Clinical Efficacy of Recombinant Activated Factor VII in Postpartum Hemorrhage

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Purpose: This study was aimed to investigate the clinical efficacy of recombinant activated factor VII (rFVIIa) for patients with intractable postpartum hemorrhage.

Methods: This was a retrospective study of ten patients who were treated with rFVIIa from July 2010 to February 2012 in one tertiary center. To evaluate each case, we used a standardized case record form. The primary outcome measures were response of rFVIIa, reduction of blood product requirement, changes of coagulation parameter. The response of rFVIIa was categorized to three groups: “complete responder”, “partial responder”, “poor responder”.

Results: After the administration of rFVIIa, effect for bleeding was completely responded in 4 patients, partially responded in 6 patients, and poorly responded in none. A certain amount of reduction in blood product requirements was noted following rFVIIa administration, although no significant differences were observed statistically between before and after rFVIIa administration except RBC ($P<0.01$). Fibrinogen and INR were significantly reduced in all case types, but other coagulation parameters were not ($P<0.01$).

Conclusion: The present results suggest that rFVIIa is a beneficial therapeutic option that could reduce blood loss and contribute to reduction of maternal morbidities and mortalities in patients with massive postpartum hemorrhage.

Key Words: Clinical efficacy, Postpartum hemorrhage, Recombinant activated factor VII

Recombinant activated factor VII (rFVIIa) was initially developed for the treatment of hemophilia with coagulation factor inhibitors.¹ It has since also been approved for the treatment of acquired hemophilia and other inherited bleeding diathesis such as Glanzmann thrombasthenia and factor VII deficiency.² Licensed in many countries, it acts by enhancing coagulation at the site of bleeding by triggering and augmenting the thrombin burst, ultimately leading to formation of a stable fibrin clot.³,⁴ Since its action was reported to be direct and localized at damaged sites, interest in the potential use of rFVIIa in cases of hemostatic failure with the standard treatments has become widespread as an off-label indications,⁵ such as trauma,⁶ intracranial hemorrhage,⁷ major surgery⁸,⁹ and obstetrical hemorrhage.¹⁰⁻²³

However, any case reports documenting the use of rFVIIa for Korean patients with postpartum hemorrhage (PPH) have not been published to date. Therefore, data on single center cases with intractable PPH in which rFVIIa had been administered were collected. In this initial report, our experiences with the use of rFVIIa for PPH management are reported.

Materials and Methods

Between July 2010 and February 2012, thirty-two women with PPH were referred to our institution for
control of bleeding.

The medical records for all the cases of PPH during that period were collected. Ten patients received rFVIIa (NovoSeven®, NovoNordisk, Bagsvaerd, Denmark) as an adjuvant therapy for PPH refractory to the conventional treatments. All patients were thoroughly informed about off-label indication and major significant adverse events of rFVIIa and written consents were obtained from the patient or her family.

Every medical record was reviewed to assess the following clinical, biochemical and hematological parameters: age, parity, gestational age, delivery method, suspected causes of bleeding. All patients received primary management in the obstetric department, including vaginal gauze packing, uterine massage, manual extraction of the placenta, detailed vaginal examination using a retractor, intravenous administration of oxytocin, methyl-ergonovine, intra-rectal misoprostol. Infusion of crystalloids and transfusion of packed red cells were used for correction of hypovolemic shock. Control of disseminated intravascular coagulation (DIC) was based on infusion of fresh frozen plasma (FFP), fibrinogen, and platelet concentrates. Infusion of 80 μg/kg or 85 μg/kg of rFVIIa was performed once in those cases in which obstetric and radiologic interventions and drug therapy had failed to control bleeding. 24 For evaluation of treatment response, dosage of rFVIIa administration, other medical treatments, and physical interventions were collected. Transfusion information was also collected for the 24 hours preceding and after administration of rFVIIa. Laboratory test results including hematologic parameters such as fibrinogen, platelets and international normalized ratio (INR) were collected for the closest tests taken before and after administration of rFVIIa.

Responses were assessed at 20 minutes after administration of rFVIIa by each patient’s vital sign, the amount of vaginal bleeding, laboratory results. The amount of vaginal bleeding was counted by number of wet pads. Clinicians assessed the effect of rFVIIa on bleeding at each administration using three categories: “complete responder”, “partial responder”, “poor responder”. The response was defined “complete responder” if the bleeding after its administration was 1,000 mL or less, systolic blood pressure (BP) was higher than 70 mmHg and pulse rate was lower than 110 bpm. The “partial responder” was defined to meet one of the two that the bleeding after its administration was 1,000 mL or less, systolic BP was higher than 70 mmHg and pulse rate was lower than 110 bpm. The response was defined “poor responder” if there are still uncontrolled bleeding and unstable vital signs.

Individual pairs of coagulation parameters and blood product requirements before and after rFVIIa administration were compared using Wilcoxon matched-pairs signed rank tests. Statistical analyses were carried out using SPSS 18.0 (SPSS Inc., Chicago, IL). Data were presented as medians, and \( P<0.01 \) was considered statistically significant.

### Results

The demographic characteristics and obstetric history of ten patients are summarized in Table 1. Nine patients were nulliparas, and one patient was multipara. Six had a spontaneous vaginal delivery and the other four underwent a cesarean delivery. There were no multiple pregnancies. Forceps and vacuum were not employed. Uterine atony, the leading cause of PPH, was revealed in five cases, and genital tract injury was discovered in three cases. The rest of causes included