hemophilia A may not need factor infusions for minor surgery. Their disease often is managed with ε-aminocaproic acid, an antifibrinolytic agent, using 4 g every 4 to 6 hours with or without infusions (0.3 μg/kg) of DDAVP.

Most patients with hemophilia require factor infusions prophylactically or at times of surgery or trauma. Factor VIII products are infused every 8 to 12 hours, and 1 U/kg of factor VIII concentrate raises plasma factor VIII activity by 2%; 50 U/kg of factor VIII theoretically yields 100% factor VIII activity in a patient with severe hemophilia A. Factor IX has a longer half-life and is infused every 18 to 24 hours; factor IX requires 2 U/kg for a 2% increase in factor IX activity (i.e., 100 U/kg for 100% activity). Major surgery in patients with hemophilia requires intensive factor therapy to achieve normal factor levels (>80%) in the intraoperative period and the early postoperative period to prevent wound hematoma formation. The dose of factors (see E-Table 51-3) is adjusted downward from this intensity, depending on the severity of the insult, the patient's response to previous factor infusions, and whether factor inhibitors have developed.

Patients with severe hemophilia A or B can develop alloantibodies (inhibitors) directed against factor VIII or IX. Standard doses of factor do not reverse the coagulopathy because administered factors are rapidly cleared and bleeding persists. Several therapies have been developed to bypass the intrinsic pathway of coagulation, thereby eliminating the need for active factor VIII or IX in the coagulation cascade. FEIBA has been employed for this purpose at doses of 50 to 100 U/kg.

Another widely used bypass agent is activated factor VII (fVIIa), a recombinant factor protein. For a patient with hemophilia A or B and a strong factor inhibitor who has bleeding, fVIIa is usually administered at 90 μg/kg every 2 hours until the bleeding is controlled. This agent has been quite successful at controlling bleeding in hemophilia inhibitor populations, in patients with congenital factor VII deficiency, and those with acquired coagulation factor inhibitors. Based on its success in treating bleeding associated with hemophilia, trials of fVIIa have been performed for non–hemophilia-associated bleeding. Because of their limited success, the FDA has approved the use of fVIIa only in the setting of factor VII deficiency (15 to 30 μg/kg) or for treatment of bleeding associated with a factor inhibitor or Glanzmann's thrombasthenia.

Several virally inactivated, intermediate-purity factor VIII concentrate products (not recombinant or monoclonal antibody purified) are available. These factors usually contain large amounts of vWF (e.g., Humate-P) and are particularly useful for bleeding or prophylaxis in moderate to severe vWD, as effective replacement immediately before major invasive procedures, or in vWD patients who have failed or do not qualify for DDAVP therapy.

Cryoprecipitate Transfusion Therapy

Cryoprecipitated antihemophiliac factor (i.e., cryoprecipitate or cryo) is an often overlooked but important blood product for the treatment of a variety of bleeding disorders. Cryoprecipitate is prepared by thawing frozen plasma at very cold temperatures and removing the precipitated portion. It contains a narrow array of coagulation factors, but fibrinogen, fibronectin, factor VIII, vWF, and factor XIII occur in high concentrations. A major advantage of cryoprecipitate is that the average single unit is only 10 to 20 mL (E-Fig 51-3).

Based on its contents and small volume, cryoprecipitate is useful for the replacement of fibrinogen in DIC or in patients with hypofibrinogenemia or dysfibrinogenemia. The product may be helpful for isolated factor XIII deficiency or factor XIII consumption in DIC. Mounting evidence suggests that the vWF and factor VIII in cryoprecipitate can be used to overcome bleeding in uremia by enhancing the adhesive properties of circulating platelets.

Cryoprecipitate is most frequently administered for hypofibrinogenemia, and appropriate dosing should take into account a patient's total plasma volume, baseline fibrinogen levels, and goal fibrinogen levels. For most bleeding associated with hypofibrinogenemia, a concentration of more than 100 mg/dL of fibrinogen is reasonable. For a 70-kg adult with a fibrinogen level less than 100 mg/dL, a 10-unit pool (total volume of about 150 to 200 mL) should be sufficient to provide adequate fibrinogen and enhance other hemostatic properties. For more advanced dosage protocols, such as for children, large patients, or those with extreme hypofibrinogenemia, consultation with the transfusion service is strongly recommended for specific calculations.

PROSPECTUS FOR THE FUTURE

Novel modalities continue to be developed for the diagnosis of patients with bleeding disorders. For instance, assays measuring thrombin generation offer a quantitative view of coagulation that may provide greater insight into the source of abnormal bleeding than current tests. Alternatives and improvements in transfusion are also being developed, including cells harvested from induced progenitor cells that can be customized for specific needs and fibrin-coated albumin particles that can evade immune-mediated platelet destruction while yielding important therapeutic impact. Progress continues to be made in the development and application of human-derived and recombinant coagulation factors for the treatment of hemophilia, with a focus on preparation of factors that are less immunogenic and therefore less prone to induce the development of significant inhibitors.

SUGGESTED READINGS

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