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Hematocrit trial

To the Editor:

We read with interest the report by Ootaki and associates,[1] as well as the correspondence by Shuhaiber[2] in reference to the article by Habib and colleagues.[3] Ootaki and coworkers[1] applied a transfusion protocol in which blood was not transfused during cardiopulmonary bypass unless hematocrit was less than 15%. They found that patients with a hematocrit of less than 20% had a higher lactate level than patients with a higher hematocrit but imply that this has no functional significance.

In their critique of the article by Habib and associates,[3] which emphasized the value of the lowest hematocrit as a predictor of outcome, Shuhaiber[2] implied that a hematocrit of 20% is a useful transfusion trigger. They also called for a prospective randomized study of hematocrit, as did Habib's group.

At the 2002 meeting of the American Association for Thoracic Surgery, we presented the results of a prospective randomized trial of 2 hemodilution strategies.[4] This study was shut down by the Data and Safety Monitoring Board of the National Institutes of Health because of a strongly positive outcome. Infants who had a mean hematocrit of 27.8% ± 3.2% (n = 73) had significantly better motor skills at 1 year of age relative to patients whose lowest hematocrit on bypass was 21.5% ± 2.9% (n = 74). A significantly greater percentage of patients at 1 year of age were classified as developmentally delayed with respect to motor skills relative to patients perfused at a higher hematocrit. The lactate level 1 hour after bypass was significantly lower with the higher hematocrit.

The findings of our prospective randomized study are consistent with several previous reports derived from our laboratory work in this area.[5-7] Studies using near-infrared spectroscopy suggest that acute hemodilution during cardiopulmonary bypass results in cerebral hypoxia. It is important to remember, before discarding the significance of our clinical trial as being irrelevant to adults because it was performed in infants, that the mature brain is significantly more sensitive to hypoxic injury than the neonatal and infant brain. Nevertheless, we strongly endorse the call for a prospective randomized trial of hematocrit in adults undergoing cardiopulmonary bypass, including sensitive end points such as assessment for cognitive dysfunction. In the meantime, we strongly recommend that a hematocrit of at least 25% and preferably closer to 30% should be used during cardiopulmonary bypass.

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Randomized prospective trial for blood transfusion during adult cardiopulmonary bypass surgery

To the Editor:

Hemoglobin dilution is an expected physiologic response during cardiopulmonary bypass (CPB) surgery. Current controversy, however, centers around this question: what is a safe hematocrit level during CPB before the patient sustains less than an expected outcome? The main reason for the lack of consensus regarding blood transfusion may stem from the lack of a direct cause (hematocrit level) and effect (morbidity and mortality) relationship or an association or both causality and association. Although it has been found that low preoperative hemoglobin levels are correlated with poorer outcome,[1] it does not mean that correcting this number will result in improved outcome. This same argument holds true for intraoperative hematocrits with the understanding that new-onset intraoperative anemia is reversible and mainly caused by dilution, whereas preoperative anemia is pathologic and mainly caused by nondilutional processes. Also, despite understanding the reversibility concept, most decisions of intraoperative transfusion stem from personal and institutional experience, with no defined dimensions. In May 2004, the National Heart, Lung, and Blood Institute working group published an executive summary regarding future directions in cardiac surgery.[2] Creating a cardiovascular surgery clinical research network was one of the pillars, and I hope that the working group and the National Institutes of Health–sponsored workshop for neurocognitive changes after cardiac surgery will consider this trial an important direction toward filling an existing critical gap.

Why Is a Hematocrit Trial Timely?

The patient's physiologic status must be the underlying cause for a transfusion, and the outcome of the transfusion (effect) must also be considered. The practicing surgeon, including those in training, is currently confused with the paradigm of cause and effect that seems to argue that mortality is higher among patients with low hematocrit (<25% in women and <23% in men[3,4]) and high hematocrit (>34%).[5] Randomization is lacking in the adult cardiac surgery group thus far, despite a clear benefit of increased hematocrit for neurologic outcome in pediatric heart surgery (mean intraoperative hematocrit: 27.8% vs 21.5%).[6]

Moreover, despite the benefit of increased oxygen-carrying capacity with increased hematocrit, we must be aware that blood transfusions expose patients to a variety of potential cellular and hu-

moral antigens. Conservation of blood during surgery will always be important because of the shortages of donor blood, the risks associated with the use of allogenic blood products, and the costs of these products.

At this stage, the outcome measured needs to be better studied in a larger group of patients to determine whether a beneficial effect is achieved when the cause is simply a new-onset decrease in hematocrit during CPB that requires the action of blood transfusion.

How Can We Define the Dimensions for Safe Intraoperative Hematocrit Level?

In the context of a study trial, all variables in a scientific study must be controlled except for a single variable that is being studied. This is an incredible task, but it can be solved with a national task force among many regional centers and coordinated in the most organized fashion. Recruitment of centers that are indifferent to institutional experience is key for eliminating bias. The center with established excellence in surgical outcome among The Society of Thoracic Surgeons risk stratification subgroups will minimize technically dependent outcome variables and maximize the weighted effect of a single variable—hematocrit. The patient population description should include elective surgical patients who require primary or redo CPB coronary, valve, or both types of surgery; who lack hematologic causes for anemia; who have a well-defined etiology of disease process; and who lack prior blood transfusions in the last 3 months, including a well-defined level of comorbidity.

Selection of Hematocrits

Given the already available data in the literature, it is important to chose 2 pathways, each performed randomly at each collaborating surgical unit, given that neither the perfusionist nor the surgeon will be blinded. This will mathematically accommodate a range of preoperative hematocrits to better define absolute and relative risk or benefit to the population sample after transfusion or not. The 2 pathways are (1) transfusing for hematocrits below a discrete value (20%, 25%, and 30%) and (2) transfusing for hematocrits when an absolute difference in CPB hematocrits (5, 10, 15, and 20 integers) is documented during surgery.

The volume of blood transfused should be held constant, and 1 unit of allogeneic blood should be sufficient except in rare circumstances. Should the next hematocrit level respond, no further blood transfusion should be given, yet further transfusion will be given if levels keep decreasing. Time from acknowledging the hematocrit level after the intervention (blood transfusion) will need to be further defined at discussion committees, among other variables, especially regarding triggers for preoperative CPB, postoperative CPB, and intensive care unit periods with respect to 4 important groups of patients—those with left ventricular dysfunction, recent myocardial infarction, congestive heart failure, and incomplete revascularization—because such groups require a higher hematocrit level.

A host of other blood product transfusion, perfusion, and operative variables—including age of blood transfused; priming volume; length of operation; amount of blood transfusion; type of blood transfused (eg, leukocyte depleted, cytomegalovirus status, and allogeneic vs predonated autologous blood); pump run; blood-primed pump; use of preoperative antiplatelets, anticoagulants, and antifibrinolytics; duration of CPB; temperature control (hypothermia and normothermia); volume of crystalloids and colloids infused and reason for infusion; and volume of other blood products infused—will need to be adjusted after consultation with a consortium of perfusionists and hematologists who are experienced in this field.

Also, a similar policy for transfusion should be adopted after surgery to avoid the potential influence of postoperative transfusion on clinical outcome. Outcome, including neurological outcome and survival, should be temporally and qualitatively documented particularly early after surgery and several years later.

Overall, there must be a safe range of hematocrits for each patient in adult and pediatric patients. Available studies remain largely observational and cannot adjust for the effects of all the confounders. In the interim, conservative use of blood products in heart surgery is warranted because of the infectious and noninfectious complications of allogeneic blood transfusion.

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Reply to the Editor:

We would like to thank Dr Jonas for his comments on our recent article.[1] Our study was a prospective, observational study, and the patients had an uncomplicated course in which the criteria for red blood cell transfusion included anemia with a hematocrit level of less than 15% during bypass and 20% after bypass. Jonas and associates[2] conducted a randomized study, and they concluded that a higher hematocrit strategy was safe for psychomotor development in infants. Habib and associates[3] retrospectively analyzed the surgical outcomes from their 6-year experience and concluded that there was a strong association between severity of hemodilution during cardiopul-