

THE USE OF RECOMBINANT ACTIVATED FVII (rFVIIa, NOVOSEVEN®) IN THE TREATMENT OF A LIFETHREATENING RETROPERITONEAL HEMORRHAGE IN A HEMOPHILIA A PATIENT WITH INHIBITORS TO FVIII

M. J. DINIZ, M. DIAS, M. T. FALCÃO, M. CRUZ
SERVIÇO DE IMUNO-HEMOTERAPIA. HOSPITAL DE S. JOSÉ. LISBOA

INTRODUCTION

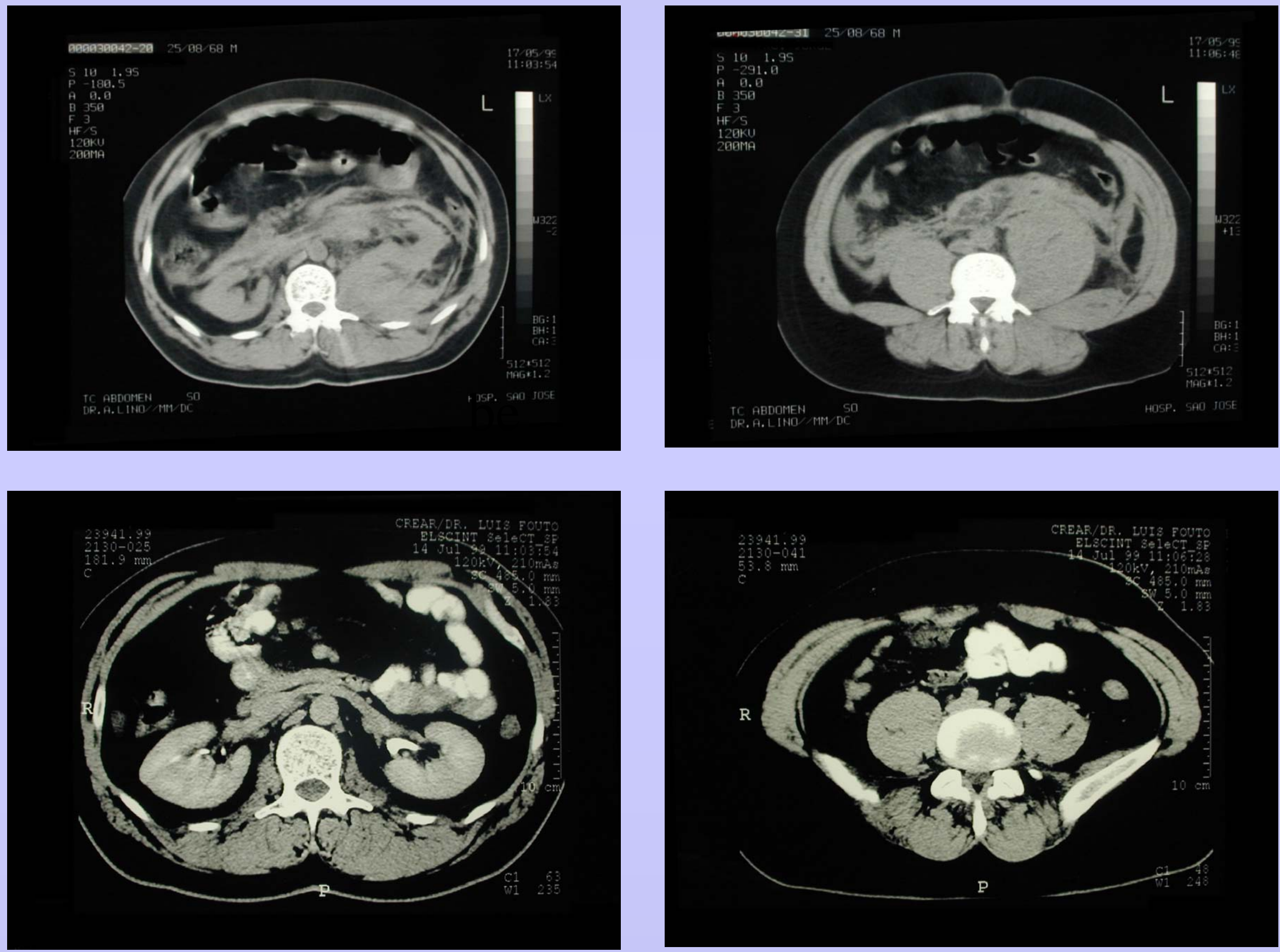
The development of inhibitors to factor VIII (FVIII) has become one of the most serious complications in the treatment of hemophilia patients, occurring in 15-30% of haemophilia A (HA) patients and 1-3% of haemophilia B (HB) patients. The management of acute bleeding episodes may use different approaches: human factor VIII or factor IX, porcine factor VIII, prothrombin complex concentrates (PCC), activated prothrombin complex concentrates (APCC) and more recently recombinant activated factor VII (rFVIIa; NOVOSEVEN). rVIIa is a potent by-passing agent which mechanism of action is most probably to provide a full thrombin burst, in the absence of FVIII/FIX, on the activated platelets and represents a major therapeutic advance in the treatment of haemophilia patients with high-titer inhibitor. Retroperitoneal haemorrhage is a significant cause of occult bleeding in the severely affected haemophiliac and is associated with a high morbidity and mortality in patients with factor VIII inhibitors. Survival of the patient often depends on rapid accurate diagnosis and replacement therapy. We report a case of a retroperitoneal haemorrhage in a patient with haemophilia A and inhibitors, successfully treated with rFVIIa.

CASE DESCRIPTION

A 30-year-old haemophilia A patient, with a long-lasting high titre inhibitor (actual inhibitor titre - 10.5 BU), was admitted to the hospital because of intense abdominal and loin pain, pallor, marked tachycardia and low blood pressure. A CT scan revealed a large retroperitoneal hematoma, extending along the iliopsoas, bilaterally. He was treated with recombinant activated FVII (rFVIIa), a loading dose of 96mcg/Kg, followed by a maintenance dose of 96mcg/Kg, in Bolus Intermittent Infusion (BII), every 2 hours, during the first 24 hours, with progressive prolongation of the intervals between doses (3-4-6 h). In the first two days he received 5 units of packed red blood cells (PRBC), because of an excessively low hemoglobin level at entry (Fig. 1). Therapy with rFVIIa was maintained during 9 days and epsilon-aminocaproic acid at day 10, when the patient was discharged.

MATERIAL AND METHODS

rFVIIa was given in BII, 96mcg/Kg every 2 hours, initially, with progressive prolongation of the intervals between doses (3-4-6 h), during 9 days. Epsilon-aminocaproic acid (Epsicapron), was given, 50mg/Kg, intravenously every 6 hours initially and, in oral doses until the patient was discharged. Laboratory monitoring included platelet count, estimations of activated partial thromboplastin time (APTT), prothrombin time (PT/INR) and factor VII:C levels. Both FVII:C and PT/INR were performed by a one-stage assay, using a rabbit brain thromboplastin.



Abdominal CT scan: extensive retroperitoneal hematoma which causes left kidney deviation and ilio-psoas thickening (upper) and 50 days later (down).

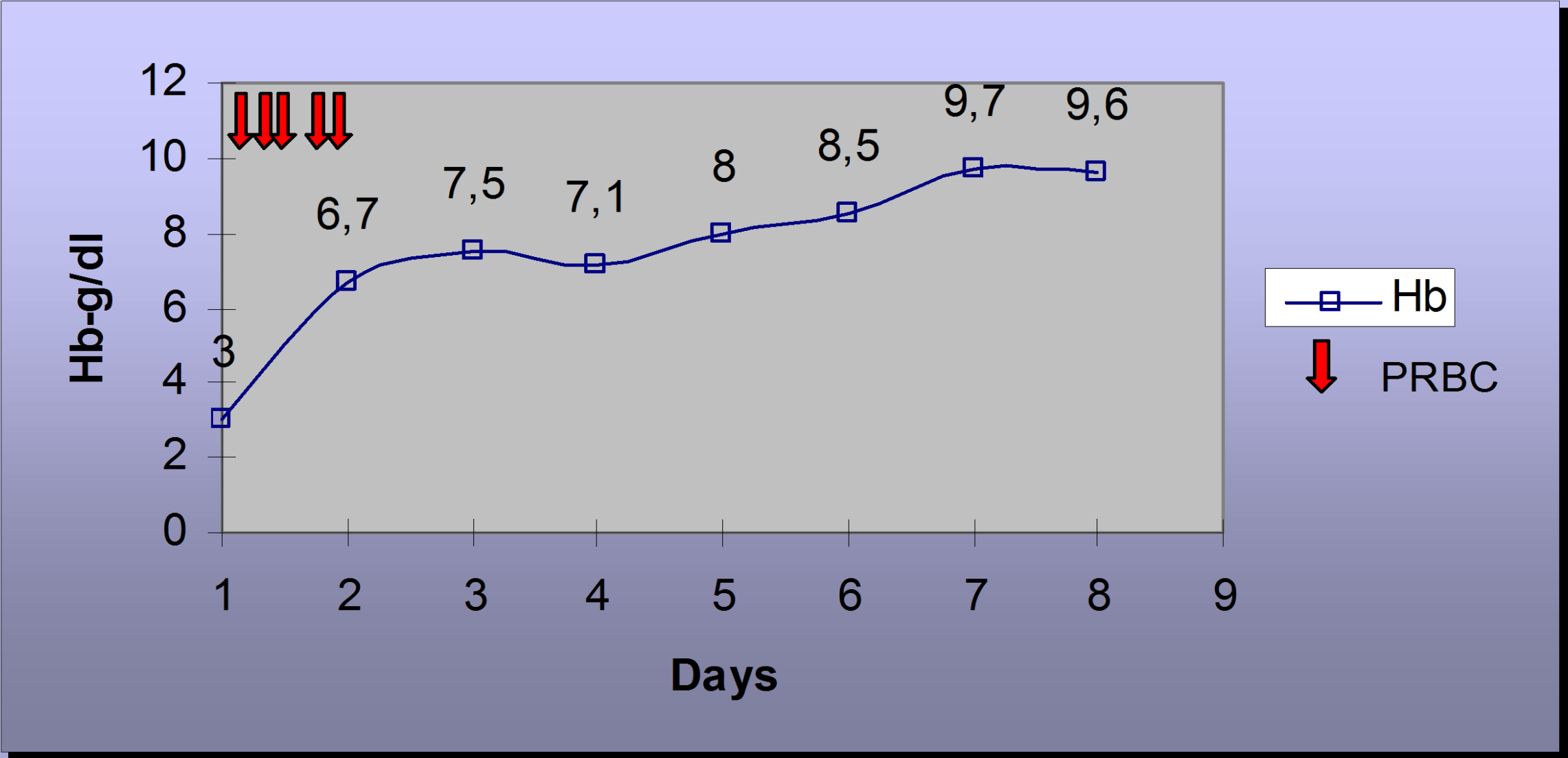


Fig.1-Hemoglobin levels and PRBC transfusions

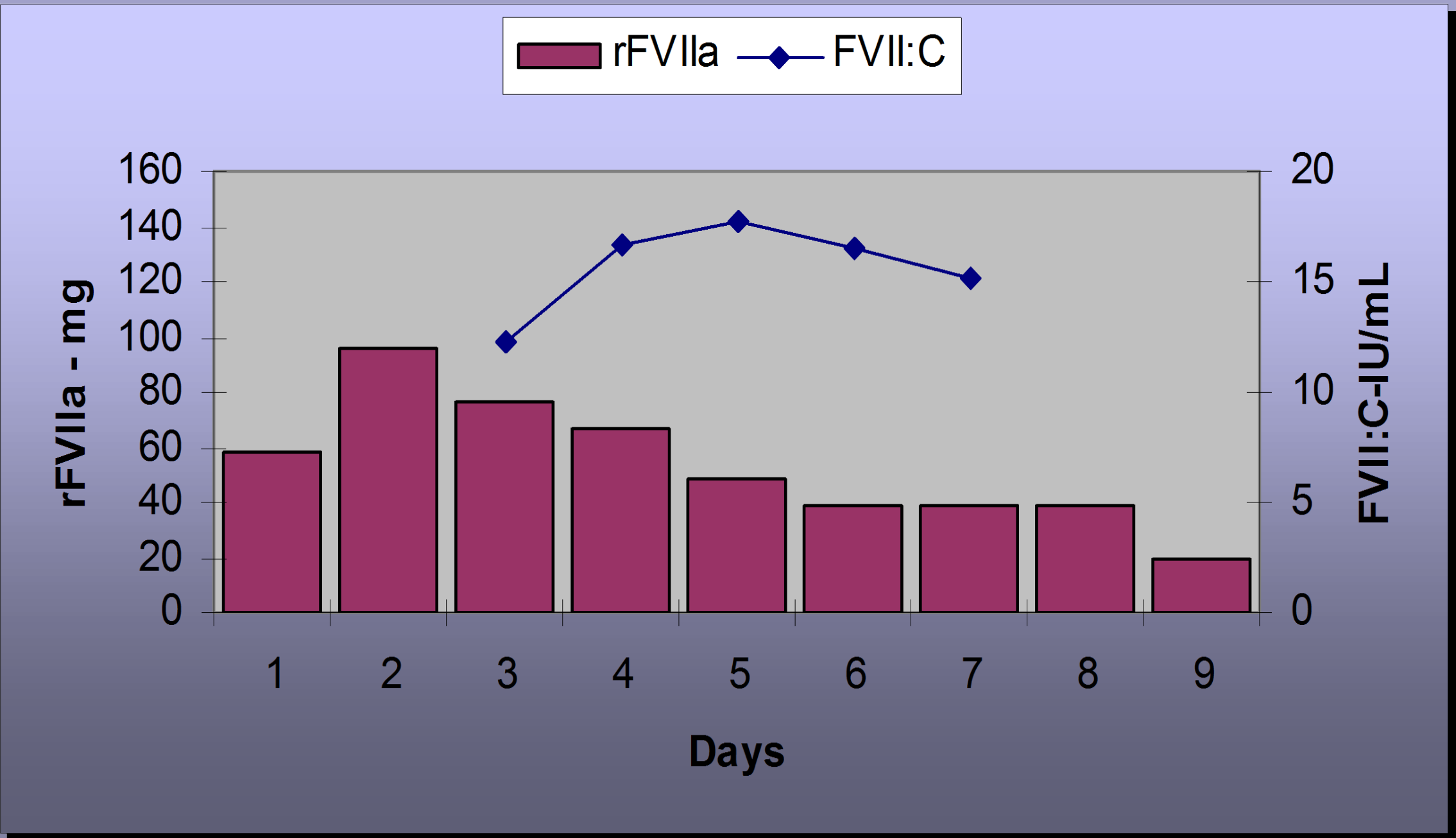


Fig.2 –FVII:C levels and rFVIIa administered.

	Days						
	1	2	3	4	5	6	7
APTT (sec.)	68	-	47.3	49.4	55	-	-
PT/INR	-	0.56	0.56	0.57	0.53	0.52	0.68
FVII:C UI/L	-	-	12.30	16.60	17.75	16.50	13.20

Table 1 – Coagulation parameters

RESULTS AND CONCLUSION

The clinical response was excellent in this patient with evident relief of pain and better mobilization in bed, less than 24 hours after the beginning of the treatment. At the second day his haemoglobin stabilized and no further transfusions with PRBC were needed (Fig.1). The therapy was prolonged during nine days and a total amount of 24000 KUI (480mg) was given. The PT-INR kept within a range of 0.68-0.52 and FVII:C levels ranged between 12.3 U/ml and 17.7/ml which were within our target range (Table 1). The APTT decreased max 18.6 sec. as the baseline value (range 49.4-68 sec.) Other haemostatic parameters did not change. Adverse reactions, such as phlebitis or other side effects were not reported. rFVIIa proved to be very safe and efficacious, but in view of the high treatment costs, especially when administered as bolus injections, the possibility of continuous infusion, leading to economic savings, has to be considered.

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