Upsala J Med Sci 93: 189–192, 1988

Swedish Transfusion Medicine in a Ten-year Perspective—A Brief Review

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ABSTRACT

Although the scientific activity within blood preservation, plasma fractionation and treatment of coagulation disorders had been quite active in Sweden before 1978, the national coordination and self support with plasma products was insufficient. A programme for research and development was initiated in 1978 and resulted in important improvements. The production and use of blood components instead of the previous whole blood transfusion rose from 15% to 93% within 10 years and the supply of high quality plasma for industrial fractionation rose from 5,500 kg in 1978 to 86,700 kg in 1986. Transfusion transmitted HIV infection came as a new threat, first in haemophiliacs treated with imported coagulation factor concentrates, later also in patients treated with products from Swedish donors. After 1985 significant improvements were obtained by the introduction of anti-HIV testing of all blood donations and methods for virus reduction of fractionated plasma products. The use of more aggressive cytostatic therapy in haematological malignancies has drastically increased the need of platelet concentrates for transfusion and has focused attention on platelet compatibility problems. The 10-year period 1978-87 has thus implied great changes in Swedish transfusion medicine with increased quality of haemotherapy and improved regional coordination.

INTRODUCTION

Before 1978 there existed no firm link in Sweden between the blood transfusion service and the production of industrially fractionated plasma products. Whole blood was the most common product for treatment of patients with blood loss. In 1978 85% of all blood units were transfused as whole blood and only 15% of the country's whole production was separated into blood components. In some of the larger blood banks 50% or more was made into components.

The demand of coagulation factor preparations, Factor VIII in particular, had been rapidly increasing during the 1970s due to the introduction of improved treatment and prophylaxis of the congenital coagulation disorders, notably haemophilia A. The country was strongly dependent on import of coagulation factor concentrates in spite of the pioneer research work which had been carried out both in plasma fractionation by the

Blombäcks, in haemophilia care by I.M. Nilsson and associates, and in blood component preparation and preservation by de Verdier, Högman and associates.

A problem was that no national transfusion service existed. Blood donation was carried out by 90 independent and uncoordinated hospital blood banks. Most of these collected less than 5000 units per year.

Representatives both from the industry and the blood transfusion services had proposed that the WHO recommendation of 1975 about national self sufficiency with blood and blood products should be taken seriously.

In 1978 the Swedish Government decided to allow 20 million SEK for research and development during a 5-year period, to be coordinated and administered by the National Swedish Board for Technical Development (STU). The project gave an important stimulus to the whole field of transfusion medicine with a large number of actitivities both scientifically and administratively. Of great importance was the interest shown by some clinicians, especially Professor Lars Thorén in whose honour this Symposium is given. In some respects the timing was perfect; an understanding had matured that something had to be done. Unfortunately the project came five years too late to avoid the transmission of HIV infection to 96 haemophiliacs, i.e. one third of all who were strongly therapy dependent. The disaster was caused by Factor VIII concentrates imported from USA and happended before AIDS had been recognized as a new virus disease.

BLOOD COMPONENT THERAPY

Separation of the donor blood into components makes it possible to optimize the storage properties. Because of the different in vivo distribution and metabolic turn-over of the blood cells and plasma proteins it is important to understand that optimal treatment is usually not to supply the components in the proportions they exist in the normal donor. Instead, those components which are needed should be transfused in sufficient quantity. Those components which are unnecessary or potentially dangerous should be avoided. A number of studies performed in our country have strongly supported these ideas (1,2,3).

The optimal additive system approach for red cell storage was developed for large scale application in our department. In 1978 we introduced the saline-adenine-glucose (SAG) solution (4) and later the same composition with addition of mannitol, SAGM or Sagman solution (5). This way of red cell storage and transfusion has now been universally accepted in our country. In 1986 93% of all blood units were produced with the Sagman system. The buffy-coat-poor red cell suspensions give more reaction free transfusions and allow 55 000 kg plasma to be saved and submitted for industrial fractionation.

Using effective leukocyte filters it is easy to remove virtually all of the remaining leukocytes from the erythrocyte preparations (7). It seems likely that not only the febrile reactions caused by contaminating leukocytes but also the immunogenic effects can be avoided in a large number of patients (7,9).

PRODUCTS FROM SINGLE DONORS VS. LARGE POOLS

Before 1985 it was generally considered that blood components from single donors were safer than products made from large pools. The latter products regularly caused liver affection indicating hepatitis B virus (HBV) or non-A, non-B-virus (NANBV) transmission in spite of the efforts to make a careful donor selection. The pooled Factor VIII concentrates also transmitted human immunodeficiency virus (HIV) infection.

After 1985 a combination of donor selection, using regular anti-HIV testing, and virus reducing treatments with heat has changed this situation drastically. Now several methods are available by which the pooled products can be made completely safe with respect to transmission of HBV, NANB and HIV.

Before July 1985 blood components used in transfusion therapy did transmit HIV infection to 72 transfusion recipients in Sweden. After the introduction of anti-HIV testing in the spring of 1985 no case of transfusion transmitted HIV infection has been observed during the period July 1985 to June 1987. Based on experience in the USA the risk of getting a transfusion transmitted HIV infection is likely to be below 1 per 1 million transfused blood units.

The risk of transfusion transmitted NANB hepatitis has also decreased and clinical cases have been found at an incidence of 0.02%. However, prospective studies indicate that subclinical cases of NANBV infection - observed as an elevation of ALAT 2.5 times normal value at two occasions - occur in the order of 4% in multitransfused patients (6).

NATIONAL SELF SUFFICIENCY WITH PLASMA

In 1978 960 kg albumin (115 g per 1000 inhabitants) was used therapeutically mainly as 20% solution (10). The supply of plasma for industrial fractionation within the country was 22,300 kg, which will correspond to about 780 kg purified albumin. In 1986 the use of albumin preparations was 1,080 kg (130 g per 1000 inhabitants), a 12% increase, only. The plasma supply was 92,100 kg (8) which would be sufficient for about 3,200 kg purified albumin. Thus, the self sufficiency with raw materials for purified albumin preparations is no longer a problem.

The situation concerning Factor VIII is quite different. In 1978 the need of Factor VIII was 7.4 million I.U., in 1986 the use had increased to 25 million I.U. (8). The supply of high quality plasma (fresh frozen) had increased from 5,500 kg in 1978 to 86,700 kg in 1986. This would have been sufficient if freeze dried cryoprecipitate or medium purity Factor VIII concentrates had been used; with 30% final yield the supply would have been sufficient for 26 million I.U. However, the treatment of haemophilia A in Sweden is completely based on the use of high purity factor VIII concentrates which have a very low final yield, particularly after introduction of heat treatment for virus reduction. The need of plasma with this policy has been estimated at 150,000 kg per year. Thus, in order to obtain self sufficiency with Factor VIII preparations, either the yield in the production has to be improved, or almost double as much plasma has to be collected. With improved

techniques for fractionation and virus reduction (HIV, HBV, NANBV) and/or new ways of producing Factor VIII (DNA hybridization technology) it seems likely that the present production of plasma will be sufficient for national self supply.

CHANGING USAGE PATTERN

The use of blood components changed drastically when the cytostatic treatment of haematological malignant diseases was driven so hard that bone marrow aplasia occurred. This has resulted in a strong increase in the use of platelet concentrates. The immunological refractoriness to platelets from random donors which appears in a large number of patients has focused attention on the platelet compatibility problems. New methods have become available to make the platelet preparations less immunogenic by removing the leukocytes effectively (9).

All these changes which have occurred within a few year period, have stressed the importance of sufficient quality control of the products and of education and information to medical staff.

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