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Case Report

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Case Report of High Dose Factor rVIIa in a Child

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ABSTRACT

The maximum tolerated dose of recombinant factor VIIa without significant toxicity is not studied in a clinical trial. Separate case reports of accidental intake of high dose recombinant factor VIIa were reported. This case report describes an exposure of an infant with congenital factor VII deficiency to a high dose of recombinant factor VIIa (300 µg. /kg).

Keywords: Factor VII Deficiency, Recombinant, Factor VIIa, Toxicity, Dose, Coagulopathy, Congenital

Introduction

Factor 7 is vitamin K dependent glycoprotein that is important for normal hemostasis in human. When Factor 7 is activated (e.g. exposure subendothelial collagen upon injury), it activates coagulation cascade (extrinsic coagulation pathway) that finally end in hemostasis [1].

It is available in 2 forms: plasma derived concentrate and recombinant form.

It can be used in different bleeding situations either to prevent or stop bleeding e.g. congenital factor 7 deficiency and congenital or acquired hemophilia (A or B) with inhibitors [2].

Repeated successive reviews of Recombinant factor VIIa in controlling bleeding in hemophiliac patients; led to initiation of its use for other bleeding conditions in non-hemophiliac patients. Now a day; it is used in critical bleeding conditions e.g. intracerebral hemorrhage, upper gastrointestinal bleeding, warfarin toxicity with bleeding, bleeding after cardiopulmonary bypass, bleeding after cardiopulmonary bypass, obstetrical bleeding and in Glanzmann's thrombocytopenia [3-7].

Many case reports have been issued accidental intake of high doses of recombinant factor VII a and few studies are issued. More studies are needed to investigate safety of this medication

Case Presentation

Seven months old boy; full term, spontaneous vaginal delivery; was diagnosed at first day of life as a case of factor 7 deficiency. He has a family of history of factor 7 deficiency (his two older sibling). His coagulation profile at birth was abnormal but with no bleeding. PT was 22.8 seconds, PTT: 48 second and INR: 1.9. Factor 7 level was requested and it was 0.1. physical examination was unremarkable. He was put on regular follow up with no active issues.

At age of 7 months old was admitted to pediatric ward for circumcision as per family request. He was admitted one day before surgery for preparation. The plan by hematology team was to give recombinant factor VIIa in a dose 30 µg/kg/ 4 hours for 24 hours before surgery and for 24 hours after surgery

On physical examination: his weight was 8 kg, temperature: 36.8, blood pressure: 95/55, pulse rate 96, respiratory rate 24 and O2 saturation: 99%. Chest, abdominal, cardiac and neurological examinations were normal with good central and peripheral pulsation with no color changes.

Table: Laboratory Results of Our Case Post Wrong Dose of Recombinant Factor VIIa

	PT	PTT	INR	D. Dimer	Fibrinogen	Factor VII level
Normal range	12.6-14.6	29.9-40.34	0.9-1.15	0.17-0.64	2.07-4.17	60-150%
Hour :1	<10	40.7	< 0.9	0.29	1.88	300

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Hour: 5	11	42.4	< 0.9	0.55	1.62	205
Hour: 9	14.5	39.5	1.1	---	1.57	46
Hour: 13	23.5	37.4	2	0.65	1.71	3
Hour: 17	37	29.4	3.5	---	1.48	---

Laboratory work up was done. WBCs count was: 6.6, hemoglobin: 9.6, platelet count: 855, PT:43 SEC., PTT: 40.1 SEC., INR: 1.8, fibrinogen level: 1.89 gm./L, factor7 level:2%, serum urea:2.3 Serum creatinine :32 u.mol/L, ALT:11 U/L, AST:14 U/L and total bilirubin: 8.1 u.mol/L

Preoperative doses were given then surgery was done the next day without bleeding or any other complication. Unfortunately, the fifth dose after surgery was given; by mistake; in a dose of 300 µg/kg. All next doses were hold. Immediate coagulation profile and factor 7 level were done. Then the patient was put on maintenance IV fluid, continuous cardiovascular monitoring, coagulation profile q 4 hours and neuro observation q 2 hours. He was observed for 24 hours without any recorded complication then discharged home with outpatient follow in pediatric hematology clinic after 2 days. Red flags were instructed to his parents.

Discussion

Recombinant factor VIIa is a vitamin K-dependent glycoprotein that was got approved by the US Food and Drug Administration in treatment of bleeding episodes in hemophilia patients and patient with hemophilia A and B with inhibitors in 1999 [1,2].

The main and the most serious complications of rFVIIa are the thromboembolic complications. It can lead to thrombotic myocardial and cerebral ischemia, deep venous thrombosis or pulmonary thromboembolism. The rate of thromboembolic adverse events (TAEs) related to the use of rFVIIa in hemophiliacs has been 5% to 7%. The risk for thromboembolic complications were strongly associated with the use of higher doses of rFVIIa and for "off-label" indications [8-11].

Many case reports have been issued accidental intake of high doses of recombinant factor VII a and few clinical studies are available now. In one single center study, Kenet and colleagues confirmed the efficacy and safety of 300 ug/kg rFVIIa as a treatment for bleeds in three young hemophilia patients with inhibitors [12].

Abshire recommended that dose of 300ug/kg can be considered effective and safe for uncomplicated bleeding episodes in children if given within a few hours of bleed onset [14].

The HRS investigated efficacy and safety of high dose rFVIIa therapy in hemophilia patients with inhibitors. 556 bleeding episodes were investigated with a median dose of 360 ug/kg administered over 72 hours was given. This dose was effective in 97% of episodes and safe in 100% of episodes [13].

In our study; a single mega dose of 300 ug/kg was given by mistake in 7 months old boy with factor 7 deficiency as prophylactic dose post circumcision. Patient was put on close follow up for 24 hours in pediatric ward and for 72 hours in clinic. no complication was reported.

The above-mentioned studies and reports in addition to our case experience may potentiate that the dose of 300 um/kg may be safe in pediatric age.

Conclusion

High dose recombinant factor VII a up to (300 µg/kg/ dose) could be safe in pediatric age but further studies and reported cases are advised.

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