Do we need protocols, guidelines or personalized therapy?

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Conflicts of interest

Octapharma
Haemorrhage and coagulopathy is associated with significant mortality……..
Functional Haemostasis

Haemostasis can only be adequately assessed in WHOLE BLOOD
Plasma-based tests?

INR/PT  EXTRINSIC PATHWAY  INTRINSIC PATHWAY  APTT

...developed to monitor heparin and vitamin K antagonists...
Cell based model of haemostasis

Haemostasis should be analyzed in whole blood!!

Hoffman et al. Blood 1996
Whole blood analysis
Measures the viscoelastical properties of the clot
Multiple endpoints reflecting clot formation, strength and degradation
Real-time (15 min.)
Thrombin generation and clot strength

The thrombin burst determines the physical qualities of the clot

TEG correlates with thrombin generation and, hence, identify coagulopathies secondary to impaired thrombin generation

Scientific explanation for why TEG is superior to conventional coag’s!!
Transfusion packages

- Stored thawed AB RhD negative plasma immediately available for transfusion.
- Transfusion Package **5 RBC : 5 FFP : 2 Platelet Concentrates** (ratio ~ 1 : 1 : 1)
- Results in
  - Haematocrit ~ 30%
  - Coagulation factor concentration >30%
  - Platelet count of 80 $10^9$/L
  - Normal TEG®
- The packages are to be used until surgical control

**For patients with uncontrollable haemorrhage**

Johansson, Stensballe et al. Transfusion 2007

The Copenhagen Concept
Validated in > 5,000 patients at Rigshospitalet
The Copenhagen Concept

Blood bank - analyze

Blood bank specialist on call 24/7

OR

Trauma centre

CT/LAB

ICU
Effect of Haemostatic Control Resuscitation on mortality in massively bleeding patients: a before and after study

P. I. Johansson & J. Stensballe

1Department of Clinical Immunology, Blood Bank, and 2Department of Anaesthesia, Centre of Head and Orthopedics, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark

Number at risk

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Log-rank, \( P < 0.0001 \)
ACIT3: 2010-11: 182 trauma patients in Copenhagen

Haemorrhagic mortality < 15% in severely injured trauma patients

Johansson et al. Transfusion 2013
Current guidelines

Are there evidence enough for this approach?

NOT YET!
TACTIC 1:1:1?

PROPPR finalized Dec. 2013

clinicaltrials.gov NCT01545232

Lead by prof J.B. Holcomb, Houston, USA
...but do we *really* believe that......
Targeted Action Curing Trauma Induced Coagulopathy
International Trauma Research Network

Pär Johansson

Copenhagen (CPH)

Carel Gosling
Amsterdam (AMS)

Simon Stanworth
Oxford (JRH)

Karim Brohi
London (RLH)

Marc Maegele
Cologne (COL)

Carl Wahlgren
Stockholm (STK)

Tina Gaarder
Oslo (OSL)
## TACTIC Partners

<table>
<thead>
<tr>
<th>Participant no.</th>
<th>Participant legal name</th>
<th>Country</th>
<th>Organisation type</th>
<th>Name of the scientific person in charge, describe briefly the role(s) in the consortium</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Rigshospitalet, Region Hovedstaden.</td>
<td>Denmark</td>
<td>Hospital</td>
<td>Prof. Pär Johansson. World expert in critical bleeding &amp; transfusion medicine. Tissue repository &amp; genomics lead.</td>
</tr>
<tr>
<td>2</td>
<td>Academic Medical Centre, Amsterdam.</td>
<td>Netherlands</td>
<td>Hospital</td>
<td>Prof. J. Carel Goslings. Specialist in early treatments for injury, member of several international advisory committees. Lead for practice management guidelines development and dissemination.</td>
</tr>
<tr>
<td>3</td>
<td>University of Witten-Herdecke</td>
<td>Germany</td>
<td>University</td>
<td>Prof. Marc Maeggele. Expert in trauma registry-based research. Lead for comparative study of existing management of trauma haemorrhage and coagulopathy.</td>
</tr>
<tr>
<td>4</td>
<td>Oslo University Hospital Ulleval</td>
<td>Norway</td>
<td>Hospital</td>
<td>Dr Tina Gaarder. International instructor of Definitive Surgical Trauma Care. Lead for randomised control trial comparing personalised, targeted management with existing empiric transfusion.</td>
</tr>
<tr>
<td>5</td>
<td>Queen Mary &amp; Westfield College.</td>
<td>United Kingdom</td>
<td>Hospital</td>
<td>Prof. Karim Brohi. Global research leader in trauma induced coagulopathy. Academic lead for the development of clinical decision support software.</td>
</tr>
<tr>
<td>6</td>
<td>University of Oxford</td>
<td>United Kingdom</td>
<td>University</td>
<td>Dr Helen Campbell. Expert in health economics. Lead for costing work and cost-effectiveness analysis of personalised management.</td>
</tr>
<tr>
<td>7</td>
<td>Haemonetics Corporation.</td>
<td>USA</td>
<td>Industry</td>
<td>Laurel Omert. Trauma surgeon &amp; Medical Director. Lead for development of TEG data visualisation &amp; decision support.</td>
</tr>
<tr>
<td>8</td>
<td>TEM Innovations GmbH</td>
<td>Germany</td>
<td>SME</td>
<td>Axel Schubert. CEO and lead for development of ROTEM data visualisation &amp; decision support.</td>
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TACTIC Program

€5.9 m European Union Framework Programme 7 Health INNOVATION 2013

Starting in Nov’13, INTRN will continue to work alongside the key industry leads in haemostatic diagnostics for this 5-year programme to:

1. Compare coagulation & outcomes in response to different existing transfusion strategies
2. Specify different disease profiles underlying Trauma Induced Coagulopathy
3. Develop personalised strategies for targeted transfusion
4. Compare existing practices with personalised, targeted treatment of coagulopathy
5. Deliver guidelines and support for the clinical management of coagulopathic bleeding
The TACTIC research resolves around:

1. An observational study of approximately 2,000 trauma patients with blood samples, functional haemostatic & clinical data already completed before TACTIC commence

2. A randomized controlled trial where 1,800 trauma patients are screened and 400 randomized to goal-directed interventions based on TEG/TOTEM vs. standard therapy
YES

..........we need to develop guidelines and protocols for personalized therapy........