

Utilization review of Novoseven in a University hospital : room for improvement

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Introduction

Recombinant factor VIIa (Novoseven®, rFVIIa) is indicated for treatment of bleeding in hemophilic or non hemophilic patients with antibodies against factor VIII or IX.

Relative contra-indications include major surgical procedures, liver failure, extensive soft tissues injuries, cranio-cerebral trauma, septicemia, cancers, or advanced arteriosclerosis, because intravascular coagulation or thrombosis can occur.

Recently, this drug has been used as a last resort treatment in patients with severe hemorrhages, in some cases at high dose. As drug acquisition cost is high, its benefit must be well-documented.

Patients and methods

All consecutive patients treated with rFVIIa in our hospital in 2004 were included in a drug utilization review process.

Results

In 2004, rFVIIa was administered in 9 patients (6 men, 3 women), age range 0-82 years.

Table 1

Characteristics, diagnosis, comorbidity and source of bleeding of individual patients

Eight patients experienced bleeding after a surgical procedure and one after rupture of esophageal varices. Only one patient suffered from a congenital deficiency in factor VII.



Patient Nr	Gender	Age (yr)	Diagnosis	Comorbidity	Source of bleeding
1	F	53	Hydronephrosis	Fibrosing mediastinal and peritoneal disease Vena cava syndrome	Liver hematoma after ureteral bypass
2	M	71	Aortic and mitral valves stenosis and insufficiency Coronary stenosis	End stage renal disease Malnutrition	Hemorrhagic shock after cardiac surgery (bypass and valve replacement)
3	M	20	Polytrauma	Cranial fractures and coma Pulmonary hemorrhage Splenic fracture	Diffuse abdominal bleeding
4	M	25	Polytrauma	Thoracic fractures Liver laceration Splenic fracture	Diffuse abdominal bleeding
5	F	25	Cesarian section	Paroxysmal hemoglobinuria Budd Chiari syndrome	Uterus + abdominal wall
6	M	82	Coronary stenosis	Myelodysplastic syndrome	Diffuse cardiac bleeding after bypass surgery
7	M	44	Thyroid adenoma	Factor VII deficiency	Diffuse bleeding after thyroid surgery
8	F	33	Oesophageal varices rupture	Kidney failure Liver cirrhosis (Child C)	Diffuse bleeding
9	M	0	Congenital aortic valve stenosis	Foramen ovale Arterial canal	Cardiac bleeding after cardiac surgery

Table 2

Treatment and outcome of individual patients

Bleeding stopped in all patients, but 7/9 died.

The only survivors were the woman who gave birth and the patient with elective thyroid intervention.

Some of these patients, including the survivors, showed evidence of thrombosis, which was extensive in one of them.

These complications occurred mainly in patients receiving high drug dose.

Patient Nr	Novoseven administration			Outcome			
	Dose/kg (µg)	Total dose (mg)	Recognised indication	Bleeding	Thromboembolic complication	Death	Interval to death
1	300	24	No	Stop	Likely	Yes	12h
2	300	18	No	Stop	No	Yes	6d
3	300	21.6	No	Stop	Likely	Yes	2d
4	300 + 90	31.2	No	Stop	No	Yes	12h
5	300	19	No	Stop	Yes	No	-
6	90	5.4	No	Stop	No	Yes	4d
7	30	1.2	Yes	Stop	No	No	-
8	90	4.8	No	Stop	No	Yes	21d
9	90	0.3	No	Stop	No	Yes	7d

Conclusion

rFVIIa utilization review showed that the drug was used outside its registered indication in the vast majority of cases, as a last resort treatment, when all other treatment had failed or been applied in a non-optimal sequence.

If it was effective in stopping bleeding, only 2/9 (22%) of patients survived, and 3/9 (33%) experienced thromboembolic complications, especially after high drug dose administration.

Given the poor patient outcome and the high drug acquisition price, clinicians should be more involved in reviewing these cases in order to improve patient care in these dramatic situations and to optimize the use of this last chance treatment.