Performance evaluation: Hemochron elite and i stat ACT devices during CPB

NABEEL RAZZAQ
Why Anticoagulate?

Allows the safe conduct of any form of extracorporeal circulation

Prevent

- Activation of Coagulation Cascade - foreign bypass circuit
- Clots into the patient - Multiple organ dysfunction
- Clots in circuit can trigger DIC
- Clot off the oxy and cease extracorporeal support
- Death

Electron microscope blood clot and fibrin on oxygenator

The need for checking

Monitor is essential

- Speed of clotting affected by: Temperature, Heamodilution, Thrombocytopenia, Coagulopathies, Heparin resistance, Kidney function
- POC - Quick and reproducible test needed in this TH environment
- Heparin- Most common anticoagulant for CPB / ACT
- **Reliability** is essential for any POC ACT device
Background

Currently most machines already out there have a mechanical endpoint
• Medtronic: HMS, Act plus - Plunger speed
• Helena: Magnet rotation
• Hemochron: Fluid movement
• (Abbott POC: istat- Amperometric Electroactive Endpoint)

Research already out there
• (Schussler et al 2003) 128 data points
• (Paniccia et al 2003), et al 168 samples
• (Lewandrowski et al 2011) 242 data points cardiac surgery range
• (Ojito et al 2012) 400 data points none above ACT 250
Our Study

International Multi-Centre Study

• Papworth Hospital
• Basel
• Cape Town

This is the Preliminary data- 171 Patients, 2071 data points to date

• Planned for 400 patients with 5000 data points
Hemochron

Detection mechanism - Mechanical endpoint
• Waste removed / uses 15 microliters out of 50
• Sample warmed / clot formation activated by Kaolin or Celite
• The sample is moved back and forth through the test channel

Clot detection mechanism
• Flow is measured through the narrowing of channel by a series of LED optical detectors
  When flow reaches below predetermined rate set by Hemochron- thus proposing a fibrin clot, the test stops
• Papworth range - > 400 seconds for bypass
Detection mechanism: Thrombin generation
- Electrochemical - Amperometric endpoint

- Cartridge contains a Thrombin substrate that has an amide linkage which mimics the amide linkage in fibrinogen which thrombin cleaves.

- Substrate: H-D-phenylalanyl-pipecolyl-arginine-p-amino-p methoxydiphenylamine
  Structure: Phenylalanine - Pipecolic acid - Arginine \(\text{-- NH - C6H4} - \text{NH - C6H4 - OCH3}\)

- 2 drops of blood into cartridge, close flap and insert into machine - warms/mixes

- Thrombin cleaves amide bond at carboxy-terminus of arginine in this compound as it would in fibrinogen.
Abbott- istat

• Thrombin - Substrate reaction produces the electrochemically inert tripeptide Phenylalanyl - Pipecoly – Arginine

and the electroactive compound: NH3+ - C6H4 - NH - C6H4 - OCH3

• Detected amperometrically by the electrochemical sensors as the compound produces an electrical current which stops the test

• Test measured in seconds

• Istat calibrates itself each cycle/ database management

• Can use for Arterial Blood Gases too
Method

- All standard Bypass Cases- In house surgery/ same day admissions.
- Whole blood used from the same syringe used for all 4 tests
- Duplicate ACTS 2 istats, 2 Hemochrons
- Standard Protocol and times
  - TF1- Baseline
  - TF2- After heparin (300iu/kg)
  - TF3-TF6- On bypass (every 30 mins)
  - TF7- Post protamine
- Data recorded in database
## Results - Coefficient of variation

<table>
<thead>
<tr>
<th></th>
<th>Device 1 (H)</th>
<th>Device 2 (IS)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>mean ACT</td>
</tr>
<tr>
<td>TF1</td>
<td>166</td>
<td>119</td>
</tr>
<tr>
<td>TF2</td>
<td>167</td>
<td>596</td>
</tr>
<tr>
<td>TF3</td>
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<td>589</td>
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<td>TF4</td>
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<td>548</td>
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<td>TF5</td>
<td>132</td>
<td>509</td>
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<tr>
<td>TF6</td>
<td>84</td>
<td>502</td>
</tr>
<tr>
<td>TF7</td>
<td>164</td>
<td>121</td>
</tr>
<tr>
<td>Total</td>
<td>1043</td>
<td>418</td>
</tr>
</tbody>
</table>

Figure 1: Table showing Coefficients of variation, (which are a standardised measure of dispersion allowing direct comparison) CVs at varying time frames

- CV% - The gold standard for comparing reliability = (SD/Mean)
- Istat is more reliable overall CV% consistently <8.5%, Hemochron can be high as 22%
- TF2-TF6, The danger zone- need reliability!
- Reliability is better for both devices at TF1 (baseline) and TF7 (post protamine)
- Also, Device 2 is systematically higher than Device 1
Results - Scatter diagram

- Visual representation of reliability
- Intra device comparison- one on each axis
- Straight line would indicate agreement between means

- Istat is the most reliable machine, more agreement
- Each dot represents a patient, further away from the line is more unreliable >400- danger zone!
- Disagreement increases with increasing ACT values
Results - Scatter diagram

- 1888 paired measurements in 171 patients
- Hemochron on x axis / istat on y axis
- Showing differences of means between devices
- Straight line if no difference in means - High level of disagreement at higher ACT’s
• The Gold standard for comparing different devices
• X axis - The mean of the Hemochron and the istat
• Y axis - (H-istat/average) as a % due to magnitude of difference increasing with increasing ACT
• 9.2% systematic bias - Hemochron reads lower than Istat
• High 95% CI limits of agreement between devices - big disagreement
Clinical Impact

Current practice- do I need to give more heparin? Which is it 330/400/470???

Better to be safe?- Too much Heparin
- More Heparin and Protamine being used
- Heparin/Protamine complex- Type 1 immune reactions
- Both anticoagulants – too little or too much protamine more risk of bleeding- more transfusions
- More time in hospital

Too little heparin/ protamine
- Clots and dangers as mentioned previously
Conclusion

• We found the Abbott Istat to be a more reliable device than the Hemochron elite when measuring ACTs on CPB using 2071 data points; in both non-anticoagulated patients and in fully heparinised patients.

• Reliability decreases in both devices as ACT increases.

• The istat and hemochron should not be used interchangeably to measure ACT due to their high levels of disagreement.

• Safe ranges for CPB would need to be adjusted when using istat to measure ACT.
References


Questions?

Thank you very much for listening