Hyperacute: treatment of intracerebral haemorrhage (ICH) - PATCH

Rustam Al-Shahi Salman
Professor of clinical neurology
MRC senior clinical fellow
& honorary consultant neurologist
Disclosures
“From bench to bedside… ...and beyond”
Promising non-randomised observational studies

- No RCTs of platelet transfusion for acute ICH
- Systematic review of observational studies

<table>
<thead>
<tr>
<th>Study name</th>
<th>Statistics for each study</th>
<th>OR and 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ducruet et al\textsuperscript{11}</td>
<td>2.444, 0.416-14.379, 0.989, 0.323</td>
<td></td>
</tr>
<tr>
<td>Creutzfeldt et al\textsuperscript{12}</td>
<td>1.724, 0.789-3.771, 1.365, 0.172</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.825, 0.892-3.734, 1.648, 0.099</td>
<td></td>
</tr>
</tbody>
</table>

BMJ Open 2012;2:e000588
Methods

- PROBE parallel group RCT
  - Acute ICH associated with antiplatelet drugs
  - 1:1 platelet transfusion vs. open control
  - Modified Rankin Scale (mRS) at 90 days
- Netherlands Trial Register NTR1303
- Protocol published *BMC Neurol* 2010;10:19
- Multicentre
  - The Netherlands, n=36
  - Scotland (UK), n=13
  - France (EU), n=11

Methods

Inclusion criteria

• Spontaneous supratentorial ICH (no AVM, aneurysm, trauma)
• ≥18 years
• GCS 8-15
• Antiplatelet therapy use for ≥7 days before ICH
• Platelet transfusion could be given <1.5hrs of CT and <6hrs of onset

Exclusion criteria

• Planned surgery <24h
• Vitamin K antagonist
• Thrombocytopaenia
• Transfusion reaction
• mRS ≥2 before ICH
• Death appears imminent

Lancet 2016;387:2605-13
CONSORT flow diagram

190 patients enrolled

190 randomised

97 randomly assigned to platelet transfusion

4 did not receive platelet transfusion
1 refused
1 ineligible
1 died before transfusion
1 transfusion arrived late

93 received platelet transfusion

97 included in intention-to-treat analysis

95 included in as-treated analysis

93 randomly assigned to standard care

2 received platelet transfusion
1 due to deterioration
1 due to misinterpretation of treatment allocation

91 received standard care

93 included in intention-to-treat analysis

95 included in as-treated analysis

Lancet 2016;387:2605-13
## Baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>Transfusion n=97</th>
<th>Standard care n=93</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (mean, SD)</strong></td>
<td>74.2 (9.8)</td>
<td>73.5 (11.1)</td>
</tr>
<tr>
<td><strong>Gender (female)</strong></td>
<td>42 (43.3%)</td>
<td>36 (38.7%)</td>
</tr>
<tr>
<td><strong>Co-morbidities</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>cerebral infarction</td>
<td>38 (38.4%)</td>
<td>40 (40.0%)</td>
</tr>
<tr>
<td>hypertension</td>
<td>68 (72.3%)</td>
<td>67 (72.8%)</td>
</tr>
<tr>
<td>diabetes</td>
<td>15 (15.5%)</td>
<td>17 (18.9%)</td>
</tr>
<tr>
<td>myocardial infarction</td>
<td>23 (23.6%)</td>
<td>22 (24.4%)</td>
</tr>
<tr>
<td>peripheral arterial disease</td>
<td>16 (16.5%)</td>
<td>4 (4.4%)</td>
</tr>
<tr>
<td><strong>Pre-ICH antiplatelet therapy</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cox-inhibitor (aspirin) alone</td>
<td>71 (73.2%)</td>
<td>78 (83.9%)</td>
</tr>
<tr>
<td><strong>GCS (median, IQR)</strong></td>
<td>14 (13 – 15)</td>
<td>15 (13 – 15)</td>
</tr>
<tr>
<td><strong>NIHSS (median, IQR)</strong></td>
<td>12 (7 – 19)</td>
<td>13 (7 – 17)</td>
</tr>
</tbody>
</table>

## Baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>Transfusion n=97</th>
<th>Standard care n=93</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICH location</td>
<td></td>
<td></td>
</tr>
<tr>
<td>supratentorial deep</td>
<td>62 (64.6%)</td>
<td>70 (76.1%)</td>
</tr>
<tr>
<td>supratentorial lobar</td>
<td>32 (33.3%)</td>
<td>22 (23.9%)</td>
</tr>
<tr>
<td>infratentorial</td>
<td>2 (2.1%)</td>
<td>0</td>
</tr>
<tr>
<td>ICH volume (mL) median (IQR)</td>
<td>13.1 (5.4 – 42.4)</td>
<td>8 (4.4 – 25.8)</td>
</tr>
<tr>
<td>Intraventricular extension</td>
<td>12 (12.6%)</td>
<td>20 (21.7%)</td>
</tr>
<tr>
<td>ICH score (median, IQR)</td>
<td>1 (0 – 2)</td>
<td>1 (0 – 1)</td>
</tr>
</tbody>
</table>
Primary outcome

Adjusted common OR 2.05 (95%CI 1.18 to 3.56), p=0.0114
mRS 4-6, OR 2.04 (95%CI 1.12 to 3.74), p=0.0195

Lancet 2016;387:2605-13
“This edition includes updated evidence published since 2012, with literature searches completed up to September 2015 and with some major publications since that date also included.”
What to do about antiplatelet-associated ICH now?

http://tich-2.org

http://www.restarttrial.org
Thank you…

• Sites and their teams
  – Southern General Hospital, Glasgow (Keith Muir)
  – Aberdeen Royal Infirmary (Mary Joan Macleod)
  – Edinburgh Royal Infirmary & Western General Hospital, Edinburgh (me)
  – St John’s Hospital, Livingston (Scott Ramsay)

• Stroke Research Network
• Trial managers and outcome assessors
Edinburgh Stroke Winter School

20th-22nd February 2017

Learn to develop and answer questions in clinical stroke research

To apply Send CV and 100 word motivation to judi.clarke@ed.ac.uk
Research fellows welcome!

Clinical care and audit

Research

Education & teaching

Public engagement

Neurology  Statistics  Nursing  Radiology

www.RUSH.ed.ac.uk  @BleedingStroke  .../bleedingstroke