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Treatment of severe coagulopathy after gunshot injury to the head using recombinant activated factor VII

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Abstract

Purpose: Patients with severe penetrating head injury often have a coagulopathy that is difficult to correct. In this report, we describe 3 such patients who were treated with activated factor VII (FVIIa) to stop ongoing hemorrhage that was refractory to conventional treatment.

Subjects and Methods: We treated 3 patients with severe head injury secondary to gunshot wounds to the head. All 3 patients had ongoing bleeding secondary to a severe consumptive coagulopathy that was refractory to treatment with fresh frozen plasma, platelets, and cryoprecipitate. Recombinant FVIIa was then administered to achieve hemostasis.

Results: Administration of FVIIa (90-120 μg/kg) was successful in rapidly achieving hemostasis and correcting abnormal laboratory parameters indicative of coagulopathy in all patients. Although all 3 patients died, control of bleeding made organ donation possible in 2 patients.

Conclusion: In patients with a severe head injury and coagulopathy, use of FVIIa may help in correction of coagulopathy and decrease transfusion requirements. In patients where ongoing bleeding precludes the declaration of brain death, the use of this agent might help in achieving hemodynamic stability and preserve the possibility of organ donation. The ethical implications of using FVIIa in this situation are discussed.

1. Introduction

Patients with severe head injury often develop coagulopathy [1-4], which is associated with poor prognosis, even progression to brain death [5]. The transfusion of blood products such as platelets, fresh frozen plasma (FFP), and cryoprecipitate to correct coagulopathy is often ineffective and can cause transfusion-related acute lung injury [6,7]. Recombinant activated factor VII (FVIIa) (NovoSeven; Novo Nordisk A/S, Bagsvaerd, Denmark) is indicated for the treatment of bleeding episodes in patients with hemophilia A or B with inhibitors to factor VIII or factor IX. It has also been used to treat severe uncontrolled bleeding in patients with multisystem trauma, pediatric cerebral injury, and during neurosurgical procedures [8-11]. The coagulopathy associated with head trauma is similar to that seen in

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patients with multisystem trauma, and therefore, FVIIa might be useful in head-injured patients with an associated coagulopathy [12]. The purpose of this report is to describe the use of FVIIa to correct coagulopathy and stop ongoing bleeding in 3 patients with severe head injury secondary to gunshot wound (GSW) to the head where conventional treatment of consumptive coagulopathy using blood products was unsuccessful in achieving hemostasis.

2. Subjects and methods

This is a retrospective case report of 3 patients with GSW to the head and refractory bleeding. This study was approved by the human studies committee of Washington University in St Louis.

2.1. Case 1

A 33-year-old man was admitted after a self-inflicted GSW to the head. The Glasgow Coma Scale (GCS) score was 2T. Pupils were bilaterally dilated (8 mm) and nonreactive. Corneal, cough, and gag reflexes and spontaneous respiratory effort were absent. There was an actively bleeding 1.2-cm right temporal entrance wound and a 1.5-cm left temporal exit wound with a hematoma around it. A computed tomographic (CT) scan of the head revealed diffuse subarachnoid hemorrhage, multiple bullet and bone fragments in both cerebral hemispheres, and diffuse cerebral edema. Both the entrance and exit wounds were sutured and pressure dressings were applied to both sites but they were ineffective in stopping the bleeding.

Serial hematologic parameters are illustrated in Table 1. The patient was transfused 4 U of packed red blood cells (RBCs), 6 U of random donor platelets (RDPs), and 4 U of FFP but continued to bleed profusely. The international normalized ratio (INR) increased from 1.89 to 2.31 with a fall in the platelet count and decrease in the fibrinogen level to 48 mg/dL (normal, 150-400 mg/dL). The patient was not acidotic, and normothermia had been maintained. A decision was made to infuse 4.8 mg of FVIIa (90 μg/kg) and 1 U of cryoprecipitate. There was an immediate correction in the coagulopathy (within 15 minutes), and the hemorrhage stopped. The patient later met neurologic criteria for death. The family consented to organ donation, and the left kidney, pancreas, heart, and liver were successfully transplanted. After a follow-up period of 8 months, the recipients were all doing well except for the heart recipient who died secondary to noncompliance with medications.

2.2. Case 2

A 27-year-old man was transferred from an outside hospital after sustaining a GSW to the head followed by a motor vehicle accident. On admission, he was hypotensive (blood pressure, 97/48 mm Hg) and tachycardic (pulse rate, 155/min). His GCS score was 2T with absent brainstem reflexes. He had a left parietal entry wound with brisk bleeding, which persisted even after suturing of the wound and the application of a pressure dressing. There was also brisk bleeding from both nares despite packing. The head CT scan revealed multiple bullet fragments in the left frontal area, subarachnoid and intraventricular hemorrhage, diffuse cerebral edema, and multiple fractures of the cranium.

The initial hematologic parameters revealed evidence of severe coagulopathy, with the INR, prothrombin time (PT), partial thromboplastin time (PTT), and thrombin time above

Table 1 Serial hematologic parameters before and after administration of FVIIa

		Time after admission (h:min)	Hematocrit (%)	Platelets (10^3/mm^3)	PTT (s)	PT (s)	INR	Fibrinogen (mg/dL)
Case 1	Before FVIIa	0:00	34.8	171	42.6	20.6	1.89	
		3:00	22.8	97	51.1	24.0	2.31	48
	After FVIIa	5:30	30.0	107	36.0	14.7	1.22	
		9:00	29.1	94	31.4	13.1	1.05	227
		16:00	38.5	111			1.89	
Case 2	Before FVIIa	0:00	16.4	139	>150.0	>106.0	>15.94	
		2:00	20.1	115	>150.0	>106.0	>15.94	<20
		3:00	22.9	67	107.3	30.5	3.16	
	After FVIIa	8:30	25.9	27	36.5	12.6	1.00	199
		13:00	21.8	71	32.2	13.1	1.05	
		20:30	26.9	105	34.2	14.0	1.15	
		29:30	26.5	81	34.0	15.4	1.30	
Case 3	Before FVIIa	0:00	43.3	134	85.8	24.0	2.31	53
		4:30	30.5	131	85.8	29.5	3.02	
	After FVIIa	8:00	37.4	203	40.8	13.8	1.13	
		10:45	35.6	203	36.9	15.1	1.27	