Plasma therapy: indications & recommendations in France

F. HESHMATI
3rd International congress of Transfusion Medicine
Iran, Tehran
Available types of therapeutic plasma

In France, EU & USA
Collection

Whole blood

Plasmapheresis
Collection

Whole blood

plasmapheresis

Preparation

Frozen

Liquid

Lyophilized

6-8 h
18 h
24 h
>24 h (USA: PF24, refrigerated within 8 h & PF24RT24, not pre refrigerated within 24 h)

Never frozen

Thawed, liquid conserved (5d)

Cryoprecipitate
Collection

Whole blood

Preparation

Frozen

Lyophilized

Liquid

Lyophilized

Preparation

Individual

Larges pools*

Minipools*

Plasmapheresis

Pools
Collection

Whole Blood

Plasmapheresis

Preparation

Frozen

Liquid

Lyophilized

Variable / Production & storage: Storage before freezing – Storage time – temperature, etc….

Leuco reduction

Secured

Individual

Pools

Any NAT

NAT

Secured+

PRT

Quarantine

No Secured
Important variation between countries

Collection

Preparation

Whole Blood

Plasmapheresis

Variables

Cell separators, sets, procedures – procedure

Preparation before freezing, temperature

Individual

Pools

Quarantine

Secured

VGS

Any VGS

Secured+

PRT

Secured

No Secured
French plasma

Whole Blood
- Leuco reduction (<10^4/L)
- NAT
- >99% Frozen
- <1% CTSA: Lyophilized
- 100% Secured
- ~10% screened for HEV negatif

Plasmapheresis

Quarantine

PRT: Amotosalen

Solvent-Detergent

Riboflavine

methylene Bleu
Plasmatic products hemovigilance
In France
# of probable and certain AEs declared in 2014 per labile blood component per 100,000 issued components (FFP: compared to 100,000 issued BCs, not to 100,000 issued FFP)

<table>
<thead>
<tr>
<th>Diagnostic</th>
<th>Nombre d'EIR</th>
<th>Taux de déclaration pour 100 000 PSL cédés</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Tous PSL</td>
</tr>
<tr>
<td>Allo-immunisation isolée</td>
<td>2 368</td>
<td>76,21</td>
</tr>
<tr>
<td>Allergie</td>
<td>602</td>
<td>19,37</td>
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<tr>
<td>Réaction fébrile non hémolytique (RFNH)</td>
<td>595</td>
<td>19,15</td>
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<tr>
<td>Oedème pulmonaire de surcharge</td>
<td>185</td>
<td>5,95</td>
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<tr>
<td>Incompatibilité immunologique</td>
<td>184</td>
<td>5,92</td>
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<tr>
<td>Réaction hypertensive</td>
<td>161</td>
<td>5,18</td>
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<tr>
<td>Inefficacité transfusionnelle</td>
<td>37</td>
<td>1,19</td>
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<tr>
<td>Hémosidérose</td>
<td>25</td>
<td>0,80</td>
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<tr>
<td>Accidents métaboliques</td>
<td>1</td>
<td>0,03</td>
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<tr>
<td>Diagnostic non précisé</td>
<td>20</td>
<td>0,64</td>
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<tr>
<td>Réaction hypotensive</td>
<td>18</td>
<td>0,58</td>
</tr>
<tr>
<td>Diagnostic non listé</td>
<td>11</td>
<td>0,35</td>
</tr>
<tr>
<td>Oedème pulmonaire lésionnel</td>
<td>9</td>
<td>0,29</td>
</tr>
<tr>
<td>Hémolyse autre</td>
<td>8</td>
<td>0,26</td>
</tr>
<tr>
<td>Dyspnée non liée à un oedème pulmonaire</td>
<td>6</td>
<td>0,19</td>
</tr>
<tr>
<td>Infection virale</td>
<td>6</td>
<td>0,19</td>
</tr>
<tr>
<td>Hémolyse drépanocytaire</td>
<td>5</td>
<td>0,16</td>
</tr>
<tr>
<td>Infection bactérienne</td>
<td>5</td>
<td>0,16</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>4246</strong></td>
<td><strong>136,65</strong></td>
</tr>
</tbody>
</table>
HEV seroconversion in France
From 2010 to 2013 (4 years)

- SD FFP : 5
- Amotosalen/UVA FFP : 2

- No seroconversion in 2014
Efficiency of different plasmatic products in France

- TMA (Nantes, Nancy, Paris)
- Liver transplantation (Strasbourg)
Type of plasma preparation used for plasma exchange and clinical outcome of adult patients with acquired idiopathic thrombotic thrombocytopenic purpura: a French retrospective multicenter cohort study.

Toussaint-Hacquard M1, Coppo P2,3,4, Soudant M5, Chevreux L1, Mathieu-Nafissi S1, Lecompte T1,6, Gross S1, Guillemin F5, Schneider T7.

Author information

Abstract

BACKGROUND: Plasma exchange (PE) is the first-line therapy of acquired thrombotic thrombocytopenic purpura (TTP). Several plasma preparations have been available; their equivalence in terms of outcome remains uncertain.

STUDY DESIGN AND METHODS: We performed a retrospective analysis of the cases prospectively reported from 2005 to 2010 to the national registry established by the thrombotic microangiopathies French reference center. We analyzed 108 initial episodes of acquired idiopathic TTP in adults treated with PE, 81 with solvent/detergent (S/D) plasma, and 27 with quarantine fresh-frozen plasma (qFFP). The primary endpoint was the time to platelet (PLT) count recovery.

RESULTS: Time to PLT count recovery was not significantly different with S/D plasma versus qFFP (median, 15 days vs. 19 days, respectively; p = 0.126). Complete remission rates, exacerbations, and survival were comparable. By multivariate competitive risk (Fine-Gray) analysis, the only significant association with a shorter time to PLT count recovery was the absence of additional treatment (hazard ratio, 2.06; 95% confidence interval [CI], 1.39-3.05; p < 0.001). There was a significant interaction between type of plasma and age, and for patients less than 40 years old, the use of S/D plasma was associated with a shorter time to PLT count recovery versus qFFP (median, 13 [95% CI, 9-16] days vs. 20 [95% CI, 16-64] days, respectively; p = 0.004).

CONCLUSION: The outcomes of acquired TTP treated with S/D plasma or qFFP seem similar and therefore both preparations can be used safely for PE in this indication. The faster response of S/D plasma observed in younger patients warrants confirmation in prospective studies.

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Comparative effectiveness of plasma prepared with amotosalen-UVA pathogen inactivation and conventional plasma for support of liver transplantation.

Cinquialbre J, Kientz D, Remy E, Huang N, Corash L, Cazenave JP.

Abstract

BACKGROUND: Liver transplant may require large-volume plasma transfusion with increased risk of transfusion-transmitted infection (TTI). Pathogen inactivation of plasma with amotosalen-UVA offers the potential to mitigate TTI risk.

STUDY DESIGN AND METHODS: A retrospective cohort design was used to compare the therapeutic efficacy and key safety outcomes for liver transplants supported with quarantine plasma (Q-FFP [reference]) or amotosalen-UVA plasma (IBS plasma [test]). The outcomes evaluated were volume of plasma, the numbers of red blood cell (RBC) components, and the total dose of platelets (PLTs) transfused during and 7 days after transplant. The safety outcomes were acute hepatic artery thrombosis (HAT) and mortality.

RESULTS: Transplantation and transfusion records for 212 Q-FFP transplants and 215 IBS plasma transplants were reviewed. Not all transplants required plasma; 161 received Q-FFP and 174 received IBS plasma. Among the transplants that required plasma, there were significant differences in median values between cohorts for delay to transplantation (p=0.002), model end-stage liver disease score (p<0.001), pretransplant hematocrit (p=0.006), and graft cold perfusion time (p=0.033). The median volumes of plasma transfused were not different for test and reference (2.160 L vs. 1.969 L, p=0.292). Transplants in the test cohort required a mean of 3.7% more RBC components (p=0.767) and on average a 16.5% increase in total PLT dose (p=0.518). No significant differences were observed for the frequency of acute HAT or mortality.

CONCLUSION: In this retrospective study, IBS plasma provided therapeutic support of liver transplant not different from Q-FFP.
| Indications of Plasma In France |  |
Indications in Surgery, traumatology and obstetrics

- Moderate hemorrhage, Low evolution and controlled
- Hemorrhagic choc, with risk of massive transfusion
  » Maintain of ratio 1:1 à 1:2
  » Early Transfusion then addition of CP
  » Protocol of massive Transfusion
  » Maintain of Fg~>1,5-2 g/L
- Obstetric : Maintain of Fg > 2 g/L
- Neurosurgery & neuro traumatology : If PT < 50%
- Cardiovascular Surgery
  » If bleeding + PT ≤40% or PTT < 1,8 and normal PT or if coting factors. ≤40%
  » Initial dose : 15 ml/kg
  » No defined ration for RBC/FFP
  » Biological monitoring
In Medicine
- Chronic or acute hepato cellular deficiency if bleeding or high risk manipulation
- DIC with PT <35-40% & Bleeding
- Factor V, S protein or Plasminogen deficiency and bleeding
- Specific Clotting fac concentrate not available
- TMA : 40-60 ml/kg
- TPE with colloids : for maintenance of Fg> 1 g/L ~10-30 ml/kg
- AVK over dose : if specific concentrate factors not available

Neonatology, pediatric
- DIC and severe hemorrhage : 10-20 ml/kg
- NN<29WA, clotting factors <20%
- Vit.K deficiency and Sevier hemorrhage
- Exsanguinous transfusion
Recommendations (International consensus)

- Hemorrhagic shock; Clotting Factors collapse
- Severe hemorrhagic risks: AVK overdose, Clotting factors deficiency and non-available concentrates
- TPE: TMA
- New one's
  - Severe infections & sepsis (Ebola etc.)
| therapeutics plasma principles of use |
Ig/Ab

Complement, Immune complex

Clotting factors
Neutralizing Ab
Healing Factors

Risks: Citrate, Anti HLA Ab, Infectious agents
<table>
<thead>
<tr>
<th>Pathology</th>
<th>Clotting factors</th>
<th>Ig/Ab</th>
<th>C/IC</th>
<th>Neutrilizing Ab</th>
<th>Healing Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemorrhage</td>
<td>+++</td>
<td>.</td>
<td>.</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>TMA, HUS</td>
<td>+++ *</td>
<td>++++</td>
<td>±</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>Sepsis</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>++</td>
</tr>
</tbody>
</table>

→ Different Plasma for different pathologies?
Frozen-dried lyophilized Plasma

Military institution « CTSA »

- Conservation: ambient temperature for 1 year
- Prepared exclusively by CTSA and used for OPEX
- Universal (without ABO group)
- Pathogen inactivation by IA procedure
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WAA/SFH CONGRESS
APRIL 27-29, 2016
PARIS
CAMPUS DES CORDELIERS

CONGRESS PRESIDENT: FARHAD HESHMATI
WAA PRESIDENT: PAOLO PERSEGHIN
THANK YOU
VERY MUCH

F.Heshmati, MD, PhD, ESLM, Cairo
EGYPTE 2015