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A case of severe Factor VIII deficiency

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Introduction[3,5]

Hemophilia refers to an inherited bleeding disorder caused by deficiency of coagulation factor VIII (hemophilia A), factor IX (hemophilia B), or factor XI (hemophilia C). Hemophilia A and B are X-linked recessive diseases that present in male children of carrier females.[3,4]

Hemophilia A – Inherited deficiency of factor VIII; an X-linked recessive disorder[4].

Case description

Patient is a 5-year-old male with severe factor VIII deficiency initially diagnosed, at age 3, as severe oral bleeding following a lip laceration. His factor VIII was less than 1%. Consequently, patient had been on "on demand" replacement but, due to an increase in bleeds, is being switched to prophylaxis. The main joints affected are the elbows, knees and ankles. Because of the increasing need for home factor infusion, a Port-A-Cath is being placed. His disease is considered severe. The known duration is approximately two years and is associated with spontaneous hemarthroses and bleeding. It is ameliorated with factor replacement. Patient is to receive Recombinant factor VIII 500 units IV twice a week (approximately 18 U/kg).

Before the procedure, patient received approximately 50 U/kg of recombinant factor VIII immediately before the port placement. He was intubated with an LMA and had no excessive bleeding during the procedure.

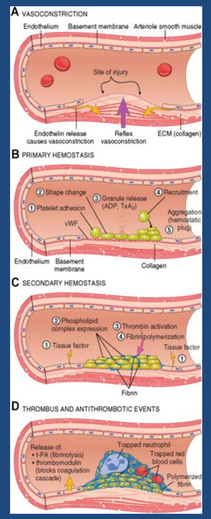

Fig. 1. Source: Bhat R, Cabey W. Evaluation and Management of Congenital Bleeding Disorders.[6] Downloaded from Clinical Key. Accessed Sept 22, 2018.

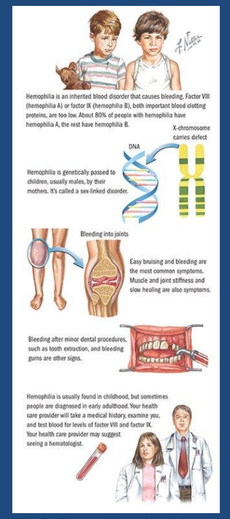

Fig. 2. Source: Managing Your Hemophilia.. Copy right © 2016 by Saunders, an imprint of Elsevier, Inc. Downloaded from ClinicalKey. Accessed Sept. 22, 2018.

Factor Replacement

→Purified factor products are the 1st choice and should be used whenever possible to avoid potential transfusion-transmitted infection and transfusion reactions.[2,4]

→However, other blood products like Cryoprecipitate can also be used. One bag of Cryoprecipitate is made from approximately 250 mL of fresh frozen plasma (FFP) and contains approximately 70 to 80 units of factor VIII in a volume of 30 to 40 mL (approximately 3 to 5 units/mL).[2]

→FFP is deemed an inadequate choice for factor replacement because 1mL of FFP contains 1unit of factor activity. A dose of 15 to 20 mL/kg will raise the factor VIII level by approximately 30 to 40 percent. This amounts to lots of bags of FFP to get the desired factor amount, which consequently exposes patient to possible fluid overload, transfusion infections and reactions.[1,2]

Therapies other than factor replacement [1,2,4]

Therapies	Use	DOSAGES
Tranexamic Acid (TXA)	Inhibit fibrinolysis by inhibiting plasminogen activation in the fibrin clot, thereby enhancing clot stability.	25 mg/kg every 6-8 hours
Epsilon Aminocaproic Acid (EACA)	Same as above	75-100 mg/kg every 6 hours, max 3-4g
Desmopressin (DDAVP)	Increases factor VIII level two-four fold. Not effective for patients with severe hemophilia A (Factor VIII activity <1%).	0.3 mcg/kg (max, 20 mcg/kg), IV or nasal

Discussion

Hemophilia A (factor VIII deficiency) is an X-linked coagulation factor disorder associated with bleeding of variable severity, from life-threatening to clinically silent. [1]

Factor VIII deficiency/Hemophilia A affects 1 in 5000 to 10,000 males; roughly 60 percent have severe disease, with factor VIII activity less than 1 percent of normal.[1,2]

The factor VIII gene is located on the X chromosome. It is one of the largest known genes. It circulates in plasma with von Willebrand factor. Cleavage of factor VIII by thrombin or factor Xa is necessary to activate factor VIII and allow it to participate in the intrinsic pathway. Activated factor VIII is inactivated by activated protein C in conjunction with proteins.[3,4,5]

In patients with hemophilia with acute bleeding, the immediate goal is to raise the factor activity to a level sufficient to achieve hemostasis.[2]

For severe bleeding, the factor activity level should be maintained above 50 percent at all times.

An initial dose of 50 units/kg to raise the factor VIII level to 100 percent should be given. The second and subsequent doses are given at intervals of approximately one half-life of the infused product for that patient. A typical half-life for standard half-life factor VIII products is approximately 8 to 12 hours.[2,3]

For patients who require perioperative factor administration, the initial dose should be timed to provide maximal coverage at the time of greatest bleeding risk (or, typically, 30 to 60 minutes before the procedure). The dose is calculated from the patient's weight, baseline factor level, desired factor level, volume of distribution, and presence of an inhibitor.[2,5]

Conclusion

- Perioperative management of Factor VIII deficiency, is dependent on the severity of the factor deficiency as well as the type of procedure being performed.[1,3]
- Factor VIII replacement with recombinant Factor VIII, 30 minutes before surgery, is the preferred method of treatment; however, alternative forms of replacement, factor related and otherwise, can be implemented.[2,4]
- Depending on the surgery, factor replacement should be given before and after surgery, as surgeries with a lot of blood loss deplete Factor VIII faster.[2,3,5]

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