Monitoring Warfarin Therapy in Lupus Anticoagulant-Positive Patients With the Chromogenic Factor X Assay

Lupus Anticoagulant

The lupus anticoagulant (LA) is one part of the antiphospholipid antibody syndrome and may be present in patients with systemic lupus erythematosus, malignancy, HIV infection, other diseases, and even in healthy persons with no manifestation of disease. The presence of a LA may predispose patients to thrombosis (venous or arterial) and subsequently, chronic treatment with warfarin is often indicated. In some LA patients, the INR can be falsely elevated by the presence of the LA (varies in different laboratories) and may result in under-treatment with warfarin. To optimally monitor warfarin therapy in such patients, an assay other than the INR is needed. Our data indicate that about 10-20% of patients with a chronic LA may have a falsely high INR artifact (see reference below). The remaining 80% of patients should be followed with the INR.

Chromogenic Factor X (CFX)

This assay is an enzymatic measurement of factor X, one of the vitamin K dependent clotting factors that is reduced by warfarin treatment. This assay is not affected by LA. By definition, normal pooled plasma has a factor X activity of 100% and all normal patients should have values greater than 70%. This test is performed daily in the Allina reference laboratory at Abbott Northwestern. This test is more expensive than an INR but it is important in those patients with an INR artifact.

The INR in the Allina Health Laboratory has been calibrated to international standards. Correlation of the CFX activity with the INR in our laboratory has shown that an INR of 2.5 is equivalent to a CFX of about 28% while the INR range of 2.0 - 3.0 corresponds to CFX of 20 - 40%. This is consistent with other published work.

Patients on chronic warfarin therapy can have periodic CFX checked and have their warfarin doses adjusted up or down using the 20-40% therapeutic range, just as one would using an INR range of 2.0 - 3.0. If the CFX is below the desired range, the warfarin dose must be **DECREASED**; if it is above, the warfarin dose must be **INCREASED**. This is the opposite response that occurs when using the INR to monitor warfarin so care must be taken to adjust the dose in the appropriate direction.
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Correlation OF CFX and INR in Non-LA Patient

<table>
<thead>
<tr>
<th>CFX (%)</th>
<th>60</th>
<th>50</th>
<th>40</th>
<th>30</th>
<th>20</th>
<th>15</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>INR</td>
<td>1.6</td>
<td>1.8</td>
<td>2.0</td>
<td>2.4</td>
<td>3.3</td>
<td>4.1</td>
<td>5.7</td>
</tr>
</tbody>
</table>

1. If a LA patient is on a stable dose of warfarin, has an INR between 2-3, and a CFX that approximately matches in the table below, we consider the INR to be accurate and the patient should be monitored with INR only.

2. If a LA patient is on a stable dose of warfarin, has an INR between 2-3, but a CFX that is clearly greater than in the table below, the patient needs to be followed with CFX.

It is possible that in a patient with a falsely high INR, after the CFX level is therapeutic and stable between 20-40% an INR could be measured to establish the relationship in that particular patient (e.g., an INR of 4.5 seems to correlate with a CFX of 30%). Thereafter, it might be reasonable to follow the INR targeting the personalized INR goal. However, if the INR becomes unstable forcing a change in the warfarin dose, repeat of the CFX measurement may be necessary to verify stability of the INR/CFX correlation.