Rapid reversal of anticoagulant bleeding- rFVIIa an option?

Recombinant factor VIIa (rFVIIa) was originally developed and approved for the treatment of bleeding episodes in patients with congenital and acquired hemophilia with inhibiting antibodies towards factor FVIII or IX. As FVIII enhances thrombin generation on activated platelets, it may help to improve hemostasis in other situations with coagulation defects or in patients with a preexistent normal coagulation system but who experience excessive bleeding.[1]

In this issue Jørgen et al.[2] bring up a new database review of cases receiving rFVIIa rescue therapy for uncontrolled bleeding in conjunction with the use of anticoagulant therapy (where traditional therapy had been ineffective).

The use of rFVIIa has been published in case reports and six clinical trials doses of 15-90 mg/kg. In rat model, rFVIIa normalized the prothrombin time and controlled warfarin-induced bleeding. Also, in 28 healthy volunteers receiving the vitamin K antagonist acenocoumarol to maintain an international normalized ratio (INR) above 2.0, rFVIIa at 5 and 320 mg/kg corrected prothrombin time and INR. The administration of rFVIIa corrects the prothrombin time or INR but still does not always correlate with cessation of bleeding. However, in several case reports and 10 case series, rFVIIa effectively arrested the bleeding in patients who were treated with oral anticoagulants. A small series of patients with intracranial hemorrhage (ICH) due to excess anti-coagulation were successfully treated with 40 mg rFVIIa and with arrest of bleeding and uncomplicated surgical drainage of the hematoma. These observations indicate that rFVIIa may be useful to reverse the effect of warfarin or other vitamin K antagonists in cases where standard therapy has been found insufficient.[3] Reversal of LMWH and UFH-induced bleeding has been done successfully with rFVIIa in a few patients after failure with protamine.[4]

The application of rFVIIa as an antidote and rescue agent in anticoagulant patients with life-threatening bleeding, in whom standard hemostatic treatments have failed is interesting and its possibilities are reported by Jørgen, et al.[2] There are several limitations of the report like small number of patients and heterogenons; different anticoagulants, variable description of bleeding and treatment with various hemostatics. In these patients there have been other hemostatic failures. We could even be sure that rFVIIa alone improved hemostasis because they have got antidotes/blood products. But it is obvious that standard treatment schedules were unsuccessful in stopping the bleeding.

RFVIIa was given as a rescue and reversed the anticoagulant
action of LMWH, UFH, coumadin and warfarin. Taken together these data create a great interest in the use of rFVIIa as a potential agent to reverse anticoagulant effects. We still need more clinical trials to assess the full potential of rFVIIa.

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**References**