NAC Companion Document to:

"Red Blood Cell Transfusion: A Clinical Practice Guideline from the AABB"

NATIONAL ADVISORY COMMITTEE ON BLOOD & BLOOD PRODUCTS

National Advisory Committee on Blood and Blood Products | Comité consultatif national sur le sang et les produits sanguins

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Overview

On April 25, 2013 the National Advisory Committee (NAC) on Blood and Blood Products recommended endorsement of the guidelines set forth in Red Blood Cell Transfusion: A Clinical Practice Guideline from the AABB (Ann Intern Med. 2012 Jul 3;157(1):49-58.) In brief, the AABB guidelines recommended:

- Adherence to a restrictive transfusion strategy (70-80 g/L) in hospitalized, stable patients
    - Adult and pediatric ICU patients: consider transfusion at 70 g/L or less
    - Post-operative surgical patients: consider transfusion at 80 g/L or less
- Adherence to a restrictive transfusion strategy (≤80 g/L) in hospitalized, stable patients with preexisting cardiovascular disease
- Considering transfusion for patients with symptoms (chest pain, orthostatic hypotension, tachycardia unresponsive to fluid resuscitation, congestive heart failure)
- Transfusion decisions should be influenced by symptoms as well as hemoglobin concentration

The last point is to be emphasized. Implicit in the phrase "adherence to a restrictive transfusion strategy" is the idea that transfusion may be **considered** at a certain hemoglobin level. A hemoglobin below this level, however, does not make transfusion obligatory; always, the clinical condition and preferences of the patient must be considered.

In the non-urgent setting, a policy of "one unit at a time" should be employed; that is, after the transfusion of a single RBC unit, there shall be clinical reassessment of the patient prior to making the decision to transfuse another.

The authors were unable to recommend either a liberal or restrictive transfusion threshold for hospitalized, hemodynamically stable patients with acute coronary syndrome. This was owing to a lack of randomized, controlled trials providing clear evidence.

In addition to patients with acute coronary syndrome, other patient populations whom the AABB guidelines do not specifically address include:

- Neonates
- Outpatients
- Patients with acute hemorrhage
- Palliative / end-of-life care patients

This first purpose of this companion document is to highlight recent advances in the literature, particularly those which may inform transfusion decisions in those who fall outside the scope of the AABB guidelines. It is important to note that this discussion is limited to appropriate transfusion thresholds, and does not address other important considerations (such as the use of irradiated RBC units). The second purpose of the document is to provide additional tools for those interested in collecting data on red cell transfusion in their practice, department, hospital or region.

Recent Advances

Please note that all hemoglobin levels have been converted into SI units.

Acute Coronary Syndrome

Although others[1] have raised methodological concerns (including the heavy reliance on observational studies), a recent metaanalysis by Chatterjee et al[2] demonstrated blood transfusion or a liberal strategy compared with no blood transfusion or a restrictive strategy was associated with higher all-cause mortality in patients with myocardial infarction.

Neonates

Kirpalani et al[3] found that in 451 infants of birth weight <1000 g, there was no difference between rates of death and major morbidity between restrictive or liberal transfusion regimens. Follow-up of the study group[4] at 18-21 months (corrected age) with post-hoc analysis using developmental delay defined as Mental Development Index score <85 showed a significant difference between the groups favouring liberal transfusion.

In contrast, Bell et al[5] found that in 100 preterm infants of birth weight between 500g and 1300g, infants in the restrictive group showed a trend for increased intraparenchymal brain hemorrhage or periventricular leukomalacia and had significantly more apneic episodes. In follow up of 56 of these infants[6], those in the liberal group performed more poorly on tests of reading, visual memory and associative verbal fluency. In a review of 44 of the infants from the original study, compared with full-term children, the liberal group showed smaller intracranial volumes (more so than the restrictive group). This difference was most marked in females.

Some authors[7] have recommended red cell transfusions be considered in premature neonates requiring mechanical ventilatory support when the hemoglobin is <120 g/L, and lower thresholds for oxygen-dependent neonates not requiring ventilation or for late anemia, dependent on gestational and post-natal age (70-100 g/L). Along these lines, a recent Cochrane

[1]Carson JL and Hebert PC. Here we go again – blood transfusion kills patients? JAMA Intern Med 2013; 173:139-140.

[2]Chatterjee S, Wetterslev J, Sharma A et al. Association of blood transfusion with increased mortality in myocardial infarction: a meta-analysis and diversity-adjusted study sequential analysis. Arch Intern Med

[3]Kirpalani H, White RK, Anderson C et al. The premature infants in need of transfusion (PINT) study: a randomized, controlled trial of a restrictive (low) versus liberal (high) transfusion threshold for extremely low birth weight infants. J Pediatr 2006;149:301-307.

[4]Whute RH, Kirpalani H, Asztalos EV et al. Neurodevelopmental outcome of extremely low birth weight infants randomly assigned to restrictive or liberal hemoglobin thresholds for blood transfusion. Pediatrics 2009;123:127-213.

[5]Bell EF, Strauss RG, Widness JA etal.Randomized trial of liberal versus restrictive guidelines for red blood cell transfusion in preterm infants. Pediatrics 2005;115:1685-1691.

[6] McCoy TE, Conrad AL, Richman LC et al. Neurocognitive profiles of preterm infants randomly assigned to lower or higher hematocrit thresholds for transfusion. Child Neuropsychol 2011;17:347-67.

[7]Venkatesh V, Khan R, Curley Anna et al. How we decide when a neonate needs a transfusion. British Journal of Haematology 2013;160:421-433.

review[8] concluded that restrictive practice does not appear to have a significant impact on death or major morbidities at first hospital discharge or at follow-up.

Outpatients

Patients with anemia should be investigated, and underlying causes treated, if possible. In patients with chronic hypoproliferative anemia in the absence of reversible etiologies, transfusion should target the lowest hemoglobin that adequately relieves clinical signs and symptoms of anemia[9]. Use of RBC transfusion to raise the hemoglobin above 100 g/L is usually inappropriate.

Hemorrhage

Villanueva et al[10] looked at 921 adult ICU patients with high clinical suspicion of upper gastrointestinal hemorrhage, with 461 assigned to a restrictive transfusion strategy (transfusion when the hemoglobin fell below 70 g/L) and 460 assigned to a liberal transfusion strategy (transfusion when the hemoglobin fell below 90 g/L). Exclusion criteria included massive exsanguinating bleeding and acute coronary syndrome. Those randomized to the restrictive strategy had lower overall mortality at 45 days, had fewer adverse events and a lower rate of further bleeding.

Palliative Care

In their review of the literature, Torres et al[11] found no clinical guidelines, reviews or consensus conferences for the use of red cell transfusion in the context of palliative care. There is no clearly established "transfusion trigger", although most of the studies they reviewed used a hemoglobin level of ≤80 g/L. Like the AABB guidelines, the authors emphasize that the hemoglobin level must not be the only factor in the decision to transfuse; the clinical situation and patient preferences must also be considered.

[8]Whyte R, Kirpalani H. Low versus high haemoglobin concentration threshold for blood transfusion preventing morbidity and mortality in very low birth weight infants. Cochrane Database Syst Rev 2011;9:CD000512. doi: 10.1002/14651858.CD000512.pub2.

[9] British Columbia Transfusion Medicine Advisory Group. Guidelines for red cell transfusion: 2014. Retrieved from: http://www.pbco.ca/images/UM/RBC/guidelines%20for%20rbc%20transfusion%20%28january%2C%202014%29.pdf

[10]Villanueva C, Colomo A, Bosch A et al. Transfusion strategies for acute upper gastrointestinal bleeding. N Eng J Med 2013;368:11-21.

[11] Torres ME, Rodriguez NJ, Ramos JL, Gomez FA. Transfusion in palliative care patients: a review of the literature. J Palliat Med 2014;17:1-17.

Other

The American College of Physicians recently published clinical practice guidelines[12] recommending a restrictive red blood cell transfusion strategy (trigger hemoglobin threshold of 70 to 80 g/L) in hospitalized patients with heart disease.

A meta-analysis by Salpeter et al[13] looking at 2364 subjects in 3 trials demonstrated that restrictive hemoglobin transfusion trigger (<70 g/L) resulted in fewer cardiac events, rebleeding, bacterial infections and total mortality, as compared with a more liberal strategy.

In a study of 139 patients >50 years old hospitalized with hip fracture[14], a liberal transfusion strategy (transfusion trigger of 100 g/L) versus a restrictive strategy (transfusion trigger of 80 g/L) was not associated with less frequent / severe delirium.

[12]Qaseem A, Humphrey LL, Fitterman N et al. Treatment of anemia in patients with heart disease: a clinical practice guideline from the American College of Physicians. Ann Intern Med. 2013;159:770-9.
[13]Salpeter SR, Buckley JS, Chattterjee S et al. Impact of more restrictive blood transfusion strategies on clinical outcomes: a meta-analysis and systematic review. Am J Med 2013;127(2):124-131
[14]Gruber-Baldini AL, Marcantonio E, Orwig D et al. Delirium outcomes in a randomized trial of blood transfusion thresholds in hospitalized older adults with hip fracture. J Am GeriatrSoc 2013;61:1286-95.

General Audit Letter – Retrospective/Prospective

DD MM YYYY

Dear _____ (Division Head/Medical Director/Chief Tech BTS)

This letter is to make you aware of an audit (either retrospective or prospective) of red blood cell (RBC) utilization that will be taking place in your province / your health region / your hospital during MM YYYY. This audit is spearheaded by the provincial Ministry of Health, with the support of the provincial Blood Coordinating Office / hospital Transfusion Safety Officer.

The purpose of this audit is to evaluate the appropriateness of RBC transfusion in your province / health region / hospital, and identify opportunities to improve the utilization of this blood product. You are being kindly requested to participate in this audit. We request that you choose any single 24 hour period during MM YYYY. During this time, please identify all patients transfused with RBCs in your hospital / health region / province, and provide data for each patient using the attached Appendix A – RBC Audit Tool.

When performing a prospective audit, there is an additional requirement by the Physician to complete a Clinic Data Request sheet – refer to Appendix B.

Any questions or clarification required regarding this audit can be directed to the contact below.

Completed audit data are to be returned to:

Name: _____

Phone:_____

Email: _____

Fax: _____

Thank you for your participation.

Audit Letter to Physician – Prospective

DD MM YYYY

Dear Doctor,

This letter is to make you aware of a prospective audit of red blood cell utilization that will be taking place in your province / your health region / your hospital during MM YYYY. This audit is spearheaded by the provincial Ministry of Health, with the support of the provincial Blood Coordinating Office / hospital Transfusion Safety Officer.

Guidelines for appropriate red blood cell transfusion were recently circulated throughout your province / health region / hospital (Ann Intern Med. 2012 Jul 3;157(1):49-58). It is not known, however, what percentage of red cell transfusions are outside of these guidelines. The purpose of this audit is to collect data on the appropriateness of red cell transfusion in your province / health region / hospital, and to allow provinces, health regions and hospitals to perform benchmarking against other comparable (anonymized) groups.

For a 24 hour period between DD MM YYYY and DD MM YYYY, hospital transfusion services will be distributing a Clinical Data Request form (see Appendix B) to each physician who orders a red cell unit for transfusion. The success of the audit in your hospital depends upon your completing these forms in a timely fashion.

If you have any questions regarding this red blood cell utilization audit, please contact:

Name: _____

Phone:_____

Email:_____

Fax:_____

Thanking you in advance for your help with this important initiative.

APPENDIX A - RBC AUDIT TOOL

Audit Date: DD MM YYYY to DD MM YYYY

HOSPITAL DATA

Province _____

Health Region _____

Hospital _____

Size (# of beds) _____

Catchment _____

Annual # crossmatches _____

Annual # transfusions _____

PATIENT DATA

Patient ID _____

Gender Male ___ Female ___

Patient Age _____

Admitting Diagnosis _____

Admission Date _____

Discharge Date _____

Comorbidities (please check)

___ Cardiac (previous MI, angina, hypertension, heart failure, pulmonary edema, peripheral vascular disease)
___ Cerebrovascular (previous CVA e.g. stroke, TIA)
___ Respiratory disease
___ Active cancer / chemotherapy
___ Acute MI / acute coronary syndrome
___ Renal disease
___ Chronic infection
___ Other (please specify) _____

Does the patient meet any of the following criteria? (Please check)

___ Thalassemia / sickle cell disease
___ Palliative patient with short-term life expectancy

APPENDIX A - RBC AUDIT TOOL - continued

Is the patient experiencing significant ongoing bleeding (>500 mL/hour or >250 mL/hour x three hours)?
☐ YES ☐ NO

Is the patient currently experiencing symptoms/signs of anemia (e.g. dyspnea, angina, palpitations, syncope, tachycardia, postural hypotension)? ☐ YES ☐ NO

LABORATORY DATA

From most recent pre-transfusion CBC (specify date): _____
Hemoglobin _____ g/L
Number of days between transfusion and most recent pre-transfusion CBC: _____

Post-transfusion CBC (specify date): _____
Hemoglobin _____ g/L
Number of days between transfusion and first post-transfusion CBC: _____

TRANSFUSION DATA

Specialty of physician who recommended transfusion? _____

Where was the patient transfused (e.g. pre-op, intraoperatively, ICU, ED, etc.)?

_____

What is the reason for the transfusion? _____

_____

How many units of RBCs were transfused? _____

Did the patient experience a transfusion reaction? ☐ YES ☐ NO

Specify type: _____

APPENDIX B - RBC AUDIT CLINICAL DATA REQUEST

Audit Date: DD MM YYYY to DD MM YYYY

To Be Completed by the Ordering Physician

Patient ID:_____

What is the patient's indication for transfusion? _____

Specialty of physician who recommended transfusion? _____

Where will the patient be transfused (e.g. pre-op, intraoperatively, ICU, ED, etc.)?_____

Is the patient currently taking:

Iron therapy? ☐ YES ☐ NO

Erythropoiesis stimulating agents (ESAs)? ☐ YES ☐ NO

Folic acid and/or vitamin B12? ☐ YES ☐ NO

Does the patient have documented / obvious evidence of ongoing significant bleeding at the time of transfusion causing symptoms as above or bleeding >500 mL/hour or 250 mL/hour x 3 hours and not stopping? ☐ YES ☐ NO

Specify:_____

Does the patient have symptoms attributable to anemia e.g. dyspnea, angina, palpitations, tachycardia, orthostatic hypotension or syncope)? Note that fatigue alone is not an appropriate symptom to prompt transfusion. ☐ YES ☐ NO

Specify:_____

Does the patient have a history of current or recent (within 3 months) cancer or chemotherapy?

☐ Yes ☐ NO

Specify:_____

Does the patient have myocardial infarction / acute coronary syndrome? ☐ Yes ☐ NO

Does the patient have cardiovascular or cerebrovascular problems (e.g. previous MI, angina, hypertension, heart failure, peripheral vascular disease, pulmonary edema) or respiratory disease?

☐ YES ☐ NO

Specify:_____