A retrospective cohort study comparing activated partial thromboplastin time versus anti-factor Xa for therapeutic monitoring of unfractionated heparin

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Disclosures

• IRB Status: Exempt
• Co-investigators
  – Christopher Gilstrap, PharmD, BCCCP
  – Jeffrey Jansen, PharmD, BCIDP
• Conflicts of Interest: none
• Project Sponsorship: none
Learning Objectives

- Indications for heparin

- Describe the differences in heparin monitoring and management
  - Antifactor Xa vs. activated partial thromboplastin time
Background

- Unfractionated heparin (UFH)- parenteral anticoagulant
  - Venous thromboembolism (VTE)
  - Acute coronary syndromes (ACS)
- First clinical use in 1935
Background

• Mechanism of action
  – Anticoagulant effect is through inhibition of thrombin and factor Xa
  – Inhibits the formation of thrombus by preventing the conversion of fibrinogen to fibrin
Background

• Monitoring
  – Variable and unpredictable nature of how it is monitored

• Activated Partial Thromboplastin Time (aPTT)
  – A measurement of the time it takes for blood to coagulate

• Antifactor Xa (anti-Xa)
  – A measurement of the inhibition of factor Xa
Background-Clinical Literature Review

• 2009: anti-Xa vs. aPTT - monitoring for safety and efficacy
  – Time to therapeutic anticoagulation: 28hrs vs. 48hrs p-value of < 0.05
  – Percentage of labs within goal: 66% vs 42%, p-value < 0.05

• 2013: anti-Xa vs. aPTT
  – Percentage of labs within goal: 69% vs 41%, p-value < 0.05
  – Fewer monitoring tests: 2.08 vs 2.73, p-value < 0.05
  – Fewer dose adjustments: 0.62 vs 1.47, p-value < 0.05

• 2018: anti-Xa vs. aPTT - major bleeding after vascular surgery
  – Major bleeding: 17% vs. 8%, p-value of 0.19
Purpose

• Evaluate the percentage of time in therapeutic goal
  – Activated partial thromboplastin time (aPTT) versus anti-factor Xa

Hypothesis

• Compared to UFH management with aPTT, management with anti-factor Xa will result in increased time in therapeutic range
Methods

- Retrospective cohort analysis
- Chart review of hospitalized patients, treated with IV unfractionated heparin
- 1/1/2017 to 8/1/2018
- St. Vincent Healthcare in Billings, MT and St. Joseph Healthcare in Denver, CO
Methods

• **Inclusion Criteria:**
  – Patients ≥ 18 year of age
  – Being treated with IV UFH for treatment of
    • Venous thromboembolism (VTE)
    • Myocardial infarction (MI)
    • Pulmonary embolism (PE)
Methods

• **Exclusion Criteria:**
  – Pregnant patients
  – Patients on heparin therapy for more than 30 days
  – Treatment interrupted for more than 10 hours
  – Anti-Xa or aPTT goal ranges outside of standard of care
## Methods-Baseline

<table>
<thead>
<tr>
<th></th>
<th>aPTT (n=355)</th>
<th>Anti-Xa (n=355)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>65 ± 13.9</td>
<td>65 ± 14.4</td>
</tr>
<tr>
<td>Male</td>
<td>219 (62%)</td>
<td>204 (57%)</td>
</tr>
<tr>
<td>BMI</td>
<td>30.5 ± 7</td>
<td>29 ± 7.6</td>
</tr>
<tr>
<td>Length of Stay (days)</td>
<td>6 ± 5.5</td>
<td>7 ± 7</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>323 (91%)</td>
<td>243 (68%)</td>
</tr>
<tr>
<td>Black</td>
<td>1 (0.3%)</td>
<td>45 (13%)</td>
</tr>
<tr>
<td>Native American</td>
<td>23 (6.5%)</td>
<td>3 (0.8%)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>3 (0.8%)</td>
<td>3 (0.8%)</td>
</tr>
<tr>
<td>Other</td>
<td>5 (1.4%)</td>
<td>61 (17%)</td>
</tr>
</tbody>
</table>
## Methods-Baseline

<table>
<thead>
<tr>
<th>Past Medical History</th>
<th>aPTT (n=355)</th>
<th>Anti-Xa (n=355)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CKD / Dialysis</td>
<td>86 (24%) / 6 (1.7%)</td>
<td>123 (35%) / 17 (4.8%)</td>
</tr>
<tr>
<td>HTN</td>
<td>127 (36%)</td>
<td>271 (76%)</td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>0 (0%)</td>
<td>138 (39%)</td>
</tr>
<tr>
<td>Bleed</td>
<td>19 (5.4%)</td>
<td>3 (0.85%)</td>
</tr>
<tr>
<td>Stroke</td>
<td>27 (7.6%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Pulmonary Embolism</td>
<td>20 (5.6%)</td>
<td>73 (21%)</td>
</tr>
<tr>
<td>Acute Coronary Syndrome</td>
<td>159 (44.8%)</td>
<td>46 (13%)</td>
</tr>
<tr>
<td>Deep Vein Thrombosis</td>
<td>25 (7.0%)</td>
<td>51 (14%)</td>
</tr>
<tr>
<td>Antiplatelet Therapy</td>
<td>287 (80.8%)</td>
<td>214 (60%)</td>
</tr>
</tbody>
</table>
## Results

<table>
<thead>
<tr>
<th>% Time Therapeutic Median, (IQR)</th>
<th>aPTT (n=355)</th>
<th>Anti-Xa (n=355)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.3% (48.7%)</td>
<td>65% (68.6%)</td>
<td>&lt;0.05</td>
<td></td>
</tr>
</tbody>
</table>
Conclusion

• Results
  – Antifactor Xa vs. aPTT
  – St. Vincent's management vs. St. Joseph’s management
Discussion

• Strengths
  – Room for improvement
    • Found from this evaluation
  – Secondary analysis

• Limitations
  – Indication for therapy
  – Dosing and differences in protocols
  – Management of adjustments
  – Confounders
Follow-Up

- MUE on St Vincent’s patients
- Average time on therapy
- Time to achieve therapeutic range
  - Do we need to adjust initial management?
  - Based on indication
- Clinical events
  - Bleeds or clots
Applications

MOA of heparin

A. Inhibition of thrombin and factor Xa preventing the conversion of fibrinogen to fibrin

B. Inhibits free Factor Xa and Factor Xa bound in the prothrombinase complex

C. Inhibits the binding of adenosine diphosphate to the platelet P2Y12 receptor

Antifactor-Xa lab value

A. Measurement of the inhibition of factor Xa

B. Measurement of time to clot

C. Ratio of prothrombin time
Applications

Mechanism of heparin

A. Inhibition of thrombin and factor Xa preventing the conversion of fibrinogen to fibrin

B. Inhibits free Factor Xa and Factor Xa bound in the prothrombinase complex

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C. Measurement of the inhibition of factor Xa
Acknowledgements

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  – Christopher Gilstrap, PharmD, BCCCP
  – Jeffrey Jansen, PharmD, BCIDP

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  – Joseph Wheeler, MS, CPA
  – Jeffrey Jansen, PharmD, BCIDP

• Other
  – Kristin Dimond, PharmD, BCPS
QUESTIONS?

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References


