Practical Aspects and Hemovigilance

Practical aspects
- Transfusion as a Process
- Quality Related Issues in Clinical Practice
- Human error and its QM

Hemovigilance
- HTC
- Belgian legislation and guidelines:
  - Legislature
  - Guidelines
- Useful examples from:
  - SHOT-database
  - National reports
Hemovigilance: an effective tool for improving the process of transfusion practice
Transfusion as a process

Safe transfusion: processes, not only products

Bloodproducts: EC, PC, Plasma
(Stable plasmaderivatives)

Bloodtransfusion: EC, PC, Plasma
(Stable plasmaderivatives)

1. donorselection
2. donorscreening
3. productselection
4. prelevation
5. processing
6. storage
7. transport
8. donor-FU

9. patientselection
10. trfs-indications
11. pre-trfs testing
12. storage (irradiation)
13. productrelease (-return)
14. transport
15. infusion
16. monitoring
17. evaluation/FU

RC

HOSP

Quality: safety donor, product quality, efficiency and safety acceptor, traceability, vigilance, reporting

Dr. prescriber
Dr. transfuser
RNurse transfuser
Dr. evaluator/-FU
Actions to improve safety / efficacy

Safe Transfusion: Processes not just product.

- Recruit
  - Screen donor
  - Collect & Prepare
  - Inf Dis tests
- Pre-tx testing
- Medical Reason for Tx
- Issue
  - Administer (bedside)
  - Monitor & Evaluate

Process

Product

Patient sample

Improvement 1
Patient sampling : avoid WBIT!

Elective trfs :

- 2 *separate* patient-samples for typing : confirmation of concordance prior to issuing bloodgroup type and antibody status (timing: as routine practice)
- *Fresh crossmatch* sample, i.e. less than 72h from effective trfs (storage of samples : to be arranged)
- *No indirect* sample transmission: e.g. no redirected samples from another lab

Urgent trfs :

- *Maximum effort* to obtain 2 separate samples for emergency typing
- If only 1 : *specific guideline* with IH-lab mandatory
- *Clinical problem 1* : unexpected important bleeding during hospitalisation (per protocol)
- *Clinical problem 2* : bleeding in a type-and-screen patient
- *Clinical problem 3* : Massive Transfusion Protocol activation
Actions to improve safety / efficacy
Release: ‘Type and Screen’ strategy or ‘Cross and Hold’ strategy
Release: Type-and-Screen

Broad applicability in pre-operative planning

Product release and shipment according to clinical need

Avoids unnecessary product release (cold chain)

Costly

Protocol mandatory

### Table I: Results of antibody screening

<table>
<thead>
<tr>
<th>Total No. of patients</th>
<th>Antibody screen</th>
<th>Cross Match</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Positive</td>
<td>Negative</td>
</tr>
<tr>
<td>354</td>
<td>04</td>
<td>350</td>
</tr>
</tbody>
</table>

### Table II: Comparison of Type and screen with Column Agglutination Technology

<table>
<thead>
<tr>
<th>T &amp; S</th>
<th>Cross Match</th>
<th></th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Compatible</td>
<td>Incompatible</td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>03</td>
<td>01</td>
<td>04</td>
</tr>
<tr>
<td>Negative</td>
<td>350</td>
<td>00</td>
<td>350</td>
</tr>
<tr>
<td>Total</td>
<td>353</td>
<td>01</td>
<td>354</td>
</tr>
</tbody>
</table>
Release: Cross-and-Hold

Broad applicability in pre-operative planning according to validated estimates of clinical need

Immediate release guaranteed with extra control

Cold chain compatible

Specific separate storage capacity needed
Release and Transport: Temperature controlled!

**RC:** cold chain issue!

**PC:** ‘room’ temperature compatible – platelet-shakers at secondary storage sites (SOC)

**Plasma:** deepfrozen status to be respected until thawing and administration – or in SOC-freezer
Administration: Infusion temperature

**EC:** thru bloodtransfusion lineset
EC warming is *not mandatory* in most elective transfusions
EC warming is preferred in patients with problematic *thermoregulation*, e.g. lengthy peroperative procedures, major surgery, infants (premature/newborns), severe trauma patients
EC warming with specific *validated equipment* only

**Plasma:** same
Plasma thawing with validated *specified equipment* only
- *Warm dry air* stoves preferred
- Specified and reserved warm *waterbaths* with temperature control for faster thawing
- Specific equipment for *emergency and large volume* plasma thawing at pre-specified SOC (e.g. Plasmatherm-R)

**PC:** same
Ambiant temperature

After thawing: retention of adequate clottingfactor activities *time-limited* (6hr+)
EC:
Slow start and observation during first minutes
Elective trfs: ‘1 drip / second’
Speeding up: only if clinically useful and if observation confirms troublefree course

9-to-5 practice, during the week!

Urgencies: according to clinical need and protocols
Rapid Infusion Systems: defined practice in experienced OR setting

Plasma and PC:
Identical practice
Drip speed can be higher if troublefree course documented

Infusion set changing:
according to observations and internal protocols?
‘Time out’ procedure
GO / NO GO

My role at this point?

// my function?
// my action points?
// my report?
Mandatory check: at bedside, ‘4 eyes’
GMP / GCP
Actions to improve safety / efficacy

Safe Transfusion: Processes not just product.

- Process
  - Product
    - Recruit
      - Screen donor
      - Collect & Prepare
        - Inf Dis tests
      - Pre-tx testing
      - Medical Reason for Tx
    - Issue
      - Administer (bedside)
      - Monitor & Evaluate

- Improvement 3
  - Patient sample
    - #######
Monitoring: short term ...

example: PC – CCI measurement
Monitoring : long term …
Example : detecting DHTR

Figure 11
Interval in days between administration of the implicated transfusion and signs or symptoms of a DHTR
Plasma products

Plasma Proteins and the Diseases They Treat

- **Albumin (25 grams*)**
  - Shock, Burns, Adult Respiratory Distress Syndrome, Cardiopulmonary Bypass Surgery

- **IVIG (Intravenous Immunoglobulin) (4 grams*)**
  - Primary Immunodeficiency Diseases, Autoimmune Diseases, Chronic Inflammatory Demyelinating Polyneuropathy, Idiopathic Thrombocytopenic Purpura

- **Alpha-1 Antitrypsin (.15 to .30 grams*)**
  - Alpha-1 Antitrypsin Deficiency (Genetic COPD)

- **Coagulation Factors**
  - (Factor VIII: 300 to 450 IUs; Factor IX: 180 to 200 IUs*)
    - Hemophilia A & B, von Willebrand Disease, Bleeding Disorders

* Plasma Protein Yields Per Liter of Plasma
Virus inactivation of plasma: MB vs SD

**MB-methode**
- Target: viral nuclear proteins and DNA/RNA are damaged
- Single unit
- Every unit is different
- Active on encapsulated and non-encapsulated viruses (parvovirus B19, HAV)

**SD-methode**
- Lipid membrane is destroyed by organic solvent (tri-n-butylfosfaat) and detergent (triton X-100)
- Pool of 350 l
- Product is QControlled
- Active only on encapsulated viruses
- No TRALI reported
- Less severe allergic reactions: observational
Figure 9
Reaction by component type (excluding 6 reactions that could not be attributed to a particular component)

Key
- Unclassified
- Hypotensive
- Mixed allergic/febrile
- Anaphylactic
- Allergic
- Febrile

Each star represents a case of:
- HLA-matched platelets
- Solvent detergent plasma
- Methylene blue plasma

Component type
- Red cells
- Platelets
- Plasma
- Multiple components

Percentage of reactions

248
27
29
14
38
52
2
3
4
2
1
2
3
4
5
11
7
6
3
2
2
100
90
80
70
60
50
40
30
20
10
0
TPE and plasma

TABLE 3. Properties of single-donor plasma as replacement fluid

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
<th>In TTP (ADAMTS13 defic/antibodies): SD-Plasma! (preliminary consensus)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All plasma proteins replaced</td>
<td>Viral transmission risk</td>
<td>In TTP (ADAMTS13 defic/antibodies): SD-Plasma! (preliminary consensus)</td>
</tr>
<tr>
<td>Frozen storage*</td>
<td>Compatible blood group required</td>
<td></td>
</tr>
<tr>
<td>Advance order and/or thawing*</td>
<td>Documentation of patient identity required</td>
<td></td>
</tr>
<tr>
<td>Citrate reactions</td>
<td>Allergic reactions</td>
<td></td>
</tr>
</tbody>
</table>

* Frozen storage and thawing are not applicable to thawed plasma.
Action plan for transfusion reactions:

- Managing observation during trfs until +6hr

- Must be reported: trfs-report, part of patientfile

-hemovigilance
MTP

Patient with excessive blood loss anticipated >10 U pRBC

→ Type and screen sent to blood bank

Need MTP?

No

→ Conventional resuscitation guided by laboratory parameters

Yes

Attending Physician activates MTP. Initial package ready in 10 min:
10 units pRBC
6 units FFP/plasma
2 apheresis plt

POC: TAG / Rotem!

→ After verbal confirmation, Blood Bank begins next MTP package (type specific):
6 units pRBC
4 units FFP/plasma
1 apheresis plt

→ Anticipate ongoing excessive bleeding?

Yes

→ Stop MTP
Continue with standard resuscitation guided by laboratory parameters

→ Review and feedback by TM physician to all participating attendings on any process issues: product wastage, failure to administer products, etc.
MTP: Anti-Fibrinolytica benefit

<table>
<thead>
<tr>
<th>Time from injury (h)</th>
<th>Tranexamic acid allocated</th>
<th>Placebo allocated</th>
<th>Risk ratio (99% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤1</td>
<td>509/3747 (13.6%)</td>
<td>581/3704 (15.7%)</td>
<td>0.87 (0.75-1.00)</td>
</tr>
<tr>
<td>&gt;1-≤3</td>
<td>463/3037 (15.2%)</td>
<td>528/2996 (17.6%)</td>
<td>0.87 (0.75-1.00)</td>
</tr>
<tr>
<td>&gt;3</td>
<td>491/3272 (15.0%)</td>
<td>502/3362 (14.9%)</td>
<td>1.00 (0.85-1.17)</td>
</tr>
<tr>
<td>(\chi^2=4.411; p=0.11)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Systolic blood pressure (mm Hg)</th>
<th>Tranexamic acid allocated</th>
<th>Placebo allocated</th>
<th>Risk ratio (99% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥90</td>
<td>702/6878 (10.2%)</td>
<td>736/6761 (10.9%)</td>
<td>0.94 (0.82-1.07)</td>
</tr>
<tr>
<td>76-89</td>
<td>280/1609 (17.5%)</td>
<td>313/1689 (18.5%)</td>
<td>0.94 (0.78-1.14)</td>
</tr>
<tr>
<td>≤75</td>
<td>478/1562 (30.6%)</td>
<td>562/1599 (35.1%)</td>
<td>0.87 (0.76-0.99)</td>
</tr>
<tr>
<td>(\chi^2=1.345; p=0.51)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>GCS</th>
<th>Tranexamic acid allocated</th>
<th>Placebo allocated</th>
<th>Risk ratio (99% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe (3-8)</td>
<td>796/1789 (44.5%)</td>
<td>860/1830 (47.0%)</td>
<td>0.95 (0.86-1.04)</td>
</tr>
<tr>
<td>Moderate (9-12)</td>
<td>219/1349 (16.2%)</td>
<td>249/1344 (18.5%)</td>
<td>0.88 (0.70-1.09)</td>
</tr>
<tr>
<td>Mild (13-15)</td>
<td>447/6915 (6.5%)</td>
<td>502/6877 (7.3%)</td>
<td>0.88 (0.75-1.04)</td>
</tr>
<tr>
<td>(\chi^2=1.387; p=0.50)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Injury type</th>
<th>Tranexamic acid allocated</th>
<th>Placebo allocated</th>
<th>Risk ratio (99% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blunt</td>
<td>1134/6788 (16.7%)</td>
<td>1233/6817 (18.1%)</td>
<td>0.92 (0.83-1.02)</td>
</tr>
<tr>
<td>Penetrating</td>
<td>329/3272 (10.1%)</td>
<td>380/3250 (11.7%)</td>
<td>0.86 (0.72-1.03)</td>
</tr>
<tr>
<td>(\chi^2=0.791; p=0.37)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>All patients</th>
<th>Tranexamic acid better</th>
<th>Tranexamic acid worse</th>
</tr>
</thead>
<tbody>
<tr>
<td>1463/10060 (14.5%)</td>
<td>0.91 (0.85-0.97)*</td>
<td></td>
</tr>
<tr>
<td>1613/10067 (16.0%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Two-sided p=0.0035
Patient management strategies when treating a major bleeding event

Time is brain / tissue!
PPSB / Octaplex stat!

Rapid and continuous assessment and reassessment of patient’s condition:
- Initiate life-saving therapy as required (i.e., intubation, ventilation, fluid resuscitation, packed red blood cells, etc.)
- Consider transfer to an intensive-care unit setting—notify required team members (e.g., radiology staff, OR staff) early in the resuscitation
- Measure the activity of the coagulation cascade, hemoglobin and platelets, electrolytes (including calcium), temperature, and hematological parameters frequently and act on observed abnormalities

Withdraw anticoagulant therapy (remove from bedside)

Administer appropriate dose of antidote (if one exists)

Address mechanical causes of bleeding—this may require:
- Radiological interventions
- Endoscopy
- Surgery

Consider administration of prohemostatic agents:
- Antifibrinolytic agents (e.g., tranexamic acid)
- Desmopressin (DDAVP)
- Recombinant factor VIIa

Consider modalities that may specifically remove the anticoagulant:
- Dialysis,
- Hemoperfusion, and/or
- Plasmapheresis

The curse of human imperfection: errors!

Hazard passes through the holes in the barriers (failed or missing), leading to a failure – James Reason

When all of the holes in each of the slices momentarily align, permitting "a trajectory of incident opportunity."
Based on ensuring that the RISK to the patient OF NOT TRANSFUSING is GREATER than the RISK OF TRANSFUSING.
Practical Aspects and Hemovigilance

**Practical aspects**
- Transfusion as a Process
- Quality Related Issues in Clinical Practice
- Human error and its QM

**Hemovigilance**
- HTC
- Belgian legislation and guidelines:
  - Legislature
  - Guidelines
- Useful examples from:
  - SHOT-database
  - National reports
Hemovigilance: an effective tool for improving the process of transfusion practice
Hemovigilance

Bloodproduct producers and providers (officially accredited)

Bloodproduct users (hospitals) thru Hospital Transfusion Committee (mandatory)

National Transfusion Platform (FGOV Health) : Board and Working Parties
Figure 2
Cases reviewed in 2010 $n = 1464$

- HSE: 239 (16.3%)
- Anti-D: 241 (16.5%)
- ATR: 510 (34.8%)
- TRALI: 15 (1.0%)
- HTR: 58 (4.0%)
- TAD: 35 (2.4%)
- TACO: 40 (2.7%)
- PTP: 1 (0.1%)
- Autologous: 15 (1.0%)
- IBCT: 200 (13.7%)
Figure 6
Cases of inappropriate and unnecessary transfusion 1996–2010

Number of reports

Year of report


1 20 31 32 56 67 51 50 76 92 110
Hemovigilance in Belgium

Report 2010

2010:

93,000 plasma transfusions

<table>
<thead>
<tr>
<th>Transfusiereactie</th>
<th>Aantal in functie van de</th>
<th>Totaal aantal</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>toegediende bloedcomponent</td>
<td></td>
</tr>
<tr>
<td></td>
<td>EC</td>
<td>PLT</td>
</tr>
<tr>
<td>Niet-hemolytische febrile transfusiereactie (temperatuur: stijging ≥2°C of &gt; 39°C)</td>
<td>49</td>
<td>9</td>
</tr>
<tr>
<td>Immunologische hemolyse</td>
<td>16</td>
<td>8</td>
</tr>
<tr>
<td>- ABO incompatibiliteit</td>
<td>8</td>
<td>-</td>
</tr>
<tr>
<td>- andere allo-antistoffen (waarvan uitgestelde reactie)</td>
<td>8</td>
<td>-</td>
</tr>
<tr>
<td>Ernstige allergische reactie</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>- angiooedeem</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>- anafylactische reactie</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Bacteriële besmetting overgedragen door transfusie</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Acuut longoedeem</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Transfusie gerelateerd acuut longletsel (TRALI)</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Niet-immunologische hemolyse</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Virale infectie overgedragen door transfusie</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Transfusie geassocieerde graft versus host ziekte</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Post transfusionale purpura</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Parasitaire besmetting overgedragen door transfusie</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Andere</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Totaal</td>
<td>85</td>
<td>23</td>
</tr>
</tbody>
</table>

EC: erytrocyteneconcentraat; PLT: bloedplaatjesconcentraat; Multip. comp.: multiple bloedcomponenten
Figure 19
Number of viral and parasitic TTI incidents, by year of report and infection type (Scotland included from 10/1998)

Key
- Malaria
- HTLV
- HIV
- HEV
- HCV
- HBV
- HAV

(Prions: ? None)
Hemovigilance in Belgium
Report 2010

Figuur 11: Risico op een transfusiereactie (NHFTR niet inbegrepen) in functie van de toegeediende bloedcomponent

Aantal bijwerk. per 100.000 bloedcomp.

2006 2007 2008 2009 2010

EC
PLT
VIVP
Totaal
Actions to improve quality and performance

**Restrictive interventions**
- e.g. delienate or limit responsibilities
- e.g. Trfs–order by guidelines only

**Persuasive interventions**
- e.g. audit-based team discussion: HTC
- Ehemovigilance analysis based meetings

**Structural interventions**
- e.g. infrastructure improvements (storage)
- e.g. ICT-applications at bedside
TRANSFUSION –

Practical Aspects and Hemovigilance

Thank you and do not ask too much questions (I don’t have all the answers)
Transfusion reactions: current risk perspective