Thromboelastography (TEG) Based Reversal of Coagulopathy and the TXA Controversy

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What We Know...

- Trauma is the leading cause of death and morbidity for children in US
- Trauma Induced Coagulopathy (TIC)
- Dysfunction of hemostatic and inflammatory systems in response to injury
- Defined as INR > 1.3
- Induced by hemorrhage
- Associated with increased morbidity and mortality

Pediatric Massive Transfusion

- Ratio of blood products that simulates the components of whole blood
- Designed to deliver blood product to the bedside as rapidly as possible with minimal product waste

Massive resuscitation protocols are great...but what about this concern for coagulopathy?
Coagulation Studies

- Bleeding time
- Activated Partial Thromboplastin Time (aPTT)
- Prothrombin Time (PT)
- Thrombin Time

Coagulation Cascade

Trauma Induced Coagulopathy

- Traditionally defined as elevated INR but inadequate as treatment target

- Viscoclastic hemostatic assays (TEG and ROTEM)
  - Monitors all phases of coagulation
  - Depicts real-time component activity rather than static values
  - Also provides information if hypercoagulability
  - Elevated INR DOES NOT NECESSARILY INDICATE a true bleeding coagulopathy

TEG-Directed Resuscitation

- Improved survival compared to MTP guided by conventional tests of coagulation cascade

- Better than traditional ratio-driven algorithms

- Utilize less plasma and platelet transfusions during resuscitation process

- When is TEG most useful?
  - Admission, OR, or ICU
What is a TEG?

Whole picture of coagulation cascade
- Clot Initiation
- Clot Kinetics
- Clot Strength
- Clot lysis

Normal TEG Tracing

Clot time (R)

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>0</th>
<th>5</th>
<th>10</th>
<th>15</th>
<th>20</th>
<th>25</th>
</tr>
</thead>
<tbody>
<tr>
<td>Value</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Note: TEG is a test used to assess coagulation in blood.

Clot time (R) is a measure of the time it takes for a clot to form.
Clot Time Irregularities

Long Clot Time (R) > 8min
- Platelet aggregation
- Reduced fibrinogen levels
- Activated factor
- Factors enzymes

Short Clot Time (R) < 4min
- Platelet aggregation
- Reduced fibrinogen levels
- Activated factor
- Factors enzymes

Clot Kinetics

Clot Kinetic Irregularities

Prolonged Kinetics
- Reduced platelet aggregation
- Reduced fibrinogen levels
- Activated factor
- Factors enzymes

Shortened Kinetics
- Increased platelet aggregation
- Increased fibrinogen levels
- Activated factor
- Factors enzymes

Clot Strength

- Platelet aggregation
- Fibrinogen levels
- Activated factor
- Factors enzymes
Clot Strength Irregularities

High MA
- Faster clotting
- Higher platelet numbers
- Coagulation defect

Low MA
- Slower clotting
- Lower platelet numbers
- Increased fibrinolytic activity

Clot Lysis

Fibrinolysis

Primary Fibrinolysis
LY38 >7.5% (or EPL >15%) with CI >1.5:
- Higher risk
- Frequent lysis
- Monitoring required

Secondary Fibrinolysis
LY38 >7.5% (or EPL >15%) with CI >1.5:
- Hyperfibrinogenemia
- Hemostatic defect
- Coagulation defect

Here comes the controversy!
**Tranexamic Acid (TXA)**

- Lysine analog thought to bind plasmin and inhibit fibrinolysis but mechanism not fully known.
- Administration within 3 hours of injury as bolus followed by drip infusion.

**Adults (18y+):**
- **Loading Dose:** 1g in 100mL over 10 minutes
- **Infusion:** 1g in 100mL infused over 8 hours

**Children (1-17y):**
- **Loading Dose:** 15 mg/kg (max 1g) in 100mL over 10 minutes
- **Infusion:** 2 mg/kg/hour (max total over 8 hours of 1g) in NS for 8 hours

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**Tranexamic Acid (TXA)**

- Clinical randomization of an antifibrinolytic in significant hemorrhage 2 study (CRASH 2) - Adult Patients:
  - Small survival benefit in patients who received TXA within 3 hours of injury.
- Pediatric Trauma and Tranexamic Acid (PEDI-TRAX):
  - Survival benefit for empiric TXA in children.
  - Large percentage of penetrating and blunt injuries.
  - Does not necessarily imply injuries in civilian population.

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**Hyperfibrinolysis vs. Shutdown**

- Fibrinolysis - physiologic process of clot breakdown required for wound healing and remodeling.
- Excessive fibrinolysis yields increased clot breakdown and can promote bleeding.
- Treated with TXA administration.
- But deficiency of fibrinolysis (shutdown) may promote thrombotic complications of DVT.
- Patients in hemorrhagic shock requiring massive transfusion most often in fibrinolysis shutdown at time of admission.

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**Why So Much Controversy?**

- Mortality risk increased by odds ratio of 1.8 for shutdown and 3.3 for hyperfibrinolysis in adults.
- Odds ratio of 6.2 in pediatric patients.
- Recent findings of increased mortality if TXA initiated >3 hours after injury or no benefit from TXA.
- Hyperfibrinolysis is rare in children, especially with TBI and blunt injury, and appears to correct with hemostatic resuscitation.
So...What's the Verdict?

- In general, aspirin administration of TXA in children remains controversial with no clear consensus.
- However, many support TEG-directed TXA administration according to hemorrhage and hyperfibrinolysis as indicated by LYT30 value.

Quick Review

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Symbol</th>
<th>Definition</th>
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<tbody>
<tr>
<td>Clotting Time</td>
<td>R</td>
<td>Time from start to 2 mm of clot amplitude (initial fibrin formation)</td>
</tr>
<tr>
<td>Clot Reactivity</td>
<td>R</td>
<td>Speed to reach 20 mm (completes initial kinetics)</td>
</tr>
<tr>
<td>Clot Firmness</td>
<td>H</td>
<td>Measure of rapidity of clot build up and cross linking (fibrinogen level)</td>
</tr>
<tr>
<td>Clot Strength</td>
<td>MA</td>
<td>Early bonds and max dynamic properties of fibrin and platelet bonding (max platelet formation)</td>
</tr>
<tr>
<td>Convert. of Factor X to Xa</td>
<td>X</td>
<td>Conversion of factor X to Xa</td>
</tr>
<tr>
<td>Coagulation Index</td>
<td>C</td>
<td>Global hemostasis index</td>
</tr>
<tr>
<td>Clot Stability</td>
<td>LYT30</td>
<td>Rate of amplitude reduction 30 min after MA</td>
</tr>
<tr>
<td>EPL</td>
<td></td>
<td>Estimates % lysed % amplitude less (LYT30) after MA</td>
</tr>
</tbody>
</table>

Example 1

[Image: Delayed clot formation, subject hypofibrinogenemia or factor deficiencies]
Example 2

Example 3

More Examples

Case Study

- 61 year-old gentleman with hepatitis C, pulmonary stenosis, and HTN presents after 20 foot fall from ladder
- Left femur fracture
- CT Abdomen: Cirrhotic appearing liver, Recanalized paravertebral vein
  Trace amount of ascites and findings of portal HTN.
Thank You!