Optimal Hemoglobin and Other Myths

Jim Wood
Grand Rounds Debate 7 Dec 2009
Philip Syng Physick (1768 – 1837)

James Blundell (1791-1878)
The Problem

• Estimated 14.6 million units of PRBC’s transfused in 2006 (total supply=15.7 mil)\(^1\)

• Approximately 50% of ICU patients receive a transfusion: average 5 units during ICU stay. \(^1\)

• 40-70% of transfusions occur in surgical pts\(^1\)

• No apparent indication for transfusion in 26% of ICU pts transfused with Hb of 9. \(^2\)

Defining the Debate

Anemia Related Morbidity

Transfusion Related Morbidity

Increasing Hb 'trigger' / Increased units of transfused blood
Defining the Debate

- Transfusion Related Morbidity
- Anemia Related Morbidity

Increasing Hb 'trigger' / Increased units of transfused blood
Defining the Debate

Is there a known transfusion ‘trigger’ or ‘threshold’ hemoglobin which minimizes BOTH anemia related and transfusion related morbidity?
For whom?

- Healthy people
- Medical ICU patients
- Cardiac surgery patients
- Orthopedic patients
- Neurosurgical patients
- Pre-op surgical patients
- Trauma patients
- Septic patients
- Critically ill surgical patients
Optimal hemoglobin concentration and high altitude: a theoretical approach for Andean men at rest

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Submitted 3 April 2003; accepted in final form 1 December 2003
How to set a transfusion threshold...
TRICC Trial:
- 838 ICU patients
- Randomized to transfusion at Hb <7 or Hb <10
- No difference in 30d mortality (incl. pts with CAD)
- Restrictive group: fewer pts w/ MI and pulm edema.

Conclusions A restrictive strategy of red-cell transfusion is at least as effective as and possibly superior to a liberal transfusion strategy in critically ill patients, with the possible exception of patients with acute myocardial infarction and unstable angina.
Is a Restrictive Transfusion Strategy Safe for Resuscitated and Critically Ill Trauma Patients?

Lauralyn McIntyre, MD, FRCPC, Paul C. Hebert, MD, MHSc, George Wells, PhD, Dean Fergusson, PhD, John Marshall, MD, Elizabeth Yetisir, MSc, and M. J. Blajchman, MD, for the Canadian Critical Care Trials Group

The Journal of TRAUMA® Injury, Infection, and Critical Care

Methods: Critically ill trauma patients with a hemoglobin concentration less than 90 g/L within 72 hours of admission to the intensive care unit were randomized to a restrictive (hemoglobin concentration, 70 g/L) or liberal (hemoglobin concentration, 100 g/L) red blood cell transfusion strategy.

Results: The 30-day all-cause mortality rates in the restrictive group were 10%, as compared with 9% in the liberal group (p = 0.81). The presence of multiple organ dysfunction (9.2 ± 6.3 vs. 9.0 ± 6.0; p = 0.81), the changes in multiple organ dysfunction from baseline scores adjusted for death (1.2 ± 6.1 vs. 1.9 ± 5.7; p = 0.44),

Conclusions: A restrictive red blood cell transfusion strategy appears to be safe for critically ill multiple-trauma patients.

Transfusion Strategies for Patients in Pediatric Intensive Care Units

Jacques Lacroix, M.D., Paul C. Hébert, M.D., James S. Hutchison, M.D., Heather A. Hume, M.D., Marisa Tucci, M.D., Thierry Ducruet, M.Sc., France Gauvin, M.D., Jean-Paul Collet, M.D., Ph.D., Baruch J. Toledano, M.D., Pierre Robillard, M.D., Ari Joffe, M.D., Dominique Biarent, M.D., Kathleen Meert, M.D., and Mark J. Peters, M.D., for the TRIPICU Investigators, * the Canadian Critical Care Trials Group, and the Pediatric Acute Lung Injury and Sepsis Investigators Network

METHODS

In this noninferiority trial, we enrolled 637 stable, critically ill children who had hemoglobin concentrations below 9.5 g per deciliter within 7 days after admission to an intensive care unit. We randomly assigned 320 patients to a hemoglobin threshold of 7 g per deciliter for red-cell transfusion (restrictive-strategy group) and 317 patients to a threshold of 9.5 g per deciliter (liberal-strategy group).

Restrictive Group: lower Hb, fewer transfx. No difference in MODS or mortality.

CONCLUSIONS

In stable, critically ill children a hemoglobin threshold of 7 g per deciliter for red-cell transfusion can decrease transfusion requirements without increasing adverse outcomes. (Controlled-trials.com number, ISRCTN37246456.)
“The principal conclusions of the task force are that RBC transfusions should not be dictated by a single Hb “trigger” but instead should be based on the patient’s risks of developing complications of inadequate oxygenation. RBC transfusion is rarely indicated when the Hb concentration is greater than 10 g/dL and is almost always indicated when it is less than 6 g/dL.”

hemoglobin level is less than 6 g/dl and strongly agree that red blood cells are usually unnecessary when the level is more than 10 g/dl. In addition, the consultants and ASA members agree that, when autologous blood is
Change in Use of Allogeneic Red Blood Cell Transfusions among Surgical Patients

Julius Cuong Pham, MD, PhD, Christina L Catlett, MD, Sean M Berenholtz, MD, MHS, Elliott R Haut, MD, FACS

CONCLUSIONS: Despite evidence supporting more restrictive use of RBC transfusions, RBC use among surgical patients has increased during the last decade. (J Am Coll Surg 2008;207:352–359. © 2008 by

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Figure 1. Proportion of surgical patients in Maryland receiving an allogeneic RBC transfusion, by year. Error bars represent 95% CI of adjusted model. Adjusted model controls for age group, gender, race, admission status, all comorbidities, surgical category, surgeon patient volume, and number of procedures coded.
What do we know?

• Acute hemorrhage (e.g. trauma, Stovall, etc.)
• Non-responsive shock
• Hemoglobin < ???
• TEG = ???

Transfuse
Transfusion Triggers: A Systematic Review of the Literature
Jeffrey L. Carson, Suzanne Hill, Paul Carless, Paul Hébert, and David Henry

Transfusion Medicine Reviews, Vol 16, No 3 (July), 2002: pp 187-199

Fig 5. Effect of restrictive transfusion triggers on cardiac events.

Fig 6. Effect of restrictive transfusion triggers on 30-day, all-cause mortality.
Systematic review

- 45 cohort studies (272,596 patients): In all but 3, the risks of transfusion outweighed benefit.
- Meta-analysis of 10 RCT’s of ‘triggers’:
  - Restrictive strategy → decrease transfusion, Hb, cardiac events (24%), mortality (20%). No difference in LOS.
  - Inadequate data on pts with cardiac, hematologic, renal ds.

Although evidence suggests that a lower transfusion threshold may be appropriate in most preoperative patients, the decision to transfuse must be individualized to the patient and the clinical setting.
Mortality and morbidity in patients with very low postoperative Hb levels who decline blood transfusion

Jeffrey L. Carson, Helaine Noveck, Jesse A. Berlin, and Steven A. Gould

### TABLE 4. Mortality or morbidity stratified by postoperative Hb level

<table>
<thead>
<tr>
<th>Postoperative Hb (g/dL)</th>
<th>Total study population</th>
<th>30-day in-hospital mortality and/or morbidity†</th>
<th>No cardiovascular disease (n = 199)</th>
<th>Cardiovascular disease (n = 57)</th>
</tr>
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<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Number</td>
<td>30-day in-hospital mortality and/or morbidity†</td>
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<tr>
<td>1.1-2.0</td>
<td>4</td>
<td>4 (100)</td>
<td>2</td>
<td>2 (100)</td>
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<tr>
<td>2.1-3.0</td>
<td>12</td>
<td>11 (91.7)</td>
<td>9</td>
<td>8 (88.9)</td>
</tr>
<tr>
<td>3.1-4.0</td>
<td>19</td>
<td>10 (52.6)</td>
<td>14</td>
<td>6 (42.9)</td>
</tr>
<tr>
<td>4.1-5.0</td>
<td>26</td>
<td>15 (57.7)</td>
<td>18</td>
<td>9 (50.0)</td>
</tr>
<tr>
<td>5.1-6.0</td>
<td>49</td>
<td>14 (28.6)</td>
<td>34</td>
<td>8 (23.5)</td>
</tr>
<tr>
<td>6.1-7.0</td>
<td>50</td>
<td>11 (22.0)</td>
<td>40</td>
<td>9 (22.5)</td>
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<tr>
<td>7.1-8.0</td>
<td>96</td>
<td>9 (9.4)</td>
<td>82</td>
<td>8 (9.8)</td>
</tr>
</tbody>
</table>

* Analysis limited to multicenter data (n = 256); postoperative Hb is prior to event.
† Defined as arrhythmia, congestive heart failure; myocardial infarction, bacteremia, pneumonia, deep wound infection, or death; 74 patients with at least one event. Data reported as number (%).
Is there an absolute minimum?

Life-threatening postoperative blood loss in a Jehovah’s Witness, treated with high-dose erythropoietin

G. Schälte¹*, H. Janz², J. Busse², V. Jovanovic³, R. Rossaint¹ and R. Kuhlen¹

Six hours after an uncomplicated extended resection of ovarian cancer, postoperative arterial bleeding led to life-threatening blood loss in a 44-yr-old Jehovah’s Witness who refused blood transfusion. Haemoglobin (Hb) decreased from 2.5 g dl⁻¹ directly after the emergency laparotomy, followed by a 10 h immeasurable period (below detectable minimum value of the analyser), to a measurable minimum of 1.5 g dl⁻¹ after 20 h. Hematopoiesis was induced by high-dose i.v.

Critical Oxygen Delivery in Conscious Humans Is Less Than 7.3 ml O₂ · kg⁻¹ · min⁻¹

Jeremy A. Lieberman, M.D.,* Richard B. Weiskopf, M.D.,† Scott D. Kelley, M.D.,‡ John Feiner, M.D.,§ Mariam Noorani, B.S.,∥ Jacqueline Leung, M.D., M.P.H.,‡ Pearl Toy, M.D.,# and Maurene Viele, M.D.**

Fig. 1. Oxygen delivery (DO₂) and oxygen consumption (VO₂) in eight healthy adults before (hemoglobin concentration, 12.5 ± 0.8 g/dl) and after (hemoglobin concentration, 4.8 ± 0.2 g/dl) isovolemic hemodilution and during intravenous infusion of a β-adrenergic antagonist, esmolol (with hemoglobin concentration of 4.7 ± 0.2 g/dl). *Indicates P < 0.05 versus baseline; ‡Indicates P < 0.05 versus hemodilution without esmolol.
Human Cardiovascular and Metabolic Response to Acute, Severe Isovoletic Anemia

Richard B. Weiskopf, MD; Maurene K. Viele, MD; John Feiner, MD; Scott Kelley, MD; Jeremy Lieberman, MD; Mariam Noorani; Jacqueline M. Leung, MD; Dennis M. Fisher, MD; William R. Murray, MD; Pearl Toy, MD; Mark A. Moore, MD

Results.—Acute, isovolemic reduction of Hb concentration decreased systemic vascular resistance and $\dot{V}O_2$ and increased heart rate, stroke volume, and cardiac index (each $P<.001$). We did not find evidence of inadequate oxygenation: $\dot{V}O_2$ increased slightly from a mean (SD) of 3.07 (0.44) mL of oxygen per kilogram per minute (mL $\text{O}_2\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$) to 3.42 (0.54) mL $\text{O}_2\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ($P<.001$) and plasma lactate concentration did not change (0.81 [0.11] mmol/L to 0.62 [0.19] mmol/L);

Conclusions.—Acute isovolemic reduction of blood Hb concentration to 50 g/L in conscious healthy resting humans does not produce evidence of inadequate systemic $\dot{V}O_2$, as assessed by lack of change of $\dot{V}O_2$ and plasma lactate concentration. Analysis of Holter readings suggests that at this Hb concentration in this resting healthy population, myocardial ischemia would occur infrequently.
Oxygen Reverses Deficits of Cognitive Function and Memory and Increased Heart Rate Induced by Acute Severe Isovolemic Anemia


Methods: Thirty-one healthy volunteers, aged 28 ± 4 yr (mean ± SD), were tested with verbal memory and standard, computerized neuropsychologic tests before and twice after acute isovolemic reduction of their hemoglobin concentration to 5.7 ± 0.3 g/dl. Two sets of tests were performed in randomized order at the lower hemoglobin concentration, with the

Conclusion: The authors confirmed that acute isovolemic anemia subtly slows human reaction time, degrades memory, increases heart rate, and decreases energy level. The findings of this study support the hypothesis that increasing PaO₂ to 350 mmHg or greater by breathing oxygen reverses all of these effects of acute anemia except for decreased energy.

Anesthesiology 2002; 96:871-7
The purpose of this study is to determine whether a higher threshold for transfusion with red blood cells improves the tissue oxygenation.

- “The purpose of this study is to determine whether a higher threshold for transfusion with red blood cells improves the tissue oxygenation.”
4. The use of only Hb level as a “trigger” for transfusion should be avoided. Decision for RBC transfusion should be based on an individual patient’s intravascular volume status, evidence of shock, duration and extent of anemia, and cardiopulmonary physiologic parameters. (Level 2)
Is there an optimal Hb?

• Maybe, but ...
• Individualized by patient and scenario.
• We have not defined it.
Is there an optimal Hb?

- Translation: NO.
- Benefits of transfusion ‘triggers’:
  - Help us to avoid thinking.
  - Should do the opposite: trigger thinking
- Blood should be transfused for a physiologic indication and not for a specific Hb ‘trigger’.

Is there an optimal Hb?

• If there is, then...

WHAT IS IT?
Figure 1. Summary of Transfusion Protocol from “Guidelines for Transfusion in the Trauma Patient.” J Trauma 2006; 61:436–439. PRBC, packed red blood cell; Pt, patient; Hgb, hemoglobin; ICU, intensive care unit; Hct, hematocrit; IV, intravenous; PA, pulmonary artery.