



Successful Treatment of Polytraumatic Bleeding with Recombinant factor VII: A Case Report

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Abstract: Recombinant activated factor VII (rFVIIa, Novoseven) enhances haemostasis in individuals, with its predominant action limited to areas of injury, apparently without systemic activation of the coagulation cascade. We report here the successful use of rFVIIa in a patient with a history of polytrauma (Road traffic accident)

KEY WORDS: Trauma; Haemorrhage, Haemodynamics, Recombinant factor VII A

Overwhelming haemorrhage due to trauma, surgery or other insults presents an immediate and challenging problem to surgeons, critical care specialist, anaesthetists and haematologists. Polytrauma patients with uncontrolled bleeding and persistent coagulopathy despite blood transfusion support and surgical intervention have mortality rates of 40 –60%. rFVIIa is a novel haemostatic agent originally developed for haemophilia patients with inhibitors to replacement factor VIII or IX. rFVIIa in therapeutic dosage maximizes thrombin burst on the activated platelets at the site of tissue injury which in turn facilitates firm fibrin clot formation at the bleeding site. Recently it has been suggested that this agent may be effective in treating non-haemophilic patients with traumatic and other types of bleed. We report here the successful use of rFVIIa in a patient sustained polytrauma with severe haemorrhage who had a rare blood group (AB, Rh -ve) with limited availability of blood and blood products.

Case Report: A 17 year old male suffered polytrauma in a high speed road traffic accident. At admission, patient had a GCS of 15/15, pulse 120bpm, extremities were cold, BP 90/60mm Hg, and was tachypnoeic. There was extensive degloving injury of right thigh and progressive haemorrhage



from the wound. The patient also had fracture pelvis and right femur. There were no signs suggestive of head trauma/maxillofacial injury/thoracic trauma or abdominal trauma. Fluid resuscitation started and pressure dressing applied over degloved part after saline wash and povidone iodine application.

Two units of packed cell and 2 units of FFP were transfused in view of ongoing blood loss. Unfortunately his blood group was found to be AB, Rh -ve and we could not make available more than 4 units of packed cell. Meanwhile requisition was sent to all nearby blood banks for compatible blood and blood products. (AB, Rh - ve, O - ve). Haemorrhage from the injured site continued with worsening of shock requiring vasopressor support. Laboratory reports showed Decreased Hb (6 gm/dl.), low haematocrit (18%), low Platelet Count (80000/mm³) and INR 1.8

Surgical team initially deferred surgical intervention, in view of the disrupted haematological architecture and ongoing bleed. In the face of unavailability of compatible blood and the overwhelming bleed with worsening of haemodynamics, it was decided to use recombinant factor VIIa. Single dose of 90 µg/ kg (6mg) was given as intravenous bolus over 2–5 minutes. Haemorrhage from wound site decreased after 15 minutes of administration and haemodynamics started improving. PT and INR were repeated after 2 hours and found to be near normal.

The haematocrit was built up in a controlled manner with appropriate blood product transfusions, which could be available only after 36 hours. Fourth day, surgical intervention for fixation of Rt femur fracture, pelvis fracture fixation and debridement of the wound was done. He required three more operative procedures in a staged manner over the next 15 days for wound care. The Pt. recovered well and was discharged from the hospital after 25 days of hospital stay.

Discussion: Trauma is the leading cause of death in young adult with 80% of all early deaths being attributable to uncontrolled haemorrhage. Patients with uncontrolled bleeding and coagulopathy have mortality rates of 40% to 60%^{1,2}. Current food and drug administration guidelines reserve the use of factor VIIa for the treatment of haemophiliacs with factor VIII and IX deficiencies (haemophiliac A and B). A number of reports have indicated the efficacy of off-label use of recombinant activated factor VII in critically ill patients with exsanguinating haemorrhage caused by coagulopathy^{3,4,5}. In the past several years there has been an explosion of publications concerning the use of rVIIa for a variety of situations leading some to claim that rVIIa is a “Pan haemostatic agent”^{6,7}.

rVIIa is a recombinant protein, with a molecular weight of 50 k Da and has the same amino acid sequence as native VII a. When infused, its half life is 2-3 hrs⁸. The dose recommended for patients with factor VIII and IX deficiencies complicated by inhibitors is 90 µg/kg⁹. This dose was chosen as it consistently produces a plasma rVIIa level > 10 U/ml., which is thought to be the level necessary for cessation of bleeding.

The mechanism of action of rVIIa remains controversial. Tissue factor is a membrane bound protein that is exposed with trauma. Coagulation is initiated when circulating VIIa binds to tissue factor. One theory of rVIIa effect is that the supraphysiological concentration of rVIIa speeds up the



tissue factor VIIa mediated reaction, such as activation of factor X and IX, resulting in more thrombin generation¹⁰. In a cell based system, rVIIa can bind to platelets and directly activate factor X and IX without the need for tissue factor¹¹. Finally recent data indicate that rVIIa can enhance platelet aggregation and adhesion via an increase in thrombin generation¹².

The most serious adverse reactions observed in patients receiving rVIIa are thrombotic events, however the extent of the risk of thrombotic adverse events after treatment with rVIIa in individuals with haemophilia and inhibitors is considered to be low¹³. The most common adverse reactions observed in clinical studies for all labelled indications of rVIIa are pyrexia, haemorrhage, injection site reaction, arthralgia, headache, hypertension, hypotension, nausea, vomiting, pain, oedema and rash. Patients who receive rVIIa should be monitored if they develop signs or symptoms of activation of the coagulation system or thrombosis. When there is laboratory confirmation of intravascular coagulation or presence of clinical thrombosis, the rFVIIa dosage should be reduced or the treatment stopped, depending on the patient's symptoms.

Due to limited clinical studies which clearly address the effect of post-haemostatic dosing, precautions should be exercised when rFVIIa is used for prolonged dosing. Factor VII deficient patients should be monitored for prothrombin time and factor VII coagulant activity before and after administration¹⁴. If the factor VIIa activity fails to reach the expected level, or prothrombin time is not corrected, or bleeding is not controlled after treatment with the recommended doses, antibody formation may be suspected and analysis for antibodies should be performed. Coagulation Factor VIIa (Recombinant) should not be administered to patients with known hypersensitivity to any of its components or known hypersensitivity to mouse, hamster, or bovine proteins.

The area with most intense focus for rVIIa use is in trauma patients. There are multiple reports confirming the use of rVIIa in trauma bleeding. It is clear that transfusion requirements are decreased after administration of rVIIa. There are preliminary results available from a randomized trial of 297 patients that compared placebo with rVIIa 200 µg/kg, followed by 100 µg/kg dose after 1 to 3 hour in massively bleeding trauma patients¹⁵. rVIIa decreased transfusion needs in blunt, but not penetrating trauma patients. Also of interest was the observation that multiorgan system failure and acute respiratory distress syndrome seems to be decreased in the rVIIa group. A larger trial is underway to better define rVIIa use in this population.

This case is reported to emphasize that we did experience a rapid and dramatic control in ongoing blood loss after single dose administration of factor rVIIa in our patient. Thus the use of factor VIIa in patients with life threatening haemorrhage is a safe and effective therapeutic modality when used as an adjunct to standard interventions for control of severe haemorrhage¹⁶.

Conclusion: Our experience regarding the efficacy of rFVIIa in this patient is consistent with a growing body of evidence suggesting a role for rFVIIa in the management of traumatic haemorrhage. Randomised studies to further assess the safety and efficacy of rFVIIa in non-haemophiliac patients with bleeding are currently underway and they should provide further insight into optimal patient selection, drug dosage and safety profile. In view of its novel mechanism of action, it may have a



possible role as a life saving tool for trauma patients in future, but it is not a substitute for conventional surgical treatment of haemorrhage due to trauma.

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