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ANEMIA ALERT

The monthly e-newsletter for medical professionals from the National Anemia Action Council.

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Anemia Alert is NAAC's monthly e-newsletter for medical professionals. Each issue contains anemia news, expert commentary, feature articles and other recently updated content from www.anemia.org.

Educating Deferred Blood Donors

Of the roughly one million monthly blood donors in the United States, about 10% are deferred from donating because their hematocrit level falls below the FDA-mandated threshold of 38%. This deferral may be the first time donors discover that they have anemia or are considered borderline anemic.

To help educate these patients about low hematocrit levels, NAAC published the *Anemia & Blood Donation* online tutorial. Take a tour to see how it can help your patients. View Tutorial

FEATURE: Advising Deferred Blood Donors About Low Hematocrit Level

For professionals, we've covered information this month that may be necessary to discuss with patients who donate blood and have been deferred due to a low hematocrit level. Many times deferred donors are not aware that it is important to discuss a low hematocrit with their doctor. Close communication with them about their medications, symptoms, and hematocrit levels will help you develop, and help your patient understand, the best plan of action to prevent or treat anemia. The article covers:

- Why a Low Hematocrit Level Leads to Deferral
- Differences in Screening Tests for Iron Levels
- Diagnosing and Managing Anemia after Deferral

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Ask the NAAC Experts

Noticeable Impact of Hemoglobin Level on Quality of Life

Question:
Is it true that the most noticeable impact on a patient's quality of life is when hemoglobin drops the first 2 g/dL?

NAAC Expert Answer:
A retrospective study in cancer patients reported that the highest incremental improvement on fatigue was obtained when hemoglobin rose from 11 to 13 g/dL. Currently there are no data on other aspects of quality of life. For many older patients, the best function is reached when hemoglobin is between 12.5 and 14.0 g/dL. It is important to note that while some results can indicate ranges of hemoglobin levels in which improved function exists, conclusions should not be made that raising hemoglobin levels improves quality of life or function for all patients. In fact, recent studies suggest that it is best not to try to correct anemia to normal hemoglobin levels above 12 g/dL.

The ranges of best function, as expressed above, have been indicated by data from clinical trials. The ranges should NOT, however, be construed as guidance for determining optimum target hemoglobin levels during anemia treatment. Practitioners should follow approved drug labeling and established clinical guidelines.

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Research Reviews of Recent Clinical Trials

Improving Oxygenation on After Severe Traumatic Brain Injury

Severe traumatic brain injury (sTBI) is a common occurrence that presents numerous health care challenges. sTBI case studies report high percentages of fatalities, as well as poor long-term prognoses in terms of cognitive abilities and patient quality of life. In particular, anemia has been shown to be injurious to the brain, and thus detrimental to patients with sTBI. However, despite the evidence showing detrimental effects, very little research has focused on determining the value of packed red blood cell transfusion to improve outcome, or to identify possible hemoglobin (Hb) target levels. Therefore, a recent study by Zygun et al evaluated the effect of packed red blood cell transfusion on cerebral oxygenation and metabolism in patients with sTBI.

This study evaluated 30 patients who presented with sTBI to an adult critical care unit from January 2003 to July 2005. On average, patients received transfusion four days after injury. Patients were randomly assigned to three Hb threshold levels (8, 9, and 10 g/dL), and were transfused with 2 units of packed red blood cells when Hb levels dropped below those thresholds. Physiologic data and Hb levels were recorded after a stabilization period of one hour, and the change in brain tissue oxygen (PbtO2) was assessed as the primary outcome. Additionally, secondary outcomes included the dependence of baseline Hb concentration and PbtO2 on the relationship of transfusion and PbtO2, as well as the effect of transfusion on lactate pyruvate ratio (LPR) and brain pH as markers of cerebral metabolic state.

In terms of PbtO2, 57% of patients experienced a significant increase in PbtO2. However, no significant association was found between PbtO2 and baseline Hb. In addition, no significant association was found between a change in LPR and change in Hb levels, nor was an increase in brain pH observed. These results indicate that transfusion of packed red blood cells may improve brain tissue oxygenation, but does not have significant effects on cerebral metabolism.

Although the study showed a significant PbtO2 increase in 57% of patients, the authors offer several limitations to be considered. First, increases in PbtO2 were most prominent in patients with LPR greater than 25. Increased LPR has recently been found to be a marker of mitochondrial dysfunction, and therefore the improvements in PbtO2 may only be seen in patients with cerebral metabolic dysfunction. Second, the results may not be representative of whole brain metabolism, because the microdialysis monitors used in this study sampled only a small portion of the brain. Finally, the study sample was small, and the duration was too short to consider the long-term effects of prestored donor erythrocytes on oxygen delivery. Thus, more comprehensive studies will be needed to evaluate transfusion strategies in sTBI patients.

Zygun DA, Nortje J, Hutchinson PJ, Timofeev I, Menon DK, Gupta AK. The effect of red

blood cell transfusion on cerebral oxygenation and metabolism after severe traumatic brain injury. Crit Care Med. 2009 Mar;37(3):1074-78.

NAAC Expert Commentary:

Reports of an association between anemia and increased mortality in severe traumatic brain injury (sTBI) patients suggest that this is a lethal combination.[1,2] To date, most treatment aimed at decreasing anemia-associated mortality has focused on increasing Hb levels with transfusion.[3] The rationale has been to prevent cerebral ischemia by maximizing the oxygen carrying capacity of blood to protect vulnerable neuronal tissues.[4]

However, success, measured as a decrease in overall mortality has been elusive. George et al reported similar mortality rates of 29% in non-transfused sTBI patients compared to 35% in those who were transfused.[5] In a study of transfusion and anemia in 1,150 sTBI patients, Salim et al showed that when both factors were taken into account, blood transfusion was significantly associated with higher mortality but anemia was not. Without transfusion, anemia was a significant risk factor for mortality.[6] Canadian investigators were unable to detect a significant decrease in mortality with a liberal (Hb maintained between 7-9 g/dL) as compared to restrictive (Hb maintained between 10-12 g/dL) transfusion strategy in critically ill trauma victims with moderate to severe head injury.[7]

Overall mortality rates may not be discriminating enough to show the potential benefit of transfusion in sTBI. Consequently, more recent investigations have focused on measures of cerebral blood flow and oxygenation. These include local cerebral blood flow (CBF) measured with a parenchymal thermal diffusion probe and brain tissue oxygen tension (PbtO2). Measurements of PbtO2 represent the product of CBF and the cerebral arteriovenous oxygen tension rather than a direct measurement of total oxygen delivery or cerebral oxygen metabolism.[8] Smith et al reported that PbtO2 increased after red cell transfusion in 26 of 35 patients. However, it decreased in 9 other matched patients.[9] Note that this same group had previously reported that red cell transfusion was associated with angiographically confirmed vasospasm and worse outcome in patients with subarachnoid hemorrhage.[10]

The current article by Zygun and colleagues addresses the impact of transfusion in sTBI as measured by PbtO2.[11] Thirty patients, randomized to one of three transfusion thresholds (8, 9, or 10 g/dL) received 2 units of red blood cells when thresholds were reached. All were studied with PbtO2 pre and post transfusion. PbtO2 increased in 57% of patients, but did not change or decreased in the remaining 43%. Although the authors concluded that transfusion of red blood cells acutely results in improved brain tissue oxygen, their data do not strongly support this conclusion. Moreover, they did not relate the Pbt02 changes to outcomes.

We know that anemia remains a major concern as a predictor of increased mortality in sTBI patients, but transfusion has not proven to be a reliable means of decreasing mortality as measured by either overall mortality or sophisticated measurements such as CBF and PbtO2. Several factors may account for the vexing problem of nonresponders in the above studies. Use of an all-cause definition of mortality may not accurately reflect the impact of anemia treatment on ischemic cerebral tissues. Although Pbt02 is a good measure of brain tissue oxygen tension in the healthy brain, its performance is affected by several variables including overall blood flow and proximity of the Pbt02 probe to ischemic brain tissue. Its value in sTBI patients needs to be clarified.

On a grander scale, mechanisms that may minimize or increase anemia-induced cerebral injury have not been clearly elucidated. In addition, protective mechanisms which may minimize cerebral injury during acute anemia have not been well defined. Vasodilatory mechanisms, such as nitric oxide, transcription factors such hypoxia inducible factor (HIF)-1alpha, cytokines, and molecules such as erythropoietin all play a role in regulating cerebral cellular responses and tissue oxygenation.[12]

The most we can conclude from these studies is that anemia remains a major concern in patients with sTBI and that red cell transfusion increases Hb levels and hematocrit, but its impact on mortality and cerebral oxygenation remains elusive. Further studies are in order.

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