USE AND ABUSE OF FRESH FROZEN PLASMA

The availability of blood components to clinicians in many disciplines has provided an increasing variety of choices for the treatment of their patients. However, the corollary is an increased potential for misuse, as there is variation in the knowledge of appropriate transfusion practices within the specialties.

Several factors are acting in concert at present to encourage a thorough review of current transfusion practices. Of these, issues of blood safety, such as the risk of transmission of infection and potential immunomodulation should be foremost in the clinician’s mind. However, with the pressure for cost containment within the Health Service, anxieties about the expense of blood component therapy are being expressed. In addition, as specialized forms of treatment are being used more widely, there is an increasing demand for specific blood components, and it is necessary to ensure the best use of the available resources. Publication by the Blood Transfusion Task Force of the British Committee for Standards in Haematology (BCSH) of Guidelines for the Use of Fresh Frozen Plasma [1] is therefore timely.

The use of fresh frozen plasma (FFP) has increased dramatically over the past decade. In the U.K., for instance, figures for one Regional Transfusion Centre show a two-and-a-half-fold increase in the past 10 years and a greater than 10-fold increase in the past 15 years. FFP is the liquid portion of a unit of donated blood which is separated and frozen within 8 h of collection. It contains all the components of the coagulation, fibrinolytic and complement systems, the proteins that maintain oncotic pressure and modulate immunity, in addition to fats, carbohydrates and minerals present in concentrations similar to those in the circulation. Historically, the widespread clinical use of plasma for the treatment of shock and restoration of plasma volume was established during World War II. Methods of storing plasma in liquid, frozen or freeze-dried forms were developed so that plasma would be available rapidly in emergency situations. After the War, the familiarity of clinicians with such use of plasma was carried over into civilian practice. Transfusion with plasma, instead of whole blood, subsequently became accepted practice for treatment of other clinical conditions such as various haemorrhagic disorders, infection and immune dysfunction.

FFP is an effective volume expander and also contains the coagulation proteins which may help to correct certain disorders of haemostasis. However, new techniques have led to the development of safer alternative treatments, for example other colloid solutions for plasma expansion, including Human Albumin Solution 4.5% and the gelatins, in addition to the specific factor concentrates which have reduced the need for FFP in many clinical situations.

Studies in the U.K. and elsewhere have shown that a significant proportion of FFP is transfused for inappropriate reasons [2-5]. Misuse has been attributed to excessive reliance on the haemostatic efficacy of FFP, underestimation of the incidence and magnitude of FFP complications and lack of knowledge amongst some clinicians of the situations in which its use is no longer indicated. In order to change and improve their attitudes and practice, education of clinicians about the appropriate use of FFP and other blood components is necessary. Information on the benefits, risks and practical use of blood component therapy is now widely available in publications such as the ABC of Transfusion of the British Medical Journal [6] and the National Blood Transfusion Service’s Handbook of Transfusion Medicine [7]. The BCSH Guidelines merit widespread distribution and their implementation should be encouraged.

This document emphasizes the fact that there are few definite indications for the use of FFP. These are limited largely to the treatment of those deficiencies of coagulation factors and inhibitors of coagulation for which specific factor concentrates are not available. Other indications include acute disseminated intravascular coagulation, emergency antagonism of warfarin [8] and vitamin K deficiency when combined factor concentrates are unavailable or unsuitable, and treatment of thrombotic thrombocytopenic purpura (TTP).

FFP is no longer indicated in several clinical situations. Many studies have been performed of the bleeding episodes which are associated with cardiopulmonary bypass procedures and in most instances the bleeding has been related to platelet dysfunction rather than deficiency of plasma coagulation factors or thrombocytopenia [9,10]. It is now accepted, and was stated as long ago as 1964 by Trimble and colleagues [11], that the routine use of FFP during or after cardiopulmonary bypass provides no known benefit. In massive blood loss, either during elective or emergency surgery or after trauma, the use of FFP has been advocated widely, but there is little evidence in support of such practice. Bleeding is associated with the duration of volume deficit, rather than the volume of blood transfused [12]. Early and repeated haemostasis studies are necessary in massively transfused patients. Following primary surgical haemostasis, continued bleeding with significantly disturbed coagulation tests or platelet counts merit energetic therapy with FFP, platelets and, if appropriate, cryoprecipitate. The use of certain drugs in cardiac surgery offers the prospect of significant reductions in perioperative blood loss. The postulated mode of action of two agents,
aprotonin and tranexamic acid, suggests that the role of fibrinolysis in non-surgical perioperative bleeding merits further study [13].

The use of FFP (or platelets) according to predetermined replacement regimens cannot be justified [14], nor can its use as a volume replacement fluid, nutritional source or replacement of immunoglobulins. More effective and safer alternatives are available. It is necessary to identify and eliminate such examples of the inappropriate use of FFP. The most important concern in this misuse is the exposure of patients to unnecessary risk. In addition, other concerns, such as the possibility of litigation following potential complications of transfusion are becoming more apparent.

Definitive rules governing the transfusion of FFP in all specific situations cannot, of course, be given precisely. For example, in patients who have haemorrhagic complications related to underlying liver disease or bleeding associated with massive transfusion, the need for FFP must be judged both by clinical assessment and results of laboratory investigations for each individual. The treatment of isolated laboratory abnormalities of coagulation or empiric treatment of bleeding without an attempt to identify the nature of the underlying haemostatic defect can no longer be justified.

There are also clinical situations, for example neonatal sepsis, in which the efficacy of treatment with FFP is unproven and needs to be determined. Studies in the future should examine these issues.

Publication of the guidelines aims to provide an up to date and comprehensive review of the present accepted use of FFP. Education programmes designed to promote the appropriate use of blood components, together with audit of transfusion practices have been shown to have a measurable effect on clinicians' attitudes [15,16]. Following such initiatives, a reduction in both the number of components transfused and the number of patients being transfused for inappropriate reasons has been reported [15].

The Guidelines provide a very useful basis for the education of all those involved in the use of blood and component therapy. Widespread adoption of the principles will be another step towards ensuring safe and efficient practice in clinical blood transfusion.

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