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ACCP Fall Meeting; October 2009; Anaheim, CA

Anticoagulation in the Presley Trauma Center

• Prophylactic UFH preferred for DVT prophylaxis
  • Head trauma, acetabulum fracture, other cases of high bleeding risk
  • May be preferred in renal dysfunction, pregnancy
• Prophylactic enoxaparin otherwise agent of choice for DVT prophylaxis
• Trauma patients at high risk of VTE, many require bridging to warfarin, long-term anticoagulation

Heparin-Induced Thrombocytopenia (HIT)

• Clinicopathologic syndrome
  – Clinical signs + laboratory confirmation
• Thrombocytopenia common in critically ill
  – Incidence: up to 40%
  – Causes confounding
• Systematic evaluation of thrombocytopenia essential to:
  – Diagnosis
  – Management


Thrombocytopenia: Differential Diagnosis in Trauma Patients

• Sepsis and HAIs
• Hemodilution
• Drugs
• Liver disease
• Hypersplenism
• DIC
• Antiphospholipid antibody syndrome / lupus anticoagulant
• ITP, TTP, PTP
• Intravascular devices

Prior to Study

• No standardized approach to managing HIT in Presley Trauma Center
• Inappropriate evaluation of thrombocytopenia and laboratory analysis performed
• Increased costs in diagnosis and treatment of suspected HIT

Preliminary Data

• 56 Patients in Trauma ICU (TICU): 1/6-1/31 2009
• 12 patients experienced thrombocytopenia (decrease in platelets >50% of baseline value)
• 1 patient qualified for HIT pathway
  – HIT antibody negative
Trauma ICU HIT Clinical Pathway

56 Patients in TICU: 1/6-1/31 2009

12 patients had thrombocytopenia, 1 patient qualified for HIT pathway

DVT/↓ Platelets > 50%†

D/C all UFH and LMWH, including heparin flushes and heparin in dialysis ports. Start Lepirudin†† Send HIT Antibody and Platelet function tests

† Platelet decrease seen within 5-14 days of starting heparin. Making final call, request number within first 4 days of initial heparin exposure, or if patient has known prior heparin exposure. Refer to TICU DVT/Thrombosed thrombus

†† Option of fondaparinux for pts who have completed sx/procedures, adj for renal dysfx

Pre-Test Probability of HIT (4Ts)

Points (0, 1, or 2 for Each of Four Categories) Maximum Possible Score = 8

<table>
<thead>
<tr>
<th>Points</th>
<th>Thrombocytopenia</th>
<th>Timing of platelet fall</th>
<th>Thrombosis</th>
<th>Other cause(s) of platelet fall</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>&gt; 50% fall to nadir 20-60 x 10^9/L</td>
<td>Days 5-10; 1 day after heparin (past 30 days)</td>
<td>New thrombosis; skin necrosis; acute reaction</td>
<td>None evident</td>
</tr>
<tr>
<td>1</td>
<td>30-50% fall; nadir 10-19 x 10^9/L</td>
<td>&gt; day 10 / timing unclear; &lt; day 1 = heparin (past 31-100 days)</td>
<td>Skin lesions; suspected thrombosis (unproven)</td>
<td>Possible</td>
</tr>
<tr>
<td>0</td>
<td>&lt; 30% fall; nadir &lt; 10 x 10^9/L</td>
<td>&lt; day 4 no heparin (past 100 days)</td>
<td>None</td>
<td>Definite</td>
</tr>
</tbody>
</table>

Pre-Test Probability of HIT (Modified 4Ts)

Points (0, 1, or 2 for Each of Four Categories) Maximum Possible Score = 8

<table>
<thead>
<tr>
<th>Points</th>
<th>Thrombocytopenia</th>
<th>Timing of platelet fall</th>
<th>Thrombosis</th>
<th>Other cause(s) of platelet fall</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>&gt; 50%</td>
<td>Days 5-14</td>
<td>New thrombosis; skin necrosis; acute reaction</td>
<td>None evident</td>
</tr>
<tr>
<td>1</td>
<td>30-50% fall</td>
<td>&lt; day 5</td>
<td>Skin lesions; suspected thrombosis (unproven)</td>
<td>Possible</td>
</tr>
<tr>
<td>0</td>
<td>&lt; 30% fall</td>
<td>&lt; day 4 no heparin (past 100 days)</td>
<td>None</td>
<td>Definite</td>
</tr>
</tbody>
</table>

HIT Treatment

<table>
<thead>
<tr>
<th>Agent</th>
<th>Cost/day</th>
<th>Adverse Effects</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Argatroban</td>
<td>$2,000-6,300</td>
<td>↑ INR (drug/lab interaction)</td>
<td>Requires close aPTT monitoring, adj in hepatic dysfx, discontinue ≥ 4 hrs before procedure</td>
</tr>
<tr>
<td>Bivalirudin</td>
<td>$688</td>
<td></td>
<td>Investigational, adj in renal dysfx, monitor aPTT</td>
</tr>
</tbody>
</table>

HIT Treatment Continued

<table>
<thead>
<tr>
<th>Agent</th>
<th>Cost/day</th>
<th>Adverse Effects</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lepirudin</td>
<td>$1200</td>
<td>Antilepirudin antibodies, may increase INR</td>
<td>Requires close aPTT monitoring, adj in renal dysfx</td>
</tr>
<tr>
<td>Fondaparinux</td>
<td>$48</td>
<td></td>
<td>Long half-life (~ 20 hrs), adj in renal dysfx</td>
</tr>
</tbody>
</table>
**HIT Laboratory Tests**

<table>
<thead>
<tr>
<th>Test</th>
<th>Location Performed</th>
<th>Turnaround Time</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIT Antibody Test</td>
<td>Baptist East</td>
<td>1-4 days</td>
<td>$146/test</td>
</tr>
<tr>
<td>Platelet Function Test</td>
<td>Lab Core Memphis</td>
<td>5-7 days</td>
<td>$220/test</td>
</tr>
</tbody>
</table>

**Limitations**

- Lepirudin agent of choice for TICU HIT Clinical Pathway based largely on cost
- Pathway not designed to recognize all types of HIT
- Pathway focuses on diagnosis and management of HIT, not prevention

**Recommendations**

- Criteria for pathway entry: Platelet values (>50% drop) and medication (timing of heparin)
- Send HIT antibody and platelet function tests
- Lepirudin as initial drug
- Coumadin x 4 weeks for HIT

**Post Study**

- Preliminary data and HIT clinical pathway presented at Trauma Conference
- Extensive trauma staff education
- Increased knowledge of HIT pathophysiology and rational approach to diagnosis and treatment
- Appropriate concern, laboratory analysis, decreased costs in diagnosis and treatment

**Conclusions**

- HIT is a clinicopathologic diagnosis, and presents a problem in trauma patients
- Proposed HIT clinical pathway helps simplify and standardize diagnosis and treatment of HIT to avoid morbidity and mortality related to this life-threatening disorder and its complications.

**Patient Example: Trauma Pt X**

- Plts on admit: 300
- Plts Day 1: 250
- Plts Day 2: 200
- Plts Day 3: 225
- Plts Day 4: 215
- Plts Day 5: 210
  - Heparin Started
- Plts Day 6: 145
  - Decrease >50% from admit value
- Plts Day 7: 75
- Plts Day 8: 70
  - Day 4 heparin, “baseline”
- Plts Day 9: 73
- Plts day 10: 80
- Plts Day 11: 100
- Plts Day 12: 105

Plts need to fall to <35 to meet criteria
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