SHOT Experience and UK Initiatives on TRALI prevention

Lorna M Williamson
University of Cambridge/National Blood Service
TRANSFUSION-RELATED ACUTE LUNG INJURY (according to SHOT)

ACUTE DYSPNOEAE WITH HYPOXIA AND BILATERAL PULMONARY INFILTRATES OCCURRING DURING OR IN THE 24 HOURS AFTER TRANSFUSION, WITH NO OTHER APPARENT CAUSE
One major cause of TRALI is leucocyte antibodies in donor plasma - either to HLA or HNA.

A male (or female) donor with a history of blood transfusion

A female donor with history of pregnancy - antibodies in 10-15%, of which 50% specific.

(MacLennan, Navarrete Lucas et al 2004)
How does TRALI occur?

- Adherence of neutrophils to pulmonary endothelium or epithelium
- Cell membrane permeabilisation
- Lung oedema
- Secretion of IL-1β, TNFα, IL-8 may amplify the reaction
TRALI cases reported to SHOT
(n = 155)
155 cases of reported TRALI

- 155 initially reported
  - 14 withdrawn
  - 139 cases analysed
  - 2 no data
    - 32 fatal (23%)
    - 11 died other causes
    - 4 partially recovered
    - 94 fully recovered (67%)
Other diagnoses with a similar clinical picture to TRALI

- fluid overload
- respiratory distress syndrome secondary to infection, trauma etc
- lung infection
- acute reaction to blood component
TRALI investigations
looking for leucocyte antibodies

• Refer to 1 of 3 specialist consultants in NBS
• Recall donors for fresh serum samples - females and transfused males first
• Patient: serum, DNA and cells for X-matching
• HLA antibodies: class I and II, specificity
• Granulocyte antibodies: HNA systems
• IgG and IgM X-match between donor serum and patient leucocytes (if available)
Profile of 139 TRALI cases

- Age range 26 d-79 yrs (median = 60)
- 12 children
- M:F = 43:57
- 48% became hypotensive
- 40% developed fever/rigors
- 72 (52%) required ICU admission
  + 25 (18%) were on ICU already
- 32 died - TRALI implicated
TRALI cases by diagnosis  (n = 139)

- Haem-onc: 38%
- Surgery: 35%
- Acute h'age: 9%
- Correctn coag: 9%
- Sepsis: 5%
- Plasma exchange: 4%
Timing of onset of symptoms (n = 108)

- **D/<2 hrs**: 63%
- **< 6 hrs**: 25%
- **<12 hours**: 7%
- **< 24 hours**: 5%
Components implicated
(n = 139)

- FFP/cryosupernate 45
- Red cells 34
- Platelets 27
- Whole blood 2
- Cryoprecipitate 2
- Other 4 (SDFFP, I/V IgG, MBFFP, buffy coat)
- Unassignable 25
Components implicated/total issues (n = 139)

HIGH PLASMA (300 MLS)
FFP /CSP  45/ 2.6 million = 1:  58,000
Platelets  27/ 1.7 million =  1:  63,000

LOW PLASMA (30 MLS)
Cryoppt  2/ 0.6 million =  1: 300,000
Red cells  34/17.8 million = 1: 523,000

Risk from ‘high plasma’ components was 5-8 times higher than from ‘low plasma’ components.
Imputability score since 1999 (1)  
(n = 100)

Highly likely:
- good history + incompatibility  = 36

Probable:
- good history + wk or neg serology
  
  OR

- weak history + incompatibility or strong specific antibody  = 18

54% in these categories!
Imputability score since 1999 (2)  
(n = 100)

Possible:
- history/serology compatible but couldn’t exclude other causes = 31

Unlikely:
- negative serology + other diagnosis to explain symptoms = 15

46% in these categories!
Probability of TRALI according to component implicated

- **FFP**
- **Platelets**
- **Red cells**

- **High**
- **Low**
Serological investigations 1998-2003

Leucocyte antibody investigations 99

- 1 or more donors positive 71
- Patient positive 8
- All donors and patient neg 19
- Inter-donor incompatibility in platelet pool 1
Positive serological investigations in donors 1998-2003  (n = 71)

71 cases

- HLA antibodies (class I or II) 50
  - Positive Xmatch 18
  - Cognate antigen 18
  - Antibodies only 14

- Both HLA and granulocyte reactive 5
  - Positive Xmatch 6
  - Cognate antigen 2
  - Antibodies only 8

- Granulocyte reactive 16
## Serology by component
### 1998-2003

<table>
<thead>
<tr>
<th></th>
<th>RED CELLS</th>
<th>FFP/PLTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>19</td>
<td>56</td>
</tr>
<tr>
<td>Ab pos donor</td>
<td>5</td>
<td>47</td>
</tr>
<tr>
<td></td>
<td>26%</td>
<td>84%</td>
</tr>
<tr>
<td>Female</td>
<td>2</td>
<td>37/37</td>
</tr>
<tr>
<td>Incompatible</td>
<td>1</td>
<td>31</td>
</tr>
<tr>
<td></td>
<td>20%</td>
<td>54%</td>
</tr>
<tr>
<td>Female</td>
<td>?</td>
<td>29/29</td>
</tr>
<tr>
<td></td>
<td>Donor selection: untransfused males/never pregnant females</td>
<td>Donor selection: males only</td>
</tr>
<tr>
<td>--------------------------------</td>
<td>----------------------------------------------------------</td>
<td>----------------------------</td>
</tr>
<tr>
<td>FFP</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Pooled platelets (plasma component)</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Apheresis platelets</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Non-OAS blood for large transfusion in neonates</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>
NBS TRALI PREVENTION PROJECT
Plea from donor care staff
No more new questions!!
SO - Oct 2003- male donations marked M & directed for FFP production

From 5th April - previously transfused donors excluded (vCJD)
Costs of male FFP

- LD filters for plasma
- sterile connectors- disposables
- staff costs- longer days
  = £2.1 million/year
(SDFFP = £25 million/year)

NB- all imported FFP for children is from male donors
Could platelet additive solution reduce TRALI risk?

- Need to retain 30% plasma - ? extent of risk reduction
- No systems yet for apheresis
- Linkage with bacterial screening:-
  - Need to confirm that additives solutions can support 7 day storage
Leucocyte antibody screening of apheresis donors

- Can we afford to lose 7% of donors?
- What to do with positives?
  - Resign completely?
  - Carry on as donors of red cells in additive solution
Large volume transfusion in neonates and infants

• How likely is TRALI in this age group?
• Would it be recognised?
• New BSCH Guidelines recommend non-SAGM blood for large volume transfusion-exchange, ECMO, cardiac surgery.
Acknowledgements

SHOT
Liz Love, Hilary Jones, Hannah Cohen, Cath Chapman, Cynthia Beatty

TRALI REDUCTION PROJECT
Michelle Ashford, Gordon Nicholson, Lindsey Lewis, Neil Beckman

LEUCOCYTE ANTIBODY DATA
Cristina Navarrete, Sheila MacLennan, Geoff Lucas
Donor serology - other findings

- HLA class II antibodies frequently implicated in TRALI
- No cases clearly associated with transfused males
- Inter-donor platelet incompatibility as a cause of TRALI is rare
  (1 reported in 1.4 million platelet doses)
SHOT AND TRALI PREVENTION

1999: A view should be taken regarding importance of TRALI in relation to other blood safety steps

2001: consider excluding female FFP donors

2002: UK Transfusion Services should take all steps possible to reduce the risk of TRALI from blood components especially FFP & platelets

2003: UKTS should continue with these.
<table>
<thead>
<tr>
<th></th>
<th>Donor selection: untransfused males/never pregnant females</th>
<th>Donor selection: males only</th>
<th>Screening for HLA antibodies</th>
<th>Platelet additive solution</th>
<th>Pooling</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FFP</strong></td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes (SDFFP)</td>
</tr>
<tr>
<td><strong>Pooled platelets (plasma component)</strong></td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td><strong>Apheresis platelets</strong></td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td><strong>Non-OAS blood for large transfusion in neonates</strong></td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Donor selection: untransfused males/never pregnant females</td>
<td>Donor selection: males only</td>
<td>Screening for HLA antibodies</td>
<td>Platelet additive solution</td>
<td>Pooling</td>
</tr>
<tr>
<td>--------------------------</td>
<td>----------------------------------------------------------</td>
<td>----------------------------</td>
<td>-------------------------------</td>
<td>---------------------------</td>
<td>---------</td>
</tr>
<tr>
<td>FFP</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes (SDFFP)</td>
</tr>
<tr>
<td>Pooled platelets (plasma component)</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Apheresis platelets</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Non-OAS blood for large transfusion in neonates</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>