## CASE REPORT

# Recombinant activated factor VII: A savior in management of postpartum hemorrhage

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## ABSTRACT

Bleeding, a major cause of morbidity and mortality, is one of the most difficult challenges for obstetricians and anesthesiologists. The management of major obstetric hemorrhage is challenging resulting in surgical and medical interventions, sometimes requiring hysterectomy. Use of Recombinant activated factor VII r(FVIIa) is a recent advancement in the control of PPH. In situations of intractable PPH, where primary measures to control hemorrhage fail, administration of rFVIIa should be considered before decision to perform a hysterectomy is undertaken. We hereby present a case report of a 21 year female presenting with post caesarean PPH refractory to standard therapy , managed successfully by rFVIIa.

**Key words:** rFVIIa; Postpartum hemorrhage management

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## INTRODUCTION

Bleeding, particularly postpartum hemorrhage (PPH) is a major cause of morbidity in obstetrics and gynaecology. Improving uterine tone and using effective transfusion therapy is the primary management of PPH. Once these primary measures fail, invasive interventions including repair of genital tract, uterine compression sutures and ultimately hysterectomy may be required as a last resort. Use of Recombinant activated factor VII r(FVIIa) is a recent advancement in the control of PPH.[1] At the site of vascular injury, the common pathway of the coagulaton cascade gets activated directly by rFVIIa which is the rationale for its use to control bleeding. We hereby present a case report of a 21 year female presenting with post caesarean PPH refractory to standard therapy , managed successfully by rFVIIa. This case report is different due to non availability of blood.

## CASE REPORT

A 21 year old second gravida weighing 50 kg underwent caesarean section under spinal anesthesia. Intraoperative period was uneventful. After surgery, hemoglobin was 9 gm%. Platelets and INR were 1.5 lakh/mm$^3$ and 1.0 respectively. Four hours after surgery, she started bleeding per vaginum in the form of clots and tone of the uterus was found to be relaxed as examined by obstetrician. Bleeding was estimated to be 200 ml. BP was 102/60 mm Hg and pulse was 96/min. Oxytocin 40 units intravenous in infusion and carboprost 250μg were administered intramuscularly. Mesoprost 800μg was administered per rectal, but the bleeding persisted. By this time blood pressure dropped to 80/50 mm Hg and pulse was 120/min. The obstetrician decided to explore. 4 units whole blood and 4 units FFP were ordered. Hydroxyethyl starch (1L) was rushed through IV line in situ. Another intravenous line was started. Blood pressure improved to 90/60 mm Hg. Rapid sequence induction was done with thiopentone sodium 200 mg and succinylcholine 75 mg and trachea was intubated successfully with endotracheal tube of internal diameter 7 mm. Fentanyl 100 μg was given intravenously. Anesthesia was maintained with isoflurane and atracurium in 67% nitrous oxide and 33% O2. Intraoperatively, on opening of abdomen, uterus was relaxed. Carboprost 250μg (intramyometrial) was given. Now tone of uterus improved but bleeding continued. By this time total blood

loss was 2 L. 2 units of whole blood and 2 units FFP were transfused alongwith Ringer Lactate (1.5 L). More blood could not be made available. Blood pressure was 96/64 mm Hg and pulse was 110/min. At this time, it was decided to give rFVIIa. rFVIIa was given in a dose of 60μg/kg. By subjective assessment, bleeding decreased and a second dose was repeated after 30 minutes. After administration of 2nd dose, bleeding stopped. Abdomen was closed and there was no further bleeding per vaginum.Blood pressure improved to 120/70 mm Hg and pulse was 90/min. The postoperative course was uneventful. She was discharged on 7th postoperative day in stable condition.

## DISCUSSION

Bleeding, a major cause of morbidity and mortality, is one of the most difficult challenges for obstetricians and anesthesiologists. The management of major obstetric hemorrhage is challenging resulting in surgical and medical interventions, sometimes requiring hysterectomy.

rFVIIa, which was initially developed for the treatment of bleeding episodes in patients with hemophilia A or B is one of the advancement in the control of PPH.[2] The first report of its use in peripartum hemorrhage was released in 2001.[3] Magon et al suggested that administration of rFVIIa could be considered in patients of PPH before considering hysterectomy. These authors also recommend administration of rFVIIa as early as possible in some specific situations like when no blood is available and before packing of the uterus or pelvis.[1] Blood could not be made available in our case, hence we decided to use rFVIIa. Recombinant factor VII has been successfully used for massive hemorrhage during radical nephrectomy by Chaudhry et al.[4] The promising results support the utility of rFVIIa for management of severe PPH in Japan.[5]

rFVIIa induces hemostasis at the site of injury. Its mechanism of action involves the binding of factor VIIa to the exposed tissue factor (TF) dependent pathway and independent of TF, it leads to activation of factor X directly on the surface of activated platelets localised to the site of injury, both of these resulting in thrombin and fibrin formation. rFVIIa does not bond to resting platelets. Therefore the effect of high dose-rFVIIa is localised to the site of vessel injury only.[6] This is particularly important in the obstetric setting where there is often bleeding from a large raw area of expoed tissue.

A 2007 review identified case reports of 65 mothers treated with rFVIIa with controversial results as 30 out of 65 patients had to undergo peripartum hysterectomy.[3] It is hence suggested thar rFVII may be used as an adjuvant to standard pharmacological and surgical treatment under guidance of a hematologist. The empirical use of rFVIIa is not advisable as it is not relevant to use this drug in low fibrinogen levels and in thrombocytopenia. The prerequisite for administration of rFVIIa is fibrinogen levels >1g/l and platelet count $>20\times10^9$.[3,7,8] Also presence of hypothermia and acidosis can lead to failure to respond to rFVIIa.[9] Franchini et al suggest that rFVIIa should always be administered before the decision of obstetric hysterectomy. If the indication still persists after its use the drug will improve the course of surgery with a reduction of surgery related blood loss. The recommended dose of rFVIIa is 60-90 μg/kg bolus which may be repeated within 30 minutes. It is reasonable to use lower doses as these doses are found to be equally effective. Also, lower doses could reduce the incidence of adverse effects.[10]rFVIIa has a thrombogenic potential. So it should be used with caution in presence of sepsis and disseminated coagulation. The best available indicator of rFVIIa efficacy is the arrest of hemorrhage judged by visual evidence, stabilisation of hemodynamic parameters and reduced demand for blood components.[11] At present, there is no satisfactory laboratory test to monitor the clinical effectiveness of rFVIIa, which is judged subjectively. The incidence of non serious adverse events is 13% and serioud adverse events are less than 1%.

We wish to highlight that in situations of intractable PPH, where primary measures to control hemorrhage fail, administration of rFVIIa could be considered before decision to perform a hysterectomy.

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