

CLINICAL OUTCOMES FROM THE EVOLUTION IN QUALITY OF PLASMA-DERIVED PRODUCTS

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Over the quarter of a century, tremendous strides that have been made in improving the quality of donated plasma. A combination of factors has been responsible for this effect, which has had obvious benefit to patients receiving labile products. These factors include the increasingly stringent selection of donors, a better understanding of transmissible infections, improved sensitivity of serological tests and the introduction of certain nucleic acid amplification tests (NAT).

These changes have also provided benefits for recipients of plasma-derived therapeutic products, such as factor VIII, factor IX, immunoglobulins and albumin. However, these patients have extra benefits from the robust, specific antiviral steps included in the purification and concentration of these normal plasma proteins. To date, specific antiviral steps are not available for labile blood products, although clinical fresh frozen plasma (FFP) can be subjected to methylene blue virus inactivation or, for pooled FFP, solvent/detergent treatment.

In addition, the technologies used in the purification processes have improved over the years, even though the principles of the methodologies may have remained unaltered. These improvements have been accompanied by more specific and sensitive assays used in-process and for final product.

The clinical outcomes for the patients have improved in two main ways as a result of these advances in donor/donation screening and production/ assay technologies.

First, the risk of virus transmission is now virtually zero. The last recorded transmissions of virus infections were about 20 years ago (an intravenous immunoglobulin and a coagulation product).

The other significant outcome related to the improved purity of products is better local and systemic tolerance, thus the number and severity of side-effects has reduced over the years. This is well-illustrated by the improved purity of intravenous immunoglobulins (IVIG). When these were first introduced, they replaced intramuscular products but, although better blood levels were achieved, this was at the expense of systemic tolerance, particularly chills, rigors and even anaphylaxis. In addition, patients who were IgA deficient could develop antibodies to IgA, because IgG products were impure and contained significant IgA. Patients with antibodies to IgA would also react to the IgA in such products. By contrast, modern IVIG products are rarely associated with rigors or anaphylaxis and some contain virtually immeasurable amounts of IgA. The overall acceptance of IVIG is confirmed by the increasing use of self-administration by patients in their own homes, in many countries.

Likewise, the purity of plasma-derived coagulation factors has improved greatly. The removal of contaminating proteins in the purification process has been associated with a reduced risk of immune function modification. Overall improvements in purity have allowed regular self-administration at home, which is now widespread in some countries, notably with regular prophylaxis for haemophiliacs.

In conclusion, the increasing pressure for continuous improvement imposed by regulation, advances in technologies, competitiveness and public pressure has brought enormous practical therapeutic benefits to patients and improved their quality of life as well as their life expectancy.