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Norwegian Knowledge Centre for the Health Services

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Plasma Product Differences

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Topics

- What is plasma
- Indications
- QC
- Different products
- Other issues
- Conclusion

Plasma

- Definition:
  - Fresh Frozen Plasma (FFP) is a component for transfusion or for fractionation, prepared either from whole blood or from plasma collected by apheresis, frozen within a period of time and to a temperature that adequately maintains the labile coagulation factors in a functional state
- Requirements and quality control
  - Factor VIII: Average after freezing and thawing. Not less than 70 IU per 100 ml
  - Residual cells

Plasma

- Preparation
  - Men vs women
- Storage
  - 36 months at below -25 C
  - 3 months at -18 C to – 25 C

What could influence the coagulation factor content?

- Natural variability in coagulation factor levels in the donor population
- Type of anticoagulant (ac) used and ratio ac/blood
- Length of time it takes to collect blood into ac
- Time from collection to freezing
- Temperature (blood and plasma)
- Residual cells in plasma prior to freezing
- Apheresis technology
- Use of filters
- Use of PRT

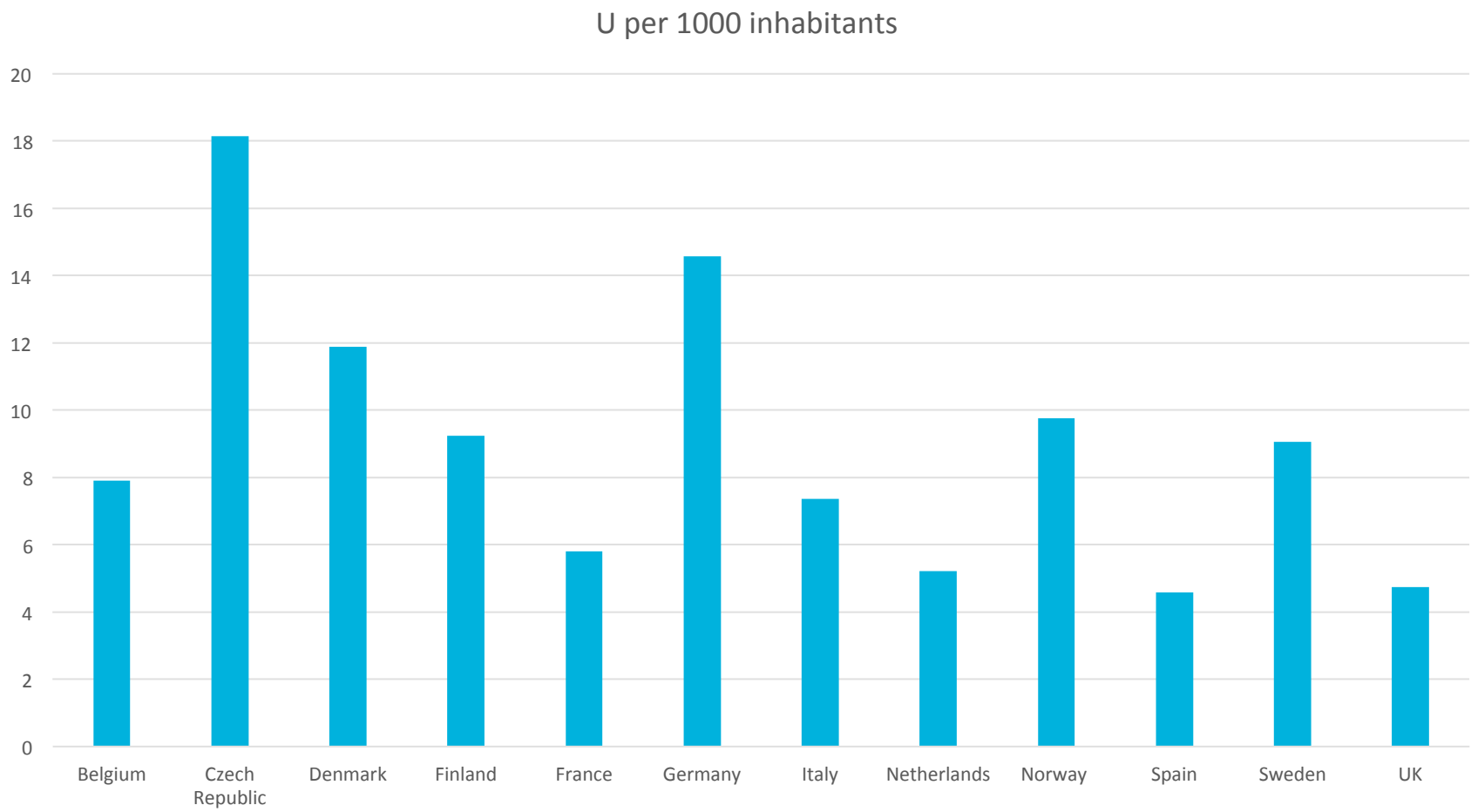
Indications (BCSH)

- Single coagulation factor deficiencies where no concentrate is available
- Multi-factor deficiencies associated with disseminated intravascular coagulation (DIC)
- Plasma exchange in thrombotic thrombocytopenic purpura (TTP)
- Surgical bleeding/massive transfusion
- Liver disease if precipitating factors such as surgery are present
- Reversal of oral anticoagulants if bleeding is present
- Neonates with multi-factor coagulation deficiencies

Quality control by transfusion indication

- Single coagulation factor deficiencies where no concentrate is available **(FV and FXI)**
- Multi-factor deficiencies associated with disseminated intravascular coagulation (DIC) **(FV, VIII, XIII, fibrinogen, protein C, protein S, antithrombin III, alfa2-antiplasmin)**
- Plasma exchange in thrombotic thrombocytopenic purpura (TTP) **(abnormally high level of high MW multimers of vWF)**
- Surgical bleeding/massive transfusion **(dilution coagulopathy ± DIC)**
- Liver disease if precipitating factors such as surgery are present **(all except vWF)**
- Reversal of oral anticoagulants if bleeding is present **(FII, VII, IX, X, protein C, protein S)**
- Neonates with multi-factor coagulation deficiencies

Plasma transfusions 2011



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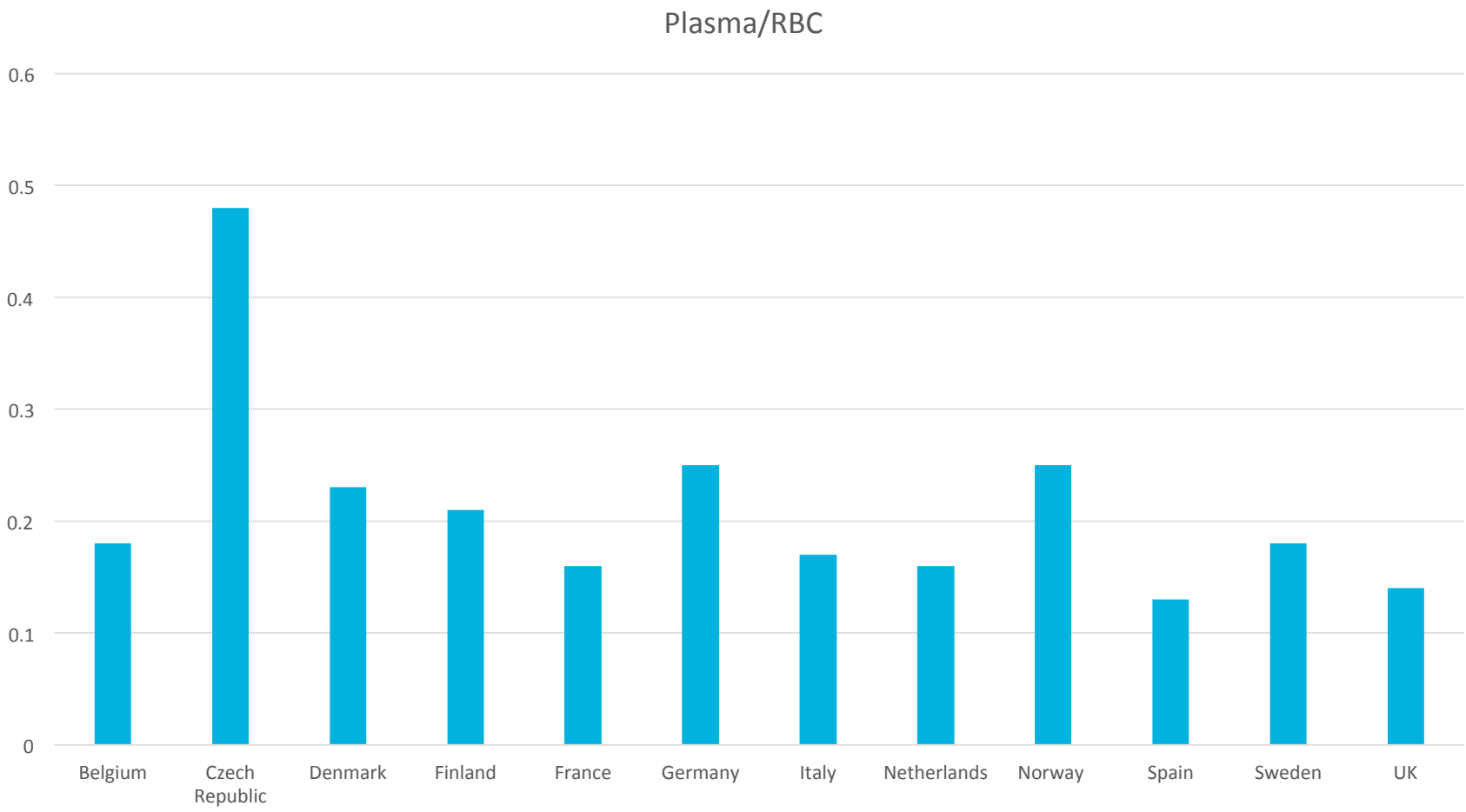
Van Hoeven, Janssen, Rautmann, Council of Europe

Ratio plasma/RBC 2011



Indications

- Yang et al. Transfusion 2012
- 80 RCTs
- …. Have investigated frozen plasma with no consistent evidence of significant benefit for prophylactic and therapeutic use across a range of indications evaluated
- Methodological quality?

Adverse reactions

- Non-haemolytic transfusion reactions (mainly chills, fever and urticaria)
- Transfusion-related acute lung injury (TRALI)
- Viral transmission (HIV, hepatitis) despite donor selection and testing)
- Sepsis due to inadvertent bacterial contamination
- Transmission of other pathogens that are not tested for or recognised
- Citrate toxicity in neonates and patients with impaired liver function
- Transfusion-associated circulatory overload
- Anaphylaxis and allergic reactions

PRT to increase safety

- Aim
  - Haemostasis
  - Effective pathogen reduction
  - Safety (toxicology)

- Issues to consider
  - Highest possible level of coagulation factors vs safety
  - Cost
  - Logistics

FFP and Quarantine FFP

- FFP – single donor, untreated
- Q-FFP – single donor, untreated, donor re-tested after a minimum time period (window phase)
- Safety only increased for those viruses we test for

- Q-FFP - Logistic problem, cost?
  - Cost depend on number of repeat donors etc

Solvent Detergent FFP (SD-FFP) (Octaplas)

- Pooled (1000+)
- SD treated and filtered.
- Refrozen in 200 ml units.
- ABO-type (or Uniplas)

- Not effective against non-lipid enveloped viruses (HAV, Parvovirus B19)
- Octaplas is the only plasma used for transfusion in Norway since 1993

Solvent Detergent FFP (SD-FFP) (Octaplas)

- vWF multimers reduced
- Protein S (Total) reduced 24 %
- Protein S activity reduced approx. 40 %
- FVIII reduced approx. 20 %

Moake 1994, Harrison 1996, Beeck 1998, Hellstern 1992, Horrowitz 1992, Piquet 1992,

Amotosalen FFP (Intercept)

- Amotosalen (a psoralen) added. Then illuminated with long wave length UVA
- Inactivates viruses (enveloped and non-enveloped), bacteria, protozoa
- 200-300 ml
- ABO-type
- Fibrinogen reduced approx 20 %
- FVIII reduced approx 25 %
- Method well known from platelet PRT

Singh 2006, Hillyer 2001, Cid 2008, Osselaer 2008, de Valensart 2009, Irsch 2010

Riboflavin treated FFP (Mirasol)

- Riboflavin (vitamin B2) plus a specific spectrum of ultraviolet (UV) light
- inactivate viruses (enveloped and non-enveloped), bacteria, parasites
- ABO-type
- 200 – 300 ml
- Fibrinogen reduced approx 25 %
- FVIII reduced approx. 25 %
- High MW vWF multimers reduced

Hornsey 2009, Larrea 2009, Smith 2010

Methylene Blue plasma (Theraflex-MB plasma)

- Add methylene blue - Illuminate plasma - Remove methylene blue
- Inactivate viruses (HIV, HBV, parvovirus B19, WNV)
- ABO-type
- 200-300 ml
- Fibrinogen reduced approx 25 %
- FVIII reduced approx 25 %
- FV reduced approx 15 %

Lambrecht 1991, Aznar 1999 and 2000, Garwood 2003, Politis 2007, Cid 2008, Cardigan 2009, Osselaer 2008, Zeiler 1994, Hornsey 2001

Cold stored liquid plasma

- Single donor
- ABO-type
- Non-frozen or tawed
- Stored at 2-6 C for 14 days
- Not pathogen reduced

Blomback 1984, Nilsson1983, Stegmayr 1985, Suontaka 1996

Freeze-Dried plasma

- German Red Cross
  - LyoPlas N-w
  - ABO type
  - Store at +2 to +25 C for 15 months
  - Rehydrate with 200 ml water in minutes
- French Military Blood Bank
  - Minipools (10 units of mixed ABO type)
  - Pathogen inactivation (amotosalen)
  - Rehydrate with 200 ml water in < 3 minutes

Other issues to consider

Cost

- FFP
- Q-FFP
- SD-plasma (Octaplas)
- Amotosalen FFP (Intercept)
- Riboflavin
- Methylene Blue
- Cold stored liquid plasma
- Freeze Dried plasma

Storage

- FFP
- Q-FFP
- SD-plasma (Octaplas)
- Amotosalen FFP (Intercept)
- Riboflavin
- Methylene Blue
- Cold stored liquid plasma
- Freeze Dried plasma

Post-transfusion mortality among recipients of ABO-compatible but non-identical plasma.

RESULTS:

- After adjustment for potential confounding factors, there was an increased mortality associated with exposure to ABO-compatible non-identical plasma, with the excess risk mostly confined to those receiving 5 or more units (relative risk, 1.15; 95% confidence interval, 1.02-1.29). Stratification by blood group indicated higher risks in group O recipients, especially when the compatible plasma was from a group AB donor.

- Shanwell A, Andersson TM, Rostgaard K, **Edgren** G, Hjalgrim H, Norda R, Melbye M, Nyrén O, Reilly M. Vox Sang. 2009

Ethics

- Universal or selective introduction
  - Who should benefit (all patients, patients with long life expectancy)
  - Who should not be exposed to added risk (children, liver transplant patients)

Conclusion

- Indications for plasma transfusions are weak, increasing the importance of adverse reactions
- Several alternative products are available, some have undergone pathogen reduction
- Ideal product may vary with indication
- Cost and storage may be important
- Quality control requirements are inadequate
- All products are OK

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