Delayed hemolytic transfusion reaction in the French hemovigilance system

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First Seminar on delayed hemolytic transfusion reaction in sickle cell disease patients
Monday, December 17th, 2018 - Créteil, France
French Hemovigilance System

• Created in 1994

• Dedicated network for labile blood products
  • Red cells, platelets, granulocytes and plasma

➢ Tracability of all transfused labile blood products in France

➢ Mandatory reporting
  • Adverse events in recipients
  • Adverse events in donors
  • Errors in transfusion protocol
  • Post-donation events
Reporting process of AE in patients

- Suspected transfusion AE in patient
  - Doctors/nurses
  - Hospital
    - Hemovigilance correspondent
    - Local AE base
  - Regional health agency
    - Hemovigilance Coordinator
  - Ministry of Health
    - Ansm
      - National AE database
    - Regional EFS
      - National EFS
    - Blood bank/EFS
      - Hemovigilance correspondent
      - Local AE base
## 2017 main figures

<table>
<thead>
<tr>
<th></th>
<th>Number</th>
<th>Rate/ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood Labile Products</td>
<td>3,082,178</td>
<td></td>
</tr>
<tr>
<td>Patients transfused</td>
<td>522,701</td>
<td>7,8/1000 inhabitant</td>
</tr>
<tr>
<td>Tracability</td>
<td>99.1 %</td>
<td></td>
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<tr>
<td>Patients adverse events</td>
<td>7,276</td>
<td>283,2/100,000 transfusions</td>
</tr>
<tr>
<td></td>
<td></td>
<td>166.6/10,000 patients</td>
</tr>
<tr>
<td>Non severe Death SCD</td>
<td>92.1%</td>
<td></td>
</tr>
<tr>
<td>patients</td>
<td>6</td>
<td>84 (1%)</td>
</tr>
</tbody>
</table>

ANSM Hemovigilance 2017 report
Major achievements of the French hemovigilance system

• **Tracability**: from 60% in 1996 to more than 99% since 2005

• **Reduction of risks**

<table>
<thead>
<tr>
<th>Incidence/ 100 000 LBP Number</th>
<th>Risk reduction</th>
</tr>
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<tbody>
<tr>
<td>2000</td>
<td>2015</td>
</tr>
<tr>
<td>ABO incompatibility Red cells and plasma</td>
<td>0,96</td>
</tr>
<tr>
<td>25 5</td>
<td>6-fold</td>
</tr>
<tr>
<td>Bacterial infection</td>
<td>0,78</td>
</tr>
<tr>
<td>20 5</td>
<td>5-fold</td>
</tr>
</tbody>
</table>

• **Recognition of unwell-known risks**
  • TRALI
  • DHTR

*ANSM Hemovigilance yearly reports*
TRALI

Identification on reporting form
National working group
Anti-HLA screening

Recommendations

Nb TRALI imput

Granulocytes
Red cells
Plasmas
Platelets


ANSM Hemovigilance yearly reports
DHTR : an under-reported event

• Under-recognized
  • Acute hemolysis in a chronic hemolytic disease
  • Mimics severe vaso-occlusive crisis
  • Link with transfusion not made because of delay
  • No alloimmunization found in some cases

• Under-reported
  • France : 2/3 of the cases identified after look-back review in a single center in France (Habibi, Am J Hematol. 2016)
  • UK : 47.8% were not diagnosed at the time of event (Vidler, BJH, 2015)

• Misclassification in the hemovigilance reporting
Hemolytic transfusion reactions

<table>
<thead>
<tr>
<th>Intravascular hemolysis</th>
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<tbody>
<tr>
<td>Fever, pain, dark urine</td>
</tr>
<tr>
<td>Unconjugated hyperbilirubinemia</td>
</tr>
<tr>
<td>Increased LDH</td>
</tr>
<tr>
<td>Decreased hemoglobin level</td>
</tr>
<tr>
<td>Abnormal decrease of HbA</td>
</tr>
<tr>
<td>With or without alloimmunization</td>
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</tbody>
</table>

Acute HTR
Within 24h

Delayed HTR
> 24h to?

Hyper hemolysis syndrome

Destruction of autologous AND transfused RBCs
Post-transfusion Hb level lower than pre-transfusion level
Life-threatening complication
Compromised future transfusions for the patient
DHTR in the French hemovigilance database

**National AE reported 2000-2016**

**HTR in SCD**

Definition criteria: at least one clinical and one biological signs
- fever, pain, hemoglobinuria
- fall in Hb, rise in LDH, fall in HbA

231

23 under-documented

26 Acute HTR onset within 24h

182 Delayed HTR
Onset between 1 and 28 days
DHTR in the French hemovigilance database
## DHTR characteristics

<p>| | |</p>
<table>
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<tbody>
<tr>
<td>N=182</td>
<td></td>
</tr>
<tr>
<td>Sex ratio F/M</td>
<td>2.1</td>
</tr>
<tr>
<td>Median Age</td>
<td>26 years (1-76)</td>
</tr>
<tr>
<td></td>
<td>84.6 % &lt; 40 years</td>
</tr>
<tr>
<td>History</td>
<td></td>
</tr>
<tr>
<td>Allo-immunisation</td>
<td>89 (48.9%)</td>
</tr>
<tr>
<td>Previous DHTR</td>
<td>37 (20.3%)</td>
</tr>
<tr>
<td>Transfusion indication (N=167)</td>
<td></td>
</tr>
<tr>
<td>Acute setting</td>
<td>129 (77.3%)</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>35 (19.2%)</td>
</tr>
<tr>
<td>Median delay</td>
<td>8 days (2-29)</td>
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<td></td>
<td>83% between 4 and 15 days</td>
</tr>
<tr>
<td>Mortality</td>
<td>10 deaths (5.5%)</td>
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Additional improvements (1)

- DHTR diagnosis and reporting
  - Elaborate guidelines for diagnosis and reporting
  - Develop specific DHTR form
    - Past history of transfusion and immunohematology
    - Hemoglobin nadir, Reticulocytes count, LDH
    - Follow-up of hemoglobin A percentage (Nomogram, Mekontso-Dessap, Am J Hematol. 2016)
    - Immuno-hematological results

- Process of reporting
  - Exhaustiveness
  - Transfusion and management of patient in different settings
  - Eliminate duplicate reporting
Additional improvements (2)

• Data quality control
  • National reviewing expert group
  • Complementary documents (hospitalization charts and immuno-hematological results)

• National register of HTR
  • DHTR and AHTR
  • SCD patients and others

• National blood transfused patients register needed

• Epidemiological studies
Conclusion

• French hemovigilance system has one of the largest cohort of DHTR in SCD patients

• Importance of coordination between clinicians, transfusion specialists and hemovigilants

• Need for common approach of reporting in Europe, and others parts of the world including Africa
Thanks you

• Clinicians
  • SCD national reference center, CHU Henri Mondor, Creteil

• Transfusion specialists
  • EFS Henri Mondor

• French hemovigilance correspondants