Donor Adverse Events

Common terminology

Frequency

Risk factors

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Canadian Blood Services
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Outline

• Donor adverse events
• Why are they important
• Definitions of adverse events
• Frequency and risk factors, vasovagal reactions
Donor adverse events

Acute
• at time of or shortly after donation
• local arm complications
• vasovagal reactions (faints)

Long term
• cumulative
• iron depletion
• possible osteopenia
Why are they important?

• Donor morbidity, extremely rarely, mortality
  • nerve injury
  • delayed vasovagal reactions most likely to lead to injury

• Decrease donor satisfaction
  • negative impact on return rate, particularly in donors early in donation career

• Should inform donor eligibility and assessment policies
Eligibility criteria

- Age
- Size (weight, estimated blood volume)
- Blood pressure, pulse
- Medications
- Heart disease
- Diabetes
- …
Mitigating actions
Donor haemovigilance

1. Compile donor reactions, characteristics
2. Determine risk factors for reactions
3. Change in eligibility or screening - mitigating actions
   - Removal of deferral criteria
4. Re-evaluation of rates

Canadian Blood Services
it's in you to give
Standard definitions

• Needed to establish baseline rates, evaluate risk factors, assess impact of changes, permit comparisons

• ISBT Working Party on Haemovigilance formed a revision subcommittee to review 2008 ISBT Standard definitions, AABB classification and related software, national systems

• Some members also part of IHN, AABB haemovigilance working group
<table>
<thead>
<tr>
<th>ISBT 2008</th>
<th>AABB</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Mild - no objective symptoms</td>
<td>• List of 12 symptoms related to pre-faint</td>
</tr>
<tr>
<td>• Moderate – objective symptoms pulse, BP, loss of consciousness (LOC)</td>
<td>• ± LOC, duration of LOC separates mild, moderate, severe</td>
</tr>
<tr>
<td>• Severe – hospitalization, significant incapacity</td>
<td>• Injury separate attribute</td>
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</table>
Aims

1. Provide simple definitions easy to apply in a standard way
2. Minimal requirements for basic surveillance international comparisons
3. Additional optional attributes process improvements, research
Complications related to blood donation

A. Local Symptoms

i. Blood outside vessel
   - Haematomata
   - Arterial puncture
   - *Delayed bleeding*

ii. Arm pain
   - Nerve injury/irritation
   - Duration < or > 12 months
   - Other arm pain
A. Local Symptoms

iii. Localized infection/inflammation of vein or soft tissue
   - *Superficial thrombophlebitis*
   - *Cellulitis*

iv. Other major blood vessel injury
   - DVT
   - Arteriovenous fistula
   - Compartment syndrome
   - Brachial artery pseudoaneurysm
B. Generalized Symptoms – vasovagal reactions

- No loss of consciousness
- Loss of consciousness
  - $< 60 \text{ sec, no complications}$
  - $> 60 \text{ sec, ± complications}$
- With or without injury
- On or off collection site
C. Related to apheresis
- Citrate reactions
- Haemolysis

D. Allergic
- Local
- Generalized

E. Other serious complications
- MI
- Cardiac Arrest
- Other cardiac
- TIA
- CVA
- Death

F. Other
Numerator and denominator data

<table>
<thead>
<tr>
<th>Numerator data about each complication</th>
<th>Denominator data about all donors</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type of donation</strong></td>
<td><strong>Total donations</strong> (proceed to phlebotomy)/year</td>
</tr>
<tr>
<td>a) Whole blood</td>
<td>a) Whole blood</td>
</tr>
<tr>
<td>i. allogeneic</td>
<td>i. allogeneic</td>
</tr>
<tr>
<td>ii. autologous</td>
<td>ii. autologous</td>
</tr>
<tr>
<td>b) Apheresis</td>
<td>b) Apheresis</td>
</tr>
<tr>
<td>i. RBC ± plasma ± platelets</td>
<td>i. RBC ± plasma ± platelets</td>
</tr>
<tr>
<td>ii. platelets ± plasma</td>
<td>ii. platelets ± plasma</td>
</tr>
<tr>
<td>iii. plasma only</td>
<td>iii. plasma only</td>
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</tbody>
</table>

Gender of donor                        
First-time vs. repeat donor            
Age group (16-18, 19-22, 23-29, 30-69, ≥ 70) 
Type of complication
Revised definitions

- Definitions have received wide endorsement
- Available as a leaflet
- We hope that their adoption will improve monitoring of donor adverse reactions and ultimately enhance donor safety
- isbtweb.org/working-parties/haemovigilance definitions
- Vox Sanguinis 2016;110(2):185-8
Long term effects – iron depletion

• Difficult to fit in haemovigilance scheme
  • not solely due to donation
  • iron levels (ferritin) not routinely measured
  • many possible mitigating strategies

• Important part of donor safety

• Can follow donation frequency, hemoglobin levels, hemoglobin deferrals over time
Frequency of donor adverse events

- Published studies
  - ~ 2-5% mild vasovagal reactions
  - ~ 4 in 1,000 syncope
  - ~ 6 in 10,000 injury

- Frequency is much higher in post-donation surveys and if donors are routinely asked about symptoms at time of next donation
Symptoms per 1,000 donors

- **Bruising**: 131 (80 first time, 41 repeat donors)
- **Tingling, numbness, weakness**: 42 (13 first time, 29 repeat donors)
- **Felt faint or weak**: 124 (25 first time, 99 repeat donors)
- **Fainted**: 19 (4 first time, 15 repeat donors)

Transfusion 2013(53):1979
Risk factors, vasovagal reactions

- Mechanisms include a direct effect of acute hypovolemia, changes in vasovagal tone and orthostatic blood pressure, psychologic stress
- Large, observational studies done at ARC and Blood Systems demonstrated risk factors for vasovagal reactions
- Similar risk factors found for delayed vasovagal reactions
## Risk factors, vasovagal reactions

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Risk of reactions, adjusted odds ratio</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>First donation</td>
<td>1.95-2.80</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>16-18</td>
<td>3.89</td>
<td>Older donors (&gt;65) examined in some studies and not at higher risk</td>
</tr>
<tr>
<td>17-20</td>
<td>2.75-4.01</td>
<td></td>
</tr>
<tr>
<td>19-24</td>
<td>2.37</td>
<td></td>
</tr>
<tr>
<td>Female gender</td>
<td>1.20-2.52</td>
<td>May be particular important risk factor for delayed reactions</td>
</tr>
<tr>
<td>Weight 110-120 lbs.</td>
<td>2.11-2.52</td>
<td>May not be independent of EBV</td>
</tr>
<tr>
<td>(50-54 kg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EBV&lt;sub&gt;1&lt;/sub&gt; &lt;3500 ml</td>
<td>2.45-2.88</td>
<td>In some studies continuous variable, with EBV &gt;5000 ml having lowest rate</td>
</tr>
<tr>
<td>Fear of donation</td>
<td>2.6</td>
<td>Donors reporting fear on a predonation survey 2.6 times more likely to experience presyncopal reactions</td>
</tr>
</tbody>
</table>
Mitigating strategies

- Both ARC and Blood Systems observed a decrease in vasovagal reaction rates after implementing several measures, often simultaneously:
  - selection of donors with EBV $\geq$ 3.5 litres
  - pre-donation water
  - muscle tensing exercises, legs and buttocks (AMT)
- Compliance is an issue for H$_2$O and AMT
- Difficult to determine efficacy of specific intervention, particularly on syncope and injury
Mitigating strategies

- Interesting studies by C. France et al on importance of donor’s psychological state, particularly young, first time donors
- Enhanced education about fear, pain, potential complications with specific instructions about preventative measures may reduce reactions
- Determination of subset of donors with higher fear factor who are at greatest risk of a reaction
Conclusions

• Donor haemogivilance plays an important role in the safety of blood donation

• Standard definitions of adverse reactions are a basic element in establishing reaction rates, risk factors

• There is incomplete understanding of the pathophysiology of vasovagal reactions

• Observational and before and after studies have shown efficacy of some measures

• Further studies needed on other mitigating strategies and their actual impact, particularly in reduction of syncopal reactions and donor injury
Thank you