DEVELOPMENT OF VIRUS-INACTIVATED PLASMA FOR INFUSION

ABSTRACT:

Öystein Fauchald

Introduction:

For plasma derived products several effective methods are in use to effectively inactivate virus. For plasma few methods have been approved. Testing alone is insufficient due to sensitivity (diagnostic window) and specificity (genetic variance of HIV and HCV).

Virus inactivated plasma with the S/D method has been introduced to the European market as a safe and standardized product. The S/D method has proven to be a robust method of inactivating enveloped virus and the use of neutralizing antibodies contributes to non-enveloped virus safety. Further, the next generation universal plasma have been developed to eliminate the risk of giving the wrong, non-ABO compatible plasma.

Rationale for developing Octaplas® and Uniplas® is to prevent viral transmission of HIV and prevent post-transfusion hepatitis caused by HBV and HCV. Further requirements were to produce a cell free, standardized coagulation active plasma for infusion in order to reduce adverse reactions and improve the therapeutic accuracy and efficacy through better planning and monitoring of treatment. Another important aspect was to prevent sepsis resulting from transient bacteremia of donors or accidental bacterial contamination during phlebotomy.

This is fulfilled through virus inactivation using solvent/detergent method. In addition, a complete removal of cells and debris is obtained by filtration steps ($1 \rightarrow 0{,}2\mu m$). In order to balance out donor- to donor variations, optimized integration of plasma is performed in all batches. (For coagulation factors ≥ 100 donations and for immune neutralizing antibodies ≥ 1000 donations are required).

Viral safety

Total removal efficacy for enveloped virus is ≥ 5 $\log^{10}$. Treatment with S/D is so potent that all viruses are inactivated within 2-3 minutes. As the infectivity of HIV-1 is beyond the limit of detection within 15 minutes of S/D treatment, there is a very high safety margin since the total time of this virus inactivation step continues for 240 minutes for every batch.

Total efficacy of immune neutralization is ≥ 8 $\log^{10}$. This is achieved through two precautionary methods. The Uniplas®, Octaplas® specification have a well defined minimum content of antibodies against HAV and B19 that secures a maximum immune neutralization capacity. Batch release in only done where the maximum titre of Parvovirus B19 DNA is ≤ 5 log, and where HAV have been found negative.

More than 7 M units have been transfused to treat more than 2 M patients with no demonstrated viral transmission including HAV and Parvovirus B19.

Other safety aspects

A further development was done through Uniplas®. The product is universally applicable and produced the same way as Octaplas® except for the optimal mixing of plasma of different blood groups prior to SD treatment. The optimal mixing is done in order to neutralize the potentially damaging anti-A and anti-B antibodies, both IgM and IgG type, by binding to free A and B substances and residual red blood cells in plasma. Being universally applicable Uniplas® can be used without taking into account the blood group of the patient.