Nationwide adoption of pathogen inactivation for platelet concentrates in Switzerland

International Haemovigilance Seminar 2012
Montreal

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Switzerland
Swiss Blood Transfusion Service

13 Regional Blood Transfusion Services (RBTS)

Population of 7’600‘000

Transfusions performed in ~200 hospitals

Units transfused in 2011:

~ 310‘000  RBC
~  60‘000  Plasma
~  30‘000  Plt concentrates

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Swiss Haemovigilance System

- Reporting is mandatory since 2002
- All reactions and events are reported
- Haemovigilance officers report to Swissmedic
Current Haemovigilance data

Number of reports 2002 - 2011

Reporting rate 2011: 3.9 reports per 1000 transfusions

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Current Haemovigilance data

TR 2011 by classification and frequency

- FNHTR: 42.6%
- Allo-immunisation: 25.2%
- Allergic TR: 19.6%
- TACO: 5.6%
- Hypotensive TR: 2.2%
- Other: 1.4%
- Haemolytic TR: 1.1%
- Infection: 0.9%
- TAD: 0.8%
- TRALI: 0.4%
- PTP: 0.1%

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Latest achievement

Nationwide implementation of the INTERCEPT® Pathogen Inactivation (PI) procedure for all platelet concentrates in Switzerland in the course of 2011

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Morbidity and Mortality due to bacterial contamination of platelet concentrates in Switzerland (2005-2009)

- 15 febrile/septic reactions (including 3 fatal)
- 130’000 transfused products (5 years)

Morbidity ~1:8’000
Mortality ~1:40’000 (~ one per 1.6 Y)

Without bacterial detection and > 90% aphaeresis PLT units
Options

Reduced storage time
• 4 instead of 5 days (e.g. Germany) → missing ~50%!!

Bacterial Screening:
• Several systems available in Europe
• BacT/ALERT® (Biomerieux) assumed as Gold Standard

Pathogen inactivation
• Only one system currently has marketing authorisation in Switzerland (Intercept ®)
Bacterial Screening

Pro

- Reduces risk
- Simple to perform
- Recognised technology
- Moderate costs

Con

- Sensitivity/specificity problem (up to ~50% false negatives)
- Issued as negative to date
  - Detected positive later
- Reduces bacterial risk only
- Loss of PLT due to sampling

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te Boekhorst PA et al; Transfusion 2005;45:514-9
Kleinman S et al; Transfusion 2009;49:903-912
Dumont LJ et al; Transfusion 2010;50:589-599
Pearce S et al; Transfusion Medicine 2011;21:25-32
Jenkins C et al; Transfusion 2011; in press
Pathogen Inactivation

Pro
- Effective for majority of bacteria, viruses, protozoa including emerging & non-tested pathogens
- Transfusion reactions
- $\gamma$-irradiation superfluous
- Stop CMV screening! & others?
- Relax donor exclusions? (travel,...)

Con
- Long term safety?
- Loss of ca. 10-15% PLT and modestly of function
- Costs (1,4 Mio $ / QALY?!)*
  (but compare: 2,7 Mio $ / QALY for additional Hep B/C & HIV – NAT)
- Monopoly of company

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- Custer B et al, Transfusion 2010;50:2461-2473
- Davidson T et al, Transfusion 2011;51:421-429
Decision

Joint decision in 2009 by Swissmedic and Swiss Red Cross Blood Transfusion Service to implement the INTERCEPT® Pathogen Inactivation (PI) procedure for all platelet concentrates in Switzerland

Nationwide implementation in 2011
Implementation

• 2010 planning and pre-validation phase

• A specific manufacturing authorisation issued to each RBTS by Swissmedic after individual validation

• Begin routine production in the three pilot centres in January 2011 (covering approx. 50% of PC production in Switzerland), the remaining 10 centres followed in the course of 2011

• Implementation completed by end 2011, now 100% supply with PI-PC
Expectations

• No more septic transfusion reactions after PC-transfusion

• Decrease in the number and severity of PC-related transfusion reactions

• An increase in platelet collection (up to ~ 15%)

• Possibly compliance problems with the clinicians
Observations 2011–Transfusion data

• ~ 80% PCs pathogen inactivated, ~ 20% conventional PCs
• 33,000 PCs transfused, increase of ~ 10.5%, due to:
  • General increase in patients needing PC transfusions (e.g. stem cell transplant patients, trauma patients, massive transfusions)
  • Precautionary raise of the transfusion trigger (from 5 to 10 G/l) for prophylactic PC transfusions in some clinics
  • PC’s transfused more readily in others (PI products considered safer)
  • Possibly lower CCI → clinical significance??
• Whole blood derived PCs increased from 14 to 23% of all PCs
  • To meet the rising need
  • As contribution to cost reduction
Observations 2011– Haemovigilance

Reports on TR for all blood components

- All reports on TR
- All HI reports
- All life-threatening TR

Reported transfusion reactions for PC

- Total reports for PC
- High Imp. reports for PC
- Grade 3 + 4 TR for PC

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Observations 2011– Haemovigilance

High imputability TR for PI-PC and conventional PC by classification

- PI-PC (60)
- conventional PC (43)

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## Risk of transfusion for PCs 2011

<table>
<thead>
<tr>
<th>Transfusion reactions</th>
<th>2011 PI-PC‘s</th>
<th>2011 conventional PC‘s</th>
<th>2010 (only conventional PCs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Units transfused</td>
<td>26‘454</td>
<td>6‘614</td>
<td>29‘900</td>
</tr>
<tr>
<td>Risk = 1 reaction per x PC transfusions</td>
<td>Reports Risk</td>
<td>Reports Risk</td>
<td>Reports Risk</td>
</tr>
<tr>
<td>All high imputability reactions</td>
<td>60 ~1: 440</td>
<td>43 ~1:150</td>
<td>98 ~1:330</td>
</tr>
<tr>
<td>High imputability grade 3 reactions</td>
<td>3 ~1:8800</td>
<td>2 ~1: 3300</td>
<td>9 ~1:3300</td>
</tr>
</tbody>
</table>

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Summary

- As expected, no transfusion transmitted bacterial infections were observed after PC transfusions in 2011.
- No reports of increased bleeding / clinical inefficiency of PC.
- Less than 2/3 of the reported TR occurred after the transfusion of PI-PC (80% of all PCs transfused), whereas the 20% conventional PC’s generated more than 30% of all PC-related reports.
- Lower risk for adverse events observed, especially for life threatening reactions (risk reduction from 1:3’300 to 1: 8’800).
- Demand for PC increased by 10.5 %
Conclusion

• PI for platelet concentrates substantially reduces the risk for bacterial TTIs and also for platelet related transfusion reactions in general

• Our findings underline the superior safety profile of pathogen inactivated PCs

• It remains to be seen how this trend towards declining platelet related TRs develops over the next few years when more Haemovigilance data become available

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Thank you for your attention
Observations 2011—Transfusion data

<table>
<thead>
<tr>
<th>Blood components</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
<th>Difference 2010 - 2011</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apheresis PC</td>
<td>26380</td>
<td>25‘876</td>
<td>25‘499</td>
<td>- 1.5 %</td>
</tr>
<tr>
<td>Whole blood derived PC</td>
<td>3220</td>
<td>7‘569</td>
<td>10‘969</td>
<td>+ 86 %</td>
</tr>
<tr>
<td>Total PC</td>
<td>29‘600</td>
<td>29‘938</td>
<td>33‘068</td>
<td>+ 10.5 %</td>
</tr>
</tbody>
</table>

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## Transfusion data Switzerland

<table>
<thead>
<tr>
<th></th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Blood components</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Red cell concentrates</td>
<td>308’470</td>
<td>313’587</td>
<td>311’521</td>
<td>308’670</td>
<td>308’627</td>
</tr>
<tr>
<td>FFP (units)</td>
<td>69’800</td>
<td>65’800</td>
<td>70’300</td>
<td>61’500</td>
<td>50’063</td>
</tr>
<tr>
<td>Platelet concentrates</td>
<td>22’900</td>
<td>27’600</td>
<td>29’600</td>
<td>29’900</td>
<td>33’068</td>
</tr>
<tr>
<td>Platelet concentrates (products)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>401’229</td>
<td>407’079</td>
<td>411’528</td>
<td>400’070</td>
<td>391’758</td>
</tr>
</tbody>
</table>

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