FFP is Ineffective for Correcting Minimally Elevated INR

Today, much plasma is ordered prophylactically to correct an elevated protime (PT) prior to an invasive procedure. Physicians performing invasive procedures want to avoid hemorrhagic complications and often regard a mild elevation of a coagulation test result as an indication to order plasma. The decision to prophylactically transfuse plasma is based on three unproven assumptions:

1. Mild prolongation of PT/INR (defined as an INR <1.7) predicts bleeding from an invasive procedure
2. Pre-procedure transfusion of plasma will correct a prolonged PT/INR
3. Prophylactic plasma transfusions result in fewer bleeding events

The evidence clearly contradicts the first assumption. PT and APTT begin to rise above the upper limit of the normal range when coagulation factor levels fall below approximately 70% of normal. When the INR increases to 1.3 - 1.5, vitamin K dependent coagulation factors are still 50% of normal. Even at an INR between 1.8 and 2.0, they remain at 30% of normal, which is still at or above the minimal hemostatic level of 20 -30%. These results explain why a mildly elevated PT/INR is not usually associated with spontaneous hemorrhage and does not increase the risk of bleeding during routine invasive procedures.

Studies during the last 20 years in patients undergoing liver biopsies, bronchoscopic biopsies, renal biopsies, central line vein cannulation, thoracentesis and angiography have repeatedly demonstrated that PT and activated plasma thromboplastin time (APTT) are not predictive of hemorrhage. However, it must be remembered that the risk of bleeding is greater if the platelet count is decreased, platelet function is abnormal, or the patient has experienced massive trauma or is undergoing extensive surgery.

Additional evidence clearly disputes assumptions 2 and 3. Prophylactic transfusion of plasma to correct a mildly elevated INR prior to an invasive procedure is often not effective. When the INR is <1.7, transfusion of plasma corrects INR an average of only 0.1 per unit transfused, largely because the INR of plasma itself ranges between 1.0 and 1.3. The difference in coagulation activity between donor plasma and patient plasma is so small that plasma transfusions produce minimal demonstrable effect on the patient’s INR.

<table>
<thead>
<tr>
<th>Pre-transfusion INR</th>
<th>INR Correction per Unit of FFP Mean (Range)</th>
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</thead>
<tbody>
<tr>
<td>1.3 – 1.7</td>
<td>0.1 (0.1 – 0.2)</td>
</tr>
<tr>
<td>1.7 – 2.3</td>
<td>0.2 (0.1 – 0.3)</td>
</tr>
<tr>
<td>2.4 – 2.9</td>
<td>0.4 (0.1 – 0.7)</td>
</tr>
<tr>
<td>3.0 – 4.3</td>
<td>0.7 (0.2 – 1.5)</td>
</tr>
<tr>
<td>4.4 – 20.0</td>
<td>3.5 (1.1 – 8.4)</td>
</tr>
</tbody>
</table>

While a patient with an INR of 1.7 or less may bleed during an invasive procedure, the medical literature clearly demonstrates that the incidence of hemorrhage is not different from that of patients with a normal INR.

In summary, plasma transfusion has minimal effect onnormalizing the INR in patients with mildly prolonged INRs for the following reasons:

- Plasma produced from healthy blood donors can have an INR as high as 1.3
- Plasma transfusion to a patient with an INR of less than 1.7 has minimal effect
- Plasma transfusion to patients with an INR of less than 1.7 does not decrease the INR more than usual medical care without plasma transfusion

In view of this information, the common practice of prescribing plasma to correct a mildly elevated INR prior to an invasive procedure needs to be reevaluated. It is not necessary or efficacious to correct an INR below 1.7 to achieve adequate hemostasis.
Monitoring Heparin Therapy

Effective July 2008, revised order sets will be in place for unfractionated heparin (UFH) therapy. These protocols will utilize the anti-factor Xa based heparin assay for monitoring and dose adjustment. This heparin assay can be used for low molecular weight heparin (LMWH) as well. Results of the heparin anti-factor Xa assay will be reported in IU/mL with the following interpretive comments:

- **Expected therapeutic range for unfractionated heparin:** 0.3 - 0.7 IU/ml (or as specified by order set or physician)
- **Expected therapeutic range for low molecular weight heparin:** 0.5 - 1.0 IU/ml (or as specified by order set or physician)

The critical value for this test will be set at 1.1 IU/ml for UFH (for non-cardiac patients).

Reflex Testing

Federal regulations require that laboratories inform physicians of their reflex test policy. Reflex testing refers to those situations where an initial test result is abnormal and the laboratory automatically performs follow-up testing when medically appropriate. Saint Luke’s Regional Laboratories (SLRL) clients should familiarize themselves with these tests by utilizing the SLRL Services Directory and make note of tests that prompt reflexive testing. In addition, some testing is sent out to specialty laboratories that perform medically appropriate reflex testing as necessary to provide information that would be essential to treat or diagnosis the patient. If additional help is needed choosing appropriate testing please contact our Client Services department at 816-932-3850.

Wound Culture Gram Stain Policy Update

Effective since December 2007, Microbiology began performing and reporting Gram stain results from all inpatient wound culture specimens. Microbiology will now extend this policy to include both inpatient and outpatient wound culture specimens.

Wound specimens represent one of the most complex cultures that the Microbiology lab interprets. Much information about adequacy of the specimen and the relevance of the organisms identified can be gained from a Gram stain of the original specimen. In general, the presence of many epithelial cells indicates a superficial collection, and the organisms identified may represent skin flora or contamination. The presence of white blood cells on the Gram stain is more indicative of pathogenic organisms from the culture.

Likelihood Ratios for Bacterial Meningitis

Based on a review of large studies of laboratory findings in patients with bacterial meningitis, the following likelihood ratios (LR) have been established for the most common tests.

<table>
<thead>
<tr>
<th>Test</th>
<th>Positive LR</th>
<th>Negative LR</th>
</tr>
</thead>
<tbody>
<tr>
<td>CSF WBC &gt;500/uL</td>
<td>15</td>
<td>0.30</td>
</tr>
<tr>
<td>CSF/blood glucose &lt;0.4</td>
<td>18</td>
<td>0.31</td>
</tr>
<tr>
<td>CSF lactate &gt;27 mg/dL</td>
<td>3.0</td>
<td>0.50</td>
</tr>
<tr>
<td>CSF protein &gt;45 mg/dL</td>
<td>1.1</td>
<td>0.90</td>
</tr>
</tbody>
</table>

The higher the positive LR, the more likely a patient has meningitis and the lower the negative LR the less likely it becomes. If the results of multiple tests are obtained, the appropriate likelihood ratios can be multiplied together to obtain the overall likelihood ratio.

For example, if a CSF specimen has a WBC count of 700/uL, CSF/blood glucose ratio of 0.2, CSF lactate of 32 mg/dL and a CSF protein of 42 mg/dL, then the overall likelihood ratio is 729, which is calculated by multiplying 15 x 18 x 3.0 x 0.9.

Reference Range Changes

The reference range for Antistreptolysin O (ASO) titer has changed from 0–200 to 0–145 IU/mL.

The reference range for rheumatoid factor has changed from 0–15 to 0–20 IU/mL.