The Clinical Utility of DDAVP trials in vWD

SS Opat, J Shortt, MB Gorniak, HA Aumann, MF Collecutt & AM Street
Background

- DDAVP secures effective haemostasis in a proportion of vWD patients undergoing haemostatic challenges
- The response to DDAVP is heterogenous
- A therapeutic trial of DDAVP is therefore recommended for vWD patients, prior to invasive procedures
Methods

- **Retrospective audit:**
  - All DDAVP trials for vWD at Alfred Hospital between 1990 & 2006
  - 129 patients in total

- **Inclusion criteria:**
  - Bleeding phenotype
  - Prior low vWF antigen, ristocetin co-factor activity or collagen binding assay

- **Exclusions:**
  - 21 patients with normal vWD parameters immediately prior to DDAVP infusion
DDAVP trial protocol

- DDAVP 0.3μg/kg in 100mL NS iv over 45 minutes
  - TPR observations: baseline, 15’ and completion
  - Monitor for common symptoms

- Blood tests taken pre-infusion and at 1 hour post DDAVP:
  - vWD parameters (FVIII, vWF: Ag, vWF: RiCof & vWF: CBA)
  - electrolytes (Na+)
  - Additional sampling performed at 24 hours in the majority of trials conducted after 2003
Patient demographics

![Bar chart showing patient demographics by age and gender](image)
vWD subtypes

- Type 1: 94 cases
- Type 2A: 8 cases
- Low vWF:RiCof: 6 cases
Examples of DDAVP responses in various vWD subtypes

Key: × FVIII  ♦ vWF:Ag  ■ vWF:CBA  ● vWF:RiCof

Dotted lines indicate levels of 30% and 50%.
Defining response

- **Complete response:**
  - An increase of all vWD parameters into the normal range (>50% activity)

- **Partial response:**
  - An increase in vWD parameters to between 30% of normal activity and the lower limit of normal

- **No response:**
  - vWD parameters <30%
<table>
<thead>
<tr>
<th></th>
<th>One hour</th>
<th></th>
<th></th>
<th>24 Hours</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>CR</td>
<td>PR</td>
<td>NR</td>
<td>n</td>
<td>CR</td>
</tr>
<tr>
<td>Type 1</td>
<td>94</td>
<td>80%</td>
<td>15%</td>
<td>5%</td>
<td>18</td>
<td>11%</td>
</tr>
<tr>
<td>Type 2A</td>
<td>8</td>
<td>0</td>
<td>0</td>
<td>100%</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Low RiCof</td>
<td>6</td>
<td>100%</td>
<td>0</td>
<td>0</td>
<td>6</td>
<td>67%</td>
</tr>
</tbody>
</table>
Summary

- **Type 1 vWD**
  - Baseline vWD parameters >20% predicted favourable response at 1 hour (55/57 CR)
  - Baseline vWD parameters <10% predicted an unsatisfactory response at 1 hour

- **Type 2A**
  - No satisfactory responders

- **Response at 24 hours:**
  - Most patients with CR at 1 hour had adequate vWD parameters at 24 hours
  - No patient with a PR at 1 hour had adequate vWD parameters at 24 hours
Conclusions

- A DDAVP efficacy trial is not indicated in:
  - Severe type 1 vWD or type 2A vWD
  - Mild type 1 vWD or an isolated low RiCof (although assessment of tolerability is still advised)

- Testing at 24 hours is indicated for:
  - Patients with a CR at 1 hour, to identify the occasional suboptimal responder

- Measurement of FVIII levels is not required

- Implementing this testing strategy would reduce the number of DDAVP trials performed by 20%
Questions?