techniques
<table>
<thead>
<tr>
<th>Value (mmol/l)</th>
<th>Conversion (g/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.0</td>
<td>6.4</td>
</tr>
<tr>
<td>5.0</td>
<td>8.0</td>
</tr>
<tr>
<td>6.0</td>
<td>9.7</td>
</tr>
</tbody>
</table>
Alternatives for blood cell transfusion

- Iron (oral or IV) -> pre-operative anaemia
- Erythropoietin -> pre-operative anaemia
- Cell savers -> intra-operative/ post-operative
- Tranexamic acid (cheap) -> pre- and during operation, IV and topical
Iron in pre-operative anaemia

• No randomized controlled studies yet

• PREVENTT: preoperative intravenous iron to treat anaemia in major surgery: study protocol for a randomised controlled trial (Trials 2015, 16; 254)

• Litton et al: Safety and efficacy of intravenous iron therapy in reducing requirement for allogeneic blood transfusion: systematic review and meta-analysis of randomised clinical trials (BMJ 2013; 347: f4822)

Fig 3 Risk of red blood cell transfusion in patients who received intravenous iron compared with oral iron and no iron.

<table>
<thead>
<tr>
<th>Study</th>
<th>No of events/total</th>
<th>Relative risk (95% CI)</th>
<th>Weight (%)</th>
<th>Relative risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>IV iron vs oral iron</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AI 2005</td>
<td>0/45</td>
<td>1/45</td>
<td>0.3</td>
<td>0.33 (0.01 to 7.97)</td>
</tr>
<tr>
<td>Auerbach 2004</td>
<td>9/78</td>
<td>10/79</td>
<td>3.7</td>
<td>0.91 (0.39 to 2.12)</td>
</tr>
<tr>
<td>Auerbach 2010</td>
<td>41/116</td>
<td>48/122</td>
<td>17.6</td>
<td>0.90 (0.65 to 1.25)</td>
</tr>
<tr>
<td>Bayoumeu 2002</td>
<td>0/24</td>
<td>1/23</td>
<td>0.3</td>
<td>0.32 (0.01 to 7.48)</td>
</tr>
<tr>
<td>Breyman 2008</td>
<td>1/227</td>
<td>0/117</td>
<td>0.3</td>
<td>1.55 (0.06 to 37.82)</td>
</tr>
<tr>
<td>Dangsuwan 2010</td>
<td>6/22</td>
<td>14/22</td>
<td>3.8</td>
<td>0.36 (0.16 to 0.82)</td>
</tr>
<tr>
<td>Froessler 2013</td>
<td>1/101</td>
<td>3/97</td>
<td>0.6</td>
<td>0.32 (0.03 to 3.03)</td>
</tr>
<tr>
<td>Gamido-Martín 2012</td>
<td>20/54</td>
<td>27/53</td>
<td>11.7</td>
<td>0.73 (0.47 to 1.13)</td>
</tr>
<tr>
<td>Henry 2007</td>
<td>11/63</td>
<td>20/124</td>
<td>5.7</td>
<td>1.08 (0.55 to 2.12)</td>
</tr>
<tr>
<td>Kochhar 2012</td>
<td>0/50</td>
<td>1/50</td>
<td>0.3</td>
<td>0.33 (0.01 to 7.99)</td>
</tr>
<tr>
<td>Meyer 1996</td>
<td>0/21</td>
<td>2/21</td>
<td>0.3</td>
<td>0.20 (0.01 to 3.93)</td>
</tr>
<tr>
<td>Steenma 2011</td>
<td>20/164</td>
<td>43/326</td>
<td>9.5</td>
<td>0.92 (0.56 to 1.52)</td>
</tr>
<tr>
<td>Welsbach 1999</td>
<td>6/30</td>
<td>5/60</td>
<td>2.3</td>
<td>2.40 (0.80 to 7.23)</td>
</tr>
<tr>
<td>Westad 2008</td>
<td>4/59</td>
<td>11/70</td>
<td>2.3</td>
<td>0.43 (0.14 to 1.28)</td>
</tr>
<tr>
<td><strong>IV iron vs no iron</strong></td>
<td>118/1054</td>
<td>186/1209</td>
<td>58.6</td>
<td>0.82 (0.67 to 1.00)</td>
</tr>
<tr>
<td>Edwards 2009</td>
<td>0/34</td>
<td>2/26</td>
<td>0.3</td>
<td>0.15 (0.01 to 3.08)</td>
</tr>
<tr>
<td>Hedensu 2007</td>
<td>2/33</td>
<td>1/34</td>
<td>0.5</td>
<td>2.06 (0.20 to 21.65)</td>
</tr>
<tr>
<td>Karkouti 2006</td>
<td>4/21</td>
<td>4/10</td>
<td>2.0</td>
<td>0.48 (0.15 to 1.52)</td>
</tr>
<tr>
<td>Kim 2007</td>
<td>12/30</td>
<td>29/45</td>
<td>9.8</td>
<td>0.62 (0.38 to 1.01)</td>
</tr>
<tr>
<td>Madi-Jebra 2004</td>
<td>17/80</td>
<td>9/40</td>
<td>5.1</td>
<td>0.94 (0.46 to 1.93)</td>
</tr>
<tr>
<td>Na 2011</td>
<td>11/54</td>
<td>29/54</td>
<td>7.3</td>
<td>0.38 (0.21 to 0.68)</td>
</tr>
<tr>
<td>Pedrazzoli 2008</td>
<td>2/73</td>
<td>5/76</td>
<td>1.1</td>
<td>0.42 (0.08 to 2.08)</td>
</tr>
<tr>
<td>Serrano-Trenas 2011</td>
<td>33/100</td>
<td>41/100</td>
<td>15.3</td>
<td>0.80 (0.56 to 1.16)</td>
</tr>
<tr>
<td><strong>Subtotal: P=0.33, I^2=14%</strong></td>
<td>81/425</td>
<td>120/385</td>
<td>41.4</td>
<td>0.64 (0.49 to 0.85)</td>
</tr>
<tr>
<td><strong>Subtotal: P=0.34, I^2=9%</strong></td>
<td>199/1479</td>
<td>306/1594</td>
<td>100.0</td>
<td>0.74 (0.62 to 0.88)</td>
</tr>
</tbody>
</table>

Edward Litton et al. BMJ 2013;347:bmj.f4822
Evidence of erythropoietin and cellsavers – Dutch study in orthopaedic patients

Dr Cynthia So-Osman
Rationale

- Hip- and knee-replacement surgery result in large blood losses
- Ageing population will result in 3 fold increase of joint replacements in 2030 (> 100,000 per year)
- Blood sparing modalities are very popular and much investigated

However:
1. NO evidence on combined effect of several modalities
2. NO evidence on effect of restrictive transfusion trigger
3. Most studies lack power, are methodologically poor
Pre-operative Haemoglobin level (Hb)

10-13 g/dL

≥ 13 g/dL

1\textsuperscript{st} randomization RHuEpo

Yes

No

2\textsuperscript{nd} randomization Cell saver

Yes

No

3\textsuperscript{rd} randomization Post-operative wound drainage

Yes

No

Yes

No

Yes

No

Yes

No

Yes

Yes

No

Control group
# Patients characteristics

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Numbers (%) or mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Evaluated patients</td>
<td>2442</td>
</tr>
<tr>
<td>Females</td>
<td>1699 (70%)</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>69 (+11)</td>
</tr>
<tr>
<td>THR</td>
<td></td>
</tr>
<tr>
<td>Of which revision</td>
<td>1462 (60%)</td>
</tr>
<tr>
<td></td>
<td>130 (5%)</td>
</tr>
<tr>
<td>TKR</td>
<td></td>
</tr>
<tr>
<td>Of which revision</td>
<td>980 (40%)</td>
</tr>
<tr>
<td></td>
<td>54 (2%)</td>
</tr>
<tr>
<td>Mean pre-operative Hb (mmol/L)</td>
<td>8.6 (+0.8)</td>
</tr>
<tr>
<td></td>
<td>13.9 (+1.3)</td>
</tr>
<tr>
<td>Epo eligible patients</td>
<td>683 (28%)</td>
</tr>
</tbody>
</table>
General results

• RBC transfusions in 11.6% of 2442 (n=284)

• If transfused: median of 2 RBC (range 1-27)
  • Intra-operatively n= 37 (range 1-12)
  • 0-14 days n= 246 (range 1-11)
  • 14 days-3 months n= 43 (range 1-27)

• Due to heterogeneity of revision patients, primary surgery group is separately reported in case of RBC use

• In case of cost analysis all patients were evaluated
Epo effect

- Significant reduction in % patients transfused: 2 times less
- Non-significant mean RBC reduction: 29%
Autologous blood re-infusion effect

No reduction in mean RBC use AND in proportion transfused (with or without epo)

No difference between cell saver and drain
## Cost analysis Epo and autologous re-infusion devices

<table>
<thead>
<tr>
<th>Costs (in Euro’s)</th>
<th>Total costs (in Euro)</th>
<th>Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=683</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low Hb (stratum I)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>with epo (n=339)</td>
<td>5615</td>
<td>785</td>
</tr>
<tr>
<td>no epo (n=344)</td>
<td>4829</td>
<td>(262-1309)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Costs (in Euro’s)</th>
<th>Total costs (in Euro)</th>
<th>Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=2442</td>
<td></td>
<td></td>
</tr>
<tr>
<td>with autologous device (n=1481)</td>
<td>4399</td>
<td>378</td>
</tr>
<tr>
<td>without autologous device (n=691)</td>
<td>4021</td>
<td>(161-595)</td>
</tr>
</tbody>
</table>
Conclusions

• Significant red blood cell (RBC) reduction by Epo, however not cost-effective

• Neither red blood cell- nor cost-reduction by autologous blood reinfusion (i.e. cell saver or postoperative drain re-infusion)
### Outcome:
Number of patients exposed to allogeneic RBC transfusion

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Cell Saver</th>
<th>Control</th>
<th>Total</th>
<th>Weight</th>
<th>Risk Ratio (M-H, Random, 95% CI)</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Events</td>
<td>Total</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.1.1 Years 1991-1999</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Majumdar 1991</td>
<td>7</td>
<td>20</td>
<td>27</td>
<td>5.3%</td>
<td>0.37 [0.20, 0.68]</td>
<td>1991</td>
</tr>
<tr>
<td>Sigals 1993</td>
<td>9</td>
<td>27</td>
<td>36</td>
<td>5.2%</td>
<td>0.50 [0.31, 0.81]</td>
<td>1993</td>
</tr>
<tr>
<td>Heddle 1992</td>
<td>10</td>
<td>39</td>
<td>50</td>
<td>5.4%</td>
<td>0.30 [0.21, 0.43]</td>
<td>1992</td>
</tr>
<tr>
<td>Ritter 1994</td>
<td>23</td>
<td>137</td>
<td>160</td>
<td>5.0%</td>
<td>0.77 [0.47, 1.29]</td>
<td>1994</td>
</tr>
<tr>
<td>Resencher 1994</td>
<td>6</td>
<td>20</td>
<td>26</td>
<td>4.3%</td>
<td>0.50 [0.22, 0.93]</td>
<td>1994</td>
</tr>
<tr>
<td>Mihail 1995</td>
<td>9</td>
<td>44</td>
<td>53</td>
<td>6.1%</td>
<td>0.43 [0.23, 0.82]</td>
<td>1995</td>
</tr>
<tr>
<td>Shenoi-Kumar 1997</td>
<td>1</td>
<td>50</td>
<td>50</td>
<td>5.1%</td>
<td>0.20 [0.10, 0.40]</td>
<td>1997</td>
</tr>
<tr>
<td>Newman 1997</td>
<td>3</td>
<td>25</td>
<td>26</td>
<td>3.4%</td>
<td>0.54 [0.40, 0.80]</td>
<td>1997</td>
</tr>
<tr>
<td>Addis 1998</td>
<td>8</td>
<td>24</td>
<td>32</td>
<td>4.3%</td>
<td>0.14 [0.04, 0.49]</td>
<td>1998</td>
</tr>
<tr>
<td>Sait 1999</td>
<td>1</td>
<td>60</td>
<td>61</td>
<td>1.6%</td>
<td>0.03 [0.00, 0.20]</td>
<td>1999</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>456</td>
<td>457</td>
<td>913</td>
<td>45.5%</td>
<td>0.39 [0.25, 0.60]</td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>84</td>
<td>232</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.38; Ch² = 34.36, df = 9 (P = 0.0001); I² = 74%
Test for overall effect: Z = 4.18 (P < 0.0001)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Cell Saver</th>
<th>Control</th>
<th>Total</th>
<th>Weight</th>
<th>Risk Ratio (M-H, Random, 95% CI)</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Events</td>
<td>Total</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.1.2 Years 2000-2009</td>
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</tr>
<tr>
<td>Thomas 2001</td>
<td>12</td>
<td>119</td>
<td>131</td>
<td>5.3%</td>
<td>0.37 [0.20, 0.67]</td>
<td>2001</td>
</tr>
<tr>
<td>Chang 2005</td>
<td>4</td>
<td>26</td>
<td>33</td>
<td>3.7%</td>
<td>0.40 [0.15, 1.09]</td>
<td>2005</td>
</tr>
<tr>
<td>Drama 2006</td>
<td>3</td>
<td>22</td>
<td>25</td>
<td>3.3%</td>
<td>0.70 [0.35, 1.39]</td>
<td>2006</td>
</tr>
<tr>
<td>Sc-Osman 2006</td>
<td>6</td>
<td>12</td>
<td>18</td>
<td>4.5%</td>
<td>0.92 [0.32, 2.60]</td>
<td>2006</td>
</tr>
<tr>
<td>Aouazakou 2007</td>
<td>13</td>
<td>52</td>
<td>65</td>
<td>5.6%</td>
<td>1.18 [0.50, 2.65]</td>
<td>2007</td>
</tr>
<tr>
<td>Zachroutou 2007</td>
<td>5</td>
<td>30</td>
<td>35</td>
<td>3.9%</td>
<td>0.50 [0.19, 1.52]</td>
<td>2007</td>
</tr>
<tr>
<td>Moonen 2007</td>
<td>1</td>
<td>45</td>
<td>46</td>
<td>1.4%</td>
<td>0.14 [0.03, 0.56]</td>
<td>2007</td>
</tr>
<tr>
<td>Amin 2008</td>
<td>12</td>
<td>92</td>
<td>104</td>
<td>4.8%</td>
<td>0.58 [0.26, 1.27]</td>
<td>2008</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>404</td>
<td>378</td>
<td>782</td>
<td>31.7%</td>
<td>0.63 [0.33, 1.22]</td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>56</td>
<td>102</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.22; Ch² = 15.32, df = 7 (P = 0.03); I² = 54%
Test for overall effect: Z = 2.72 (P = 0.007)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Cell Saver</th>
<th>Control</th>
<th>Total</th>
<th>Weight</th>
<th>Risk Ratio (M-H, Random, 95% CI)</th>
<th>Year</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Events</td>
<td>Total</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.1.3 Years 2010-present</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blatamakos 2010</td>
<td>99</td>
<td>183</td>
<td>282</td>
<td>6.9%</td>
<td>0.75 [0.45, 1.27]</td>
<td>2010</td>
</tr>
<tr>
<td>Atay 2010</td>
<td>1</td>
<td>20</td>
<td>21</td>
<td>1.5%</td>
<td>0.13 [0.02, 0.98]</td>
<td>2010</td>
</tr>
<tr>
<td>Dutil 2012</td>
<td>4</td>
<td>23</td>
<td>27</td>
<td>2.9%</td>
<td>1.09 [0.31, 3.80]</td>
<td>2012</td>
</tr>
<tr>
<td>Cip 2012</td>
<td>23</td>
<td>70</td>
<td>93</td>
<td>6.9%</td>
<td>1.00 [0.62, 1.63]</td>
<td>2012</td>
</tr>
<tr>
<td>Sc-Osman 2012</td>
<td>31</td>
<td>436</td>
<td>467</td>
<td>5.6%</td>
<td>1.25 [0.79, 2.00]</td>
<td>2012</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>712</td>
<td>818</td>
<td>1530</td>
<td>22.8%</td>
<td>0.91 [0.55, 1.51]</td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>158</td>
<td>124</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.08; Ch² = 6.83, df = 4 (P = 0.07); I² = 54%
Test for overall effect: Z = 0.51 (P = 0.61)

| Total (95% CI)    | 1572       | 1453    | 100.0% | 0.51 [0.39, 0.68]                |      |
| Total events      | 288        | 458     |        |        |                                 |      |

Heterogeneity: Tau² = 0.26; Ch² = 66.81, df = 22 (P < 0.0001); I² = 75%
Test for overall effect: Z = 4.69 (P = 0.0001)
Test for subhazard differences: Omn² = 0.90, df = 2 (P = 0.01); I² = 77.7%
Conclusions meta-analysis cell saving

Cell Saving significantly reduces

- the need for allogeneic RBC transfusion, and
- the volume of RBC transfused

However, in RCTs published more recently (2010-2012), Cell Saving does neither reduce the need for allogeneic RBC transfusion nor the volume of RBC transfused in both hip and knee surgery.
Tranexamic acid to prevent/diminish bleeding

- TXA is a synthetic lysine analogue antifibrinolytic agent. It is an antifibrinolytic that competitively inhibits the activation of plasminogen to plasmin, by binding to specific sites of both plasminogen and plasmin, a molecule responsible for the degradation of fibrin.
- Oral, intravenous or topical administration
Use of tranexamic acid

• in 2015 many randomized trials/ meta-analysis on tranexamic acid, i.e.:  
  • Trauma  
  • Postpartum haemorrhage  
  • Orthopaedic surgery (total hip and knee, spine)  
  • Upper gastro-intestinal bleeding  
  • Open heart surgery
Effect tranexamic acid in total knee arthroplasty in 34 randomized controlled trials

Effect on blood units transfused per patient
More indications for PBM than surgery?
Patient Blood Management in Europe (PaBloE)

Objectives of one of the working parties

• Data collection on current blood and blood component use and PBM practices
  • Survey of PBM practices among the PaBloE centres
  • Survey of top indications for red blood cell use
<table>
<thead>
<tr>
<th>Box a) No of units:</th>
<th>Box b) Patient's</th>
<th>Box c) Male</th>
<th>Female</th>
<th>Audited Patient No.</th>
</tr>
</thead>
</table>

### Cardiothoracic Surgery
- 1. CABG (first)
- 2. CABG (redo)
- 3. Valve replacement (+/- CABG)
- 4. ECMO
- 5. Congenital Heart Disease
- 6. Other (please state)

### ENT
- 7. ENT

### Gastrointestinal Surgery
- 8. Oesophageal
- 9. Gastric
- 10. Pancreatic

### Neurosurgery
- 11. Neurosurgery
- 12. Neurosurgery (including head injury)

### Trauma
- 13. Blunt
- 14. Penetrating
- 15. Fractured femur
- 16. Fractured pelvis
- 17. Other fracture
- 18. Other (please state)

### Urology
- 19. Urology

### Solid Organ Transplant
- 20. Solid Organ Transplant
- 21. Solid Organ Transplant (State organ)

### Vascular Surgery
- 22. Vascular Surgery
- 23. Emergency AAA repair
- 24. Elective open AAA repair
- 25. Other (please state)

### Orthopaedics
- 26. THR (first)
- 27. THR (redo)
- 28. TKR (first)
- 29. TKR (redo)
- 30. Other (please state)

### Plastic surgery
- 31. Plastic surgery

### Obstetrics & Gynaecology
- 32. Obstetrics & Gynaecology
- 33. Gynae (non malignant)
- 34. Gynae oncology
- 35. Obstetric anaemia
- 36. Obstetric haemorrhage
- 37. Neonatal/fetal
- 38. Neonatal top-up
- 39. Neonatal exchange
- 40. Neonatal large volume transfusion
- 41. Intrathecal transfusion
- 42. Other (please state)

### Haematological
- 43. Acute myeloid leukaemia
- 44. Other acute leukaemia
- 45. Chronic lymphocytic leukaemia
- 46. Other chronic lymphocytic leukaemia
- 47. Acute lymphoblastic leukaemia
- 48. Chronic myeloid leukaemia
- 49. Chronic myelomonocytic leukaemia
- 50. Chronic myeloproliferative disorders
- 51. Polycythaemia
- 52. Other (please state)

### GI bleed
- 53. Upper acute
- 54. Lower acute
- 55. Upper chronic
- 56. Lower chronic

### Anaemia due to:
- 57. Renal failure
- 58. Anaemia due to non-haematological causes
- 59. Iron deficiency
- 60. B12/folate deficiency
- 61. Chronic disorders e.g. rheumatoid arthritis

### Other Surgery
- 62. Critical care not related to surgery, trauma or GI blood loss
- 63. Other (please state)

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National Comparative Audit Program, NHS Blood & Transplant

Cardiothoracic Surgery
ENT
Gastrointestinal Surgery
Neurosurgery
Trauma
Urology
Solid Organ Transplant
Vascular Surgery
Orthopaedics
Plastic Surgery
Other Surgery
Obstetrics & Gynaecology
Neonatal/fetal
GI Bleed
Haematological
Anaemia due to other causes
8 European Hospitals

- Nijmegen, Netherlands
- Frankfurt, Germany
- Manchester, UK
- Torino, Italy
- Malta
- Odense, Denmark
- Stockholm, Sweden
- Rome, Italy

Number of beds (10,930)
Number RBC’s transfused (3366)
Where did red cells go to?

- Medical indications: 63.6%
- Surgical indications: 33.4%
- Gynaecology and Obstetrics: 3%
## Top Surgical Indications

<table>
<thead>
<tr>
<th>Indication</th>
<th>Number of red cell units transfused</th>
<th>Percentage of total (3366)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiothoracic</td>
<td>324</td>
<td>9.6%</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>193</td>
<td>5.7%</td>
</tr>
<tr>
<td>Trauma</td>
<td>133</td>
<td>4%</td>
</tr>
<tr>
<td>Orthopaedics</td>
<td>118</td>
<td>3.5%</td>
</tr>
<tr>
<td>Vascular</td>
<td>101</td>
<td>3%</td>
</tr>
</tbody>
</table>
### Top Medical Indications

<table>
<thead>
<tr>
<th>Indication</th>
<th>Number of red cell units transfused</th>
<th>Percentage of total (3366)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haematological</td>
<td>1013</td>
<td>30.1%</td>
</tr>
<tr>
<td>Gastro-intestinal bleeding</td>
<td>239</td>
<td>7.1%</td>
</tr>
<tr>
<td>Critical Care</td>
<td>147</td>
<td>6.8%</td>
</tr>
<tr>
<td>Cancer non-haematological</td>
<td>144</td>
<td>6.7%</td>
</tr>
<tr>
<td>Neonatal</td>
<td>99</td>
<td>2.9%</td>
</tr>
</tbody>
</table>
Conclusions

• Patient Blood Management = Good Clinical Practice
• A simple rule (4-5-6) may safe blood use
• Alternatives for blood transfusion may be useful, but
• Evidence is needed to implement PBM properly
• PBM had been investigated particularly in surgical patients, but
• Most red blood cells go to medical indications

More research is needed on the topic of PBM