RBC Transfusions: Benefi or Risk Factor?

The appropriate hemoglobin level at which transfusion of red blood cells is clinically indicated continues to be debated and studied. The so-called “transfusion trigger” has declined in recent years as more studies have examined the clinical effects of anemia and whether transfusion of red blood cells actually reduces morbidity or mortality. RBC transfusions are usually given to augment the delivery of oxygen to avoid deleterious effects of oxygen debt, based on the assumption that more red cells equates with more oxygen delivery to tissue. However, physiologic studies indicate that increasing hemoglobin values is not always necessary or even critical in delivering more oxygen to tissue sites since mechanisms including a shift of the oxygen dissociation curve and changes in the microcirculation can be very effective.

An important study of transfusion requirements in critical care patients was published last year. The TRICC Trial determined whether a restrictive RBC transfusion trigger (i.e. waiting until the hemoglobin was lower before transfusing) might be clinically equivalent to a liberal transfusion trigger (i.e. giving a transfusion at a higher hemoglobin level) in critically ill patients. This study was a randomized controlled trial comparing 30 day all-cause mortality in the two arms of the study using 838 critically ill anemic patients with euvolemia, enrolled when they were found to have a hemoglobin of 9.0 g/dl or less. Study subjects were enrolled within 72 hours of admission to intensive care, with 418 patients randomly assigned to the restrictive and 420 to the liberal transfusion arm. In the restrictive arm, patients were transfused for hemoglobin less than 7.0 g/dl, and were maintained between 7.0 and 9.0 g/dl. In the liberal transfusion arm, RBC transfusions were given when hemoglobin fell below 10.0 g/dl, with the level maintained between 10.0 and 12.0 g/dl.

Overall, 30 day mortality was similar in the two arms (18.7% vs 23.3%, p=0.11). However, the mortality rates were significantly lower in the restrictive RBC transfusion arm in patients who were either less acutely ill (APACHE II score < 20) or younger (<55). Mortality in the less acutely ill were 8.7% vs. 16.1% (p=0.01) in the restrictive and liberal arms respectively.

Transfusion rates were significantly different in the two arms with 2.6 RBC units transfused in the restrictive arm and 5.6 RBC units in the liberal arm (p<0.01). In addition, 33% of subjects in the restrictive arm did not receive any RBCs compared to 0% in the liberal arm.

Because two recent cohort studies suggested that anemia may increase mortality in patients with cardiovascular disease following surgery and critical illness, the impact of the two RBC transfusion triggers was also evaluated in a subgroup of 323 patients with known cardiovascular disease. Baseline characteristics were comparable in the two cardiovascular disease study arms. Overall, the 30 day mortality in the cardiovascular disease patients was similar in the two arms (20.5% vs 22.9%, p=0.68). In the less acutely ill patients (APACHE II < 20), 30 day mortality tended to be lower in the restrictive arm vs. that seen in the liberal transfusion arm (7% vs 14%, p=0.27). Based on these data, it was concluded that a restrictive RBC transfusion strategy was at least equivalent, and possibly superior, to the use of a more liberal transfusion strategy in euvolemic critically ill patients with cardiovascular disease. [It is important to note, however, that these data may not necessarily apply to patients with acute myocardial infarction, as such patients tended to be excluded from entry into the TRICC trial.]

Another subgroup of patients evaluated was the cohort on mechanical ventilation during the course of the TRICC trial. It is widely believed that in mechanically ventilated patients, correcting anemia using RBC transfusions helps with the increased oxygen demands that are presumably required by such patients, particularly during respiratory weaning. In the TRICC trial, 713 patients had been mechanically ventilated with 357 in the restrictive and 356 in the...
liberal transfusion groups. The baseline characteristics of both groups were comparable, and the mean mechanical ventilation time was 8.3 days for both arms. No difference was found in terms of respiratory weaning success between the two groups; nor was weaning success confounded by patient age or severity of illness. There was no evidence to indicate a liberal RBC transfusion strategy would improve respiratory weaning or number of days on the ventilator. A corollary of this observation is that anemia does not appear to compromise mechanical respiratory weaning nor does it appear to increase the need for mechanical ventilation.

In summary, this study set out to determine if a more conservative RBC transfusion strategy was equally safe for critically ill patients compared to a more liberal approach. Not only did they find that patients receiving conservative transfusion therapy fared as well, but that some actually did better than the group receiving more blood and maintaining a higher hemoglobin value. This is an important new twist on the issue. Not only may liberal transfusion be unnecessary; it may actually be harmful.

While this may not be the final word on the issue of a clinically appropriate transfusion trigger, it appears prudent to carefully consider whether transfusion at hemoglobin above 7.0 – 8.0 g/dl is actually helping the patient or whether it may indeed be harmful.

Timothy R. Carter, MD


PAP Smear Specimen Adequacy

General Information

One of the most important contributions of The Bethesda System for Reporting Cervical/Vaginal Cytologic Diagnoses was the standardization of criteria for specimen adequacy. There are four necessary elements for an adequate cervical/vaginal (Pap Smear) specimen: 1) Correct patient and specimen identification. 2) Pertinent clinical information especially patient age, menstrual information, and any history of prior dysplasia or malignancy. 3) Technical interpretability of the specimen. 4) Cellular composition and sampling of the transformation zone.

A “Satisfactory for Evaluation” specimen will have all of the following:
- Appropriate specimen labeling and identifying information.
- Relevant clinical information.
- Adequate numbers of well preserved and well visualized squamous epithelial cells and an adequate sampling of the endocervical/transformation zone.

A specimen is “Satisfactory for evaluation but limited by …” if:
- There is a lack of pertinent clinical information (age, date of last menstrual period and specimen source as a minimum with additional information as appropriate).
- There is obscuring blood, inflammation, thick areas, poor fixation, air-drying artifact, contaminant, etc. that precludes interpretation of approximately 50-75% of the epithelial cells.
- There is an absence of sampling of the endocervix/transformation zone.
A specimen is “Unsatisfactory for evaluation” if:

- There is a lack of patient identification on the specimen and/or the requisition form.
- The slide is broken and cannot be repaired.
- Well-preserved and well-visualized squamous epithelial cells cover less than 10% of the slide surface. (For ThinPrep slides this is adjusted to less than 40% of the slide surface.)
- Obscuring blood, inflammation, thick areas, poor fixation, air-drying artifact, contaminant, etc. precludes interpretation of 75% or more of the epithelial cells on the slide.

**Rex Cytology Laboratory Specimen Adequacy Data**

For quality assurance purposes and to comply with CLIA regulations, the Rex Healthcare Cytology Laboratory tracks specimen “Unsatisfactory” and “Satisfactory but Limited By…” rates monthly. Our “Unsatisfactory” rate consistently runs around 0.2%, well below the national mean of 0.5%. Our “Satisfactory but Limited By…” rate in the past had ranged from 15-18%. However, over the last several months we have observed an upward trend until now this rate is 22%. Nationally, the mean is approximately 10%. There are two major components to this upward trend. First is an increase in specimen requisitions that do not include the basic pertinent clinical information required by CLIA for proper interpretation and reporting of Pap Smears. The minimal clinical information needed to comply with these criteria is patient age (date of birth), date of last menstrual period, and source of the specimen (cervical/ endocervical or vaginal, etc.). The second major component of the upward trend is a marked increase in ThinPrep specimens that do not include an adequate sampling of the endocervix/transition zone.

The preferred specimen collection procedure for ThinPrep specimens involves the use of an endocervical brush/plastic spatula combination. If this set of collection devices is used then it is unusual to not obtain an adequate sampling of the endocervix/transition zone. However, when using the endocervical brush it is critical that after inserting the brush into the endocervix only a single, gentle, one-quarter of a turn of the brush is made before it is withdrawn. Being too vigorous with the endocervical brush can lead to a bloody specimen, which can then clog the filter apparatus of the ThinPrep device and lead to an Unsatisfactory sample. It is also critical that the endocervical brush be vigorously rubbed at least ten times around the inside of the ThinPrep sample bottle to insure release of all cells into the liquid suspension. Many ObGyns prefer to use a broom-like device for Pap Smear collection. When using these broom devices it is necessary to make sure that the long bristles of the device enter into the endocervix and that then the device is completely rotated ten times while in contact with the endocervix before it is withdrawn. Then, as with the brush, it is important to vigorously press and bend the broom-like device’s bristles against the bottom of the ThinPrep sample container at least ten times and then swirl the broom an additional ten times within the liquid to insure release of all cells into the liquid.

**Physician-Specific Reports**

In February, 2000, our laboratory commenced sending monthly Pap Smear summary reports to all physician clients. These reports list the number of Pap Smears from that
physician for the month and classify the abnormal specimens by diagnosis and percentages of the total. The monthly percentages of “Satisfactory” and “Satisfactory but Limited By…” specimens are also listed. In addition, by request, we can provide a monthly patient by patient list of Pap Smears for a particular physician.

For further information on these reports or for any client services information please contact Debbie Lompa at 784-3355.

Keith V. Nance, M.D.

Effective April 1, 2000, more mandated changes in laboratory panels will take effect. These result from modifications made by the American Medical Association (AMA) in CPT codes for selected test panels with subsequent reimbursement policies adopted by the Health Care Financing Administration (HCFA). Highlights of the changes include the following:

- Calcium is added to the basic metabolic panel.
- ALT (SGPT) is added to the comprehensive metabolic panel. (Carbon dioxide/bicarbonate had been added earlier when somebody finally came to their senses and realized how silly it was to have left it off the original panel configuration.)
- Total protein is added to the hepatic function panel.
- The hepatitis panel is changed to “acute hepatitis panel” with the following changes. Hep B surface antibody, Hep B core antibody (total), and Hep A antibody (total) are deleted. Hep B core antibody (IgM) and Hep A antibody (IgM) are added.
- A renal function panel is created (basic metabolic panel + albumin + PO4).
- There is no longer a thyroid panel.

While some of the changes (hepatitis panel, thyroid panel) are laudable, the others are of questionable benefit. Nevertheless, the Laboratory is obligated to adopt these changes and modify our panels accordingly. As the components of the chemistry panels seem to be changing on a relatively frequent basis, the panels will be referred to by the names adopted by the AMA (rather than trying to use alphanumeric shorthand such as M7 or M12). We regret the inconvenience these changes create for physicians, clerical staff, nursing staff, and patients. For your convenience, an insert summarizing the panels available is enclosed. Tests not included in the panels can be ordered individually. If a panel contains more tests than are medically necessary for a particular patient, a less inclusive panel or individual tests should be substituted.

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