Actionable Patient Safety Solution (APSS) #5: ANEMIA AND TRANSFUSION: A PATIENT SAFETY CONCERN

Executive Summary Checklist

Errors in the use of blood products are a significant cause of hospital patient morbidity and mortality. To eliminate these errors, we must implement an effective Patient Blood Management program, including the following actionable steps:

- A Commitment from hospital leadership to support a Patient Blood Management program that closes the performance gap by reducing unnecessary transfusions while speeding up needed blood transfusion and care for patients who truly need it.

- Clinical and safety leadership endorse the plan and drive implementation across all providers and systems.

- Establish the Patient Blood Management Committee, which replaces the traditional hospital transfusion committee, and appoint an MD chairperson to be responsible and accountable for leading this group.

- On a monthly basis, distribute the blood product usage report by clinicians across the hospital to hospital leaders.

- Develop a Patient Blood Management education program for emergency and elective hospital admissions, targeting medical students, physicians, nurses, pharmacists and other healthcare staff.

- Implement interdisciplinary blood conservation modalities, including:
  - Reductions of unnecessary laboratory tests, frequency of blood sampling, and “discard” volumes.
  - A consistent protocol for preoperative management of platelet inhibitors and other anticoagulants.
  - Technology that has been shown to improve patient care, such as continuous non-invasive hemoglobin monitoring and red cell recovery technology in the operating room (OR).

- Establish protocols for anemia management, including:
  - Screen, diagnose and appropriately treat anemia prior to surgery, allowing adequate lead time to correct the anemia before surgery.
    - Identify patients at risk for needing transfusion
    - Increase and normalize hemoglobin levels before surgery
    - Minimize the risk of hitting levels that require blood transfusions
  - When appropriate, establish single unit transfusion policy and advocate for restrictive transfusion practices.
  - Document hemoglobin levels before and after the transfusion of each RBC unit.
  - Consider alternative therapies to RBC transfusions, such as intravenous iron or erythropoietin stimulation agents (ESAs).

- Continuously monitor the effectiveness of the Patient Blood Management program, and use the results of this monitoring in medical staff educational sessions as a part of Continuous Quality Improvement (CQI).
The Performance Gap

Anemia

The healthy human body contains approximately 5 liters of blood and about 40 to 45% of blood consists of red blood cells (RBCs). Impaired blood formation, blood loss or destruction leads to anemia which represents the most common blood disorder worldwide.

About 30% of the world’s population is anemic, in other words 1 out of every 3 people are anemic.\(^1\) The underlying causes can be of various etiologies; however, 30% can be attributed to malnutrition. For example, iron-deficiency is the most prominent cause due to a chronic blood loss and low iron consumption.\(^1\) Although considered a silent disease, anemia has a list of typical symptoms such as weakness, fatigue and difficulty in concentration to name a few, resulting in reduced quality of life and productivity. Due to the natural occurrence of these symptoms in our daily life the presence of anemia is often overlooked, underdiagnosed, ignored and undertreated especially in women of childbearing years (approximately ½ a billion women).\(^2\) This frequently underestimated health problem is present in both the industrialized world as well as in developing countries\(^3\) and represents 68.3 million years lived in disability (YLD) and consumes 8.8% of all ailments worldwide.\(^1\)

In clinical practice hemoglobin (Hb) levels are used to determine anemia. The World Health Organization (WHO) defines a normal Hb level of ≥13 g/dL for men and ≥12 g/dL for menstruating women. Recent studies reveal the severe impact of anemia on surgical outcomes implicating anemia as a serious health condition and an independent risk factor for patients. Musallam et al., conducted a retrospective trial comprising 227,425 patients undergoing any kind of non-cardiac surgery. Non-anemic patients showed a 30-day mortality rate of 0.78% (over 158,000 patients).\(^4\) In contrast the presence of any anemia whether mild (Hb level of 10-13 g/dL in men and 10-12 g/dL in women) amplified patient’s mortality by a factor of 4.5 (3.52% in over 57,000 patients). Moreover, when patients were severely anemic (Hb level below 10 g/dL) 30-day mortality rate increased by factor 13 (more than 11,000 patients). Baron and coworkers analyzed medical reports of more than 39,000 patients confirming the association between the presence of mild anemia (Hb level of 10-13g/dL in men and 10-12g/dL in women) and increased mortality (+20% in multivariate models), longer duration of hospitalization and more frequent admission of intensive care.\(^5\) Longer hospital stays are associated with increased cost and patients are at an increased risk for other healthcare-associated conditions like falls and healthcare-associated infections (HAIs).

Being a worldwide epidemic with significant consequences addressed above, anemia requires prompt evaluation and treatment.\(^1\) Approximately 234 million surgeries are performed worldwide and about 70.2 million patients are anemic prior to surgery displaying additional (avoidable) risk factors.\(^6\) Of this patient population, over 21 million

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patients possess iron-deficiency and iron deficiency anemia that can be reverted by iron replacement.\(^7\)\(^8\) In addition, postoperative iron-deficiency anemia has an even higher prevalence, affecting up to 32 million patients.

Another emerging concept is Hospital-acquired (Associated) Anemia (HAA). Data from 10 Cleveland Clinic Hospitals revealed that 3 out of four patients admitted to their hospitals were anemic. Since this was a multi-hospital study, it is easily generalizable suggesting the high prevalence of this condition in hospitalized patients.\(^9\) Discharge data suggest little to no appropriate therapy for this condition except for red cell (RBC) transfusion. Moreover, presence of anemia on admission will be made worse with ongoing blood loss from surgery but most from phlebotomy for redundant and unneeded tests. More than 25 million liters of phlebotomy blood a year are discarded in sewers which is 4 times the amount we transfuse.\(^10\)

One of the if not the highest risk of anemia in hospitalized patients is the current default treatment, transfusion of RBCs. Transfusions have been demonstrated to be an independent risk factor for both morbidity and mortality and as a treatment of anemia compound the risks.\(^11\) Whitlock et al. analyzed in a retrospective study with 1,583,819 patients (41,421 transfused) the association of RBC transfusion and stroke and myocardial infarction. Transfusion of a single unit of RBC already increased the risk of perioperative ischemic stroke or myocardial infarction by 2.3 fold.\(^8\)

Transfusions

RBC transfusions are administered to patients during active bleeding, chronic blood loss or poor production in order to increase the body’s oxygen carrying capacity. Despite the perceived benefit many RBC transfusions have been deemed unnecessary resulting in risk or harm and defined as “overuse”. Overuse in healthcare has been defined by the Institute of Medicine (IOM) as use “in circumstances where the likelihood of benefit is negligible or zero, and therefore the patient is exposed to the risk of harm”. In general, health care providers as well as health policy makers are largely unaware of the significant impact that overuse in this area has on quality and safety of patients, or the cost and resource savings that can be realized by actively addressing RBC overuse.

RBC transfusion is one of the most frequent procedures performed in U.S. hospitals and Europe, with one in ten inpatients receiving one or more blood units.\(^12\) RBC transfusion practices are highly variable by institution, procedure, and physician.\(^13\) Meta-analysis from risk-adjusted observational studies has shown that RBC transfusions are associated with a 69% increase in mortality and 88% increase in morbidity.\(^14\) Restrictive transfusion practices, in which RBC transfusions are given at lower-than-usual hemoglobin threshold, have been proven safe in multiple

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randomized controlled trials. These studies done repeatedly, ignore the etiology and other available modalities to effective treat or even cure anemia. 

In response to this unmet medical need, the concept of Patient Blood Management evolved to effectively address anemia, coagulation abnormalities and assert blood conservation for all and has now shown to reduce or eliminate transfusions when applied as a multimodality approach with reduced resource utilization and improved patient outcome. 

The costs of RBC transfusion are not widely appreciated. In the past, cost was estimated and ignored as part of “doing business”. In 2010, Activity Based Costing (ABC) employed in one study revealed the cost of transfusion to be between $522 and $1,183 per unit (depending on geographic location) – the study did not account for any morbidity or mortality costs. Beyond the cost of transfusion, each RBC unit transfused is associated with increased cost of care and transfusions that occur at higher hemoglobin levels increase the cost of care more than those given at lower hemoglobin levels. As mentioned above, many transfusions are unnecessary and therefore should be avoided. A systematic, expert review of 494 studies for positive impact on health outcome showed that 59% of RBC transfusions are “inappropriate” resulting in harm to patients. Given the risk and cost of RBC transfusions, there is a growing recognition for the need to implement strategies to reduce transfusions. The Joint Commission has introduced Patient Blood Management Performance Measures that help evaluate appropriateness of transfusions as a continuous quality indicator but lack any recommendation for anemia management. The American Medical Association and the Joint Commission, with Centers for Medicare and Medicaid Services participation, recently identified RBC transfusions as one of the top five overused procedures in medicine.

Hospitals and physicians have continued to face challenges in adopting evidence-based practice guidelines for RBC transfusions. In spite of the strong need to reduce RBC transfusions, existing tools for transfusion decision making may be lacking and this paucity may contribute to inappropriate transfusions. For example, estimated blood loss during surgery is often greater than actual blood loss, leading to incorrect assessments about the need for RBC transfusion and resulting in ‘over-transfusions’.

In addition, laboratory hemoglobin values, which are used as a primary indicator for RBC transfusions, are only available intermittently and are often delayed – leading to transfusion decisions without a laboratory hemoglobin value. In addition, repeated phlebotomies for laboratory tests are associated with induction and/or aggravation of anemia resulting in RBC transfusions in hospitalized patients.

22 Joint Commission. (2012). The Joint Commission continues to study overuse issues. The Joint Commission Perspectives, 32(5), 4-8(5).
Technology to augment laboratory hemoglobin measurements, such as noninvasive and continuous hemoglobin monitoring, may provide clinicians with additional real-time trending information to determine if hemoglobin values are rising, falling, or remain stable, which may permit clinicians to make more informed and early RBC transfusion decisions.

It is estimated that the use of process changes and technology to reduce RBC transfusions can save the U.S. healthcare system in excess of five billion dollars per year, while significantly improving quality and safety. Closing the performance gap will require hospitals and healthcare systems to commit to actions that will result in better healthcare outcomes with efficient use of healthcare resources. In the so far largest multicentre trial (almost 130,000 patients) in the world it has been shown that the implementation of PBM reduces significantly the amount of transfused blood, costs and kidney damage. Overall, the implementation of PBM is safe and effective (Meybohm et al., Annals of Surgery 2016).

**Leadership Plan**

Based on sustained success of Patient Blood Management programs in USA, Australia, Europe, and Asia, proposals to implement change are listed below:

- The plan should include fundamentals of change outlined in the National Quality Forum (NQF) safe practices, including awareness, accountability, ability, and action.
- Hospital governance and senior administrative leadership must commit to increase awareness of this major performance gap in their own healthcare environment.
- Hospital governance, senior administrative leadership, and clinical/safety leadership must close their own performance gap by implementing a comprehensive approach to addressing the performance gaps identified above.

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● A time line with defined deliverables should be set to implement the plan to address the gap with measurable quality indicators - “Some is not a number. Soon is not a time.”

● Specific resource allocations for the plan should be evaluated and approved by governance boards and senior administrative leaders.

● Clinical/safety leadership should endorse the plan and drive implementation across all providers and systems.

**Practice Plan**

- Establish a Patient Blood Management Committee and appoint an individual to be responsible for leading this group.
  - Patient Blood Management Coordinator and her/his team should engage in early communication to key stakeholders (stakeholder management).
  - The committee should establish a comprehensive plan for anemia management
  - Measurable outcomes with benchmarks for individual and departmental goals

- A comprehensive education program should be developed for emergency and elective admissions. This should be targeted to medical students, physicians, nurses, pharmacists and other health care staff, and focused on Patient Blood Management program’s goals, structure, and scope.
  - Online E-Learning course and receive a “Patient Blood Management certificate”

**Interdisciplinary Blood Conservation Modalities**

- Reduce unnecessary laboratory tests, the frequency of sampling, the “discard” volume when samples are obtained from indwelling lines, and the blood waste by the use of closed blood sampling systems for arterial and central venous lines, are recommended.
- Introduce a protocol for management of platelet inhibitors and other anticoagulants preoperatively.
- Consult the appropriate blood conservation specialists early in cases with physiologic deterioration or complications.
- Guidelines, for anemia therapy including transfusion thresholds, checklists and SOPs should be established in cooperation with all stakeholders.

**Anemia Management**

- Screen, diagnose and treat appropriately all anemia including prior to surgery, allowing adequate lead time to correct the anemia.
  - Establish a system to address anemia both for outpatient and inpatient
- Prompt identification of anemia during and after surgery using all available techniques.
- Establish single unit transfusion policy.
- Implement mercurial-algorithm to calculate RBC deficit.
- Consider alternative therapies to RBC transfusions
  - Intravenous iron.
  - Erythropoietin stimulating agents (ESAs).
- Introduce a protocol for RBC transfusion decision-making.
  - Normovolemia should be checked before restrictive transfusion.
- Advocate restrictive transfusion practices.
  - Develop guidelines locally that reduce patients’ exposure to allogeneic transfusions including lower hemoglobin triggers for transfusion.
- Introduce proactive review instead of the commonly used retroactive review.

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○ Consideration of not just hemoglobin levels but also the change in hemoglobin levels from baseline, as an indicator or need for transfusion.\textsuperscript{37}

○ Transfusion decision making based on signs and symptoms, in addition to hemoglobin level - consider symptoms including chest pain, orthostatic hypotension or tachycardia unresponsive to fluid resuscitation, or congestive heart failure.\textsuperscript{39}

○ Benchmarking of hemotherapy product use by individual units and/or hospitals may be a significant tool in change management and implementation of Patient Blood Management.

- Documentation of hemoglobin before the transfusion of each RBC unit.\textsuperscript{21}
- Utilize hemoglobin monitoring technologies to augment laboratory testing to obtain additional information about patient status before transfusion decisions are made.

Figure 1: Preoperative anemia management workup algorithm.\textsuperscript{40}

Optimizing Coagulation and Reduce Bleeding

- Preoperative evaluation of coagulation abnormalities.
- Minimally invasive surgical techniques.
- Use surgical techniques to minimize bleeding including use of electrocoagulation, bipolar, and argon beam.
- Blood loss minimization techniques; for example, use of vasoconstrictors, topical coagulation agents and tourniquets.
- Maintain normothermia
- Consider controlled hypotension.
- Consider acute normovolemic hemodilution.
- Use blood salvage technologies.
- Basic conditions for hemostasis, reversal of anticoagulants, point-of-care diagnostics in coagulopathic patients, optimized coagulation management with the use of clotting factor concentrates, and the use of antifibrinolytic agents or desmopressin are further important considerations.
- In cardiac surgery, a wide spectrum of blood sparing techniques have been described, e.g. minimized extracorporeal circuits, retrograde autologous priming, modified ultrafiltration, blood cardioplegia, and meticulous hemostasis in saphenous vein graft removal.

Hemorrhage Identification and Control

- Identify patients at risk for development of hemorrhage (OB)
- A massive hemorrhage protocol should be available.
  - Where indicated, massive hemorrhage protocols should be extended by specific algorithms for different subgroups of high-risk patients, e.g. postpartum and trauma.

Technology Plan

Suggested technologies are limited to those proven to show benefit or are the only known technologies with a particular capability. As other technology options may exist, please send information on any additional technologies, along with appropriate evidence, to info@patientsafetymovement.org.

- Implement electronic health record (EHR) fields requiring documentation of clinical indication for transfusion and hemoglobin value prior to each RBC unit.21 (Decision support iForms)
- Implement noninvasive and continuous hemoglobin monitoring17,18 (SpHb® adhesive sensors connected to rainbow SET monitors with SpHb, or a multi-parameter patient monitor with SpHb, including but not limited to the Dräger® M540/Infinity Acute Care System, Welch Allyn® CVSM, Fukuda Denshi® 8500, Saadat® Aria and Alborz monitors, GE®, Philips®, and more).
- Implement cell recovery technology in the operating room (such as Cobe®, Haemonetics®, or other equivalent devices).
- Implement point of care coagulation testing (such as iStat®, TEG®, and ROTEM®).
- Implement smaller blood test tube volumes
- Reduce priming volume of extracorporeal circuits
- Implement closed blood sampling systems for arterial and central venous lines.
- Implement an IT structure for benchmarking.

Metrics

Topic:

**Anemia and Transfusion Management**
Rate of transfusion, adverse events (AE) and/or mortality for untreated and treated preoperative anemia per 1000 patients undergoing elective surgery.

**Outcome Measure Formula:**
- **Numerator:** Number of transfusion, AE and/or mortality for patients with untreated and treated preoperative anemia.
- **Denominator:** Total number of patients with transfusion, AE and/or mortality undergoing elective surgery.

*Rate is typically displayed as Mortalities/1000 Patients

**Metric Recommendations:**

**Direct Impact:**
All patients undergoing elective surgery.

**Lives Spared Harm:**

\[
\text{Lives} = (\text{Mortality Rate}_{\text{baseline}} - \text{Mortality Rate}_{\text{measurement}}) \times \text{Patients}_{\text{baseline}}
\]

**Notes:**
Patients with hemoglobin level below WHO recommendation: 41

**Table 1**

<table>
<thead>
<tr>
<th>Population</th>
<th>Non-Anaemia*</th>
<th>Mild*</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children 6 - 59 months of age</td>
<td>110 or higher</td>
<td>100-109</td>
<td>70-99</td>
<td>lower than 70</td>
</tr>
<tr>
<td>Children 5 - 11 years of age</td>
<td>115 or higher</td>
<td>110-114</td>
<td>80-109</td>
<td>lower than 80</td>
</tr>
<tr>
<td>Children 12 - 14 years of age</td>
<td>120 or higher</td>
<td>110-119</td>
<td>80-109</td>
<td>lower than 80</td>
</tr>
<tr>
<td>Non-pregnant women (15 years of age and above)</td>
<td>120 or higher</td>
<td>110-119</td>
<td>80-109</td>
<td>lower than 80</td>
</tr>
<tr>
<td>Pregnant women</td>
<td>110 or higher</td>
<td>100-109</td>
<td>70-99</td>
<td>lower than 70</td>
</tr>
<tr>
<td>Men (15 years of age and above)</td>
<td>130 or higher</td>
<td>110-129</td>
<td>80-109</td>
<td>lower than 80</td>
</tr>
</tbody>
</table>

* Adapted from references 5 and 6
* Haemoglobin in grams per litre
* "Mild" is a misnomer: iron deficiency is already advanced by the time anaemia is detected. The deficiency has consequences even when no anaemia is clinically apparent.

Data Collection:
Data may be pulled from electronic billing data. Additionally, data may be collected exclusively through manual chart review, or a hybrid method of chart review and electronic billing data.

Settings:
All in-patients (aged ≥ 18 years) undergoing a surgical procedure and with at least one overnight stay.

Mortality (will be calculated by the Patient Safety Movement Foundation).

Workgroup

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Conflicts of Interest Disclosure:
*This Workgroup member has reported a financial interest in an organization that provides a medical product or technology recommended in the Technology Plan for this APSS.