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Interest of Recombinant factor VIIa in the Management of Postpartum Hemorrhage

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Abstract

Introduction : Postpartum hemorrhage (PPH) is the leading cause of maternal mortality and morbidity in our country. The role of hemostatic treatments, particularly recombinant activated factor VII (rFVIIa), in combating coagulopathy occurring during the course of PPH has been highlighted in the literature.

Objective : To evaluate the efficacy and benefit/risk ratio of recombinant factor VIIa in the treatment of PPH.

Methods : This is a descriptive retrospective study including all parturients who received rFVIIa at the Ibn Jazzar Maternity Unit in Kairouan for PPH between January 1, 2021, and December 31, 2024.

Results : 15 patients were included. The mean age was 31 ± 5.96 years. The main risk factors for PPH were multiparity, overdistention, prolonged labor, and infection. The mean time to PPH diagnosis was 48 minutes. The most common cause of PPH was uterine atony. The mean time to rFVIIa administration was 6 hours 40 minutes. The average dose used was 78.8 ± 9.24 µg/kg. Five patients received a single dose, 8 patients received a seconde injection, and 2 patients required 3 doses. After rFVIIa administration, normalization of coagulation parameters was observed in 8 patients.

Conclusion : rFVIIa is not a first-line treatment but may be used as a single, repeatable dose if needed.

Keywords: Postpartum hemorrhage, disseminated intravascular coagulation, recombinant activated factor VII

Introduction

Postpartum hemorrhage (PPH) is the leading cause of maternal mortality and morbidity in our country [1]. Obstetric hemorrhagic emergencies are specific situations, and their management depends on several factors, particularly the etiology and severity of the bleeding. Over the last decade, the interest in hemostatic treatments, particularly recombinant activated factor VII (rFVIIa), in combating coagulopathy during PPH has been highlighted in the literature.

rFVIIa is a potent procoagulant drug that directly activates factor X on cell surfaces, leading to thrombin generation and localized coagulation at the vascular injury site. The aim of our study was to evaluate the efficacy and benefit/risk ratio of recombinant factor VIIa in the treatment of severe postpartum hemorrhage.

Materials and Methods

This is a descriptive retrospective study including all parturients who received rFVIIa at the Ibn Jazzar University Hospital Maternity Unit in Kairouan for PPH between January 1, 2021, and December 31, 2024. It was administered in cases of failure of initial obstetric and/or medical measures for PPH and after a collegial decision involving anesthetists, intensivists, and obstetricians.

Results

During the study period, 15 patients were treated with rFVIIa for PPH, averaging 3.75 new cases per year. Seven patients (46%) were transferred from peripheral maternities. The mean age of patients was 31 ± 5.96 years, ranging from 21 to 41 years. Parity ranged from 1 to 6, with a mean of 2.5. The mean gestational age was 35 weeks, ranging from 28 to 41 weeks. Cesarean delivery was performed in 10 patients, 6 of which were planned, and the others were emergency procedures. Vaginal deliveries accounted for 33.33%.

In our series, the main risk factor for PPH was multiparity in 10 cases. The mean time to PPH diagnosis was 48 minutes. Four patients (26.6%) were diagnosed within 30 minutes, while a delayed diagnosis beyond 120 minutes occurred in 11 patients (72.6%). The most frequent cause of PPH was uterine atony (5 patients). Uterine rupture and cervico-uterine tears were each observed in 3 cases. Retroplacental hematoma and placenta accreta were reported in 1 case each. Placenta previa was the cause in 2 patients.

Initial obstetric management was implemented before rFVIIa administration. Mechanical or traumatic lesions were repaired in 3 patients, uterine revision was performed in 6 patients, and one patient underwent triple vascular ligation using the Tsirulnikov technique. Seven patients (46.6%) underwent subtotal interannexial hysterectomy as first-line treatment. Indications for primary hysterectomy are detailed in Table 1.

Table 1 : Indications for primary hemostatic hysterectomy in our study population

Etiology	Number of cases	Percentage (%)
Uterine atony	3	20%
Retroplacental hematoma	1	6.66%
Uterine rupture	2	13.33%
Placenta accreta	1	6.66%

All patients had at least two large-bore peripheral intravenous lines. A central venous catheter was placed in all patients via the right internal jugular vein. An arterial catheter was placed in all patients via the radial artery for continuous blood pressure monitoring. A urinary catheter was inserted in all patients for urine output monitoring. Rapid sequence induction was performed in all patients with nasogastric aspiration. Induction drugs included ketamine 4 mg/kg and suxamethonium 1 mg/kg. Maintenance before delivery was achieved with ketamine infusion (0.5 mg/kg/min) and cisatracurium boluses (0.03 mg/kg every 15–20 min). After hemodynamic stabilization, sedation was continued with fentanyl 100 µg and midazolam 50 mg via infusion pump.

Pre- and perioperative crystalloid fluid administration averaged 1500 mL (range 500–3000 mL). All patients received maximal intravenous oxytocin and sulprostone (Nalador). Catecholamines (norepinephrine) were used to maintain a mean arterial pressure ≥ 70 mmHg. All patients received blood transfusions : mean of 5.37 red blood cell units, 7.24 fresh frozen plasma units, and 1.5 platelet units. Fibrinogen was administered to all patients (mean dose 2 g, range 2–4 g). Tranexamic acid (Exacyl) was also given to all patients (mean dose 2 g, range 1–4 g).

The mean time to rFVIIa administration was 6 hours 40 minutes (range 3–17 hours). All patients received 4.8 mg rFVIIa vials. The mean dose was 78.8 ± 9.24 µg/kg (range 64–98 µg/kg). Five patients received a single dose, 8 patients received a second dose, and 2 patients required 3 doses. After rFVIIa administration, normalization of coagulation parameters was observed in 8 patients. Hemoglobin levels were <8 g/dL in 6 patients, 8–10 g/dL in 7 patients, and >10 g/dL in 2 patients. Platelet counts were <100,000/mm³ in 5 patients, 100,000–200,000/mm³ in 6 patients, and >200,000/mm³ in 4 patients.

After a single rFVIIa injection, clinical efficacy in bleeding reduction was observed in 8 patients, whereas hemorrhage persisted or worsened in 7 patients. Transfusion requirements decreased, and coagulation parameters improved after rFVIIa administration, as detailed in Table 2.

Table 2 : Changes in transfusion requirements after rFVIIa administration

Before rFVIIa	After rFVIIa	Percentage reduction
RBC units	6.98	3.84
Platelet units	3.40	1.68
FFP units	9.58	6.14

Complications included renal failure in 7 cases (2 requiring dialysis), disseminated intravascular coagulation in 4 cases, pulmonary edema in 2 cases, multiorgan failure in 2 cases, septic shock in 1 case, and mesenteric infarction in 1 case. Mortality occurred in 3 patients:

- Septic shock following small bowel perforation and mesenteric infarction
- Multiorgan failure following hemorrhagic shock (2 cases)

Discussion

The literature reports some life-threatening PPH cases successfully treated with rFVIIa after failure of conventional therapy [2,3]. Recombinant activated factor VII is not a first-line treatment for PPH, and its use is reserved for severe cases refractory to conventional treatment. Several case series and registries have documented the use of rFVIIa in PPH [4,5].

Reported doses vary (10–170 µg/kg), with a single dose used in 78–93% of cases. In our series, clinical efficacy in bleeding reduction was observed in 3 patients after a single dose. Published series report success rates between 63–100% (median 89%). European, Italian, Australian–New Zealand, and French registries reported success rates of 86%, 89%, 76%, and 69%, respectively [4,6,7].

Retrospective comparative studies are limited and difficult to interpret. Hossain et al. [8] reported reduced transfusion requirements and mortality in women receiving rFVIIa. Overall, rFVIIa appears effective in at least three-quarters of PPH cases, but its true contribution requires prospective randomized studies.

Biological efficacy is assessed via improvement or normalization of coagulation parameters, while clinical efficacy is measured by bleeding control. Hysterectomy is considered a treatment failure; in our study, rFVIIa prevented hysterectomy in only one primiparous patient.

Several studies report reduced rates of embolization and vascular ligation after rFVIIa administration [9,10]. Bouma et al. [11] reported hysterectomy avoidance in 76% of cases. Despite promising results, available studies

are low-level evidence and do not conclusively demonstrate rFVIIa's benefit in hysterectomy reduction.

No data exist on "early" rFVIIa administration before invasive hemostatic procedures. Optimal dosing is still debated; literature reports 20–120 µg/kg, with unclear dose-response relationships [12,13]. Rare cases required multiple doses: Moscardo et al. reported 9 doses, Boehlen et al. reported 19 doses [14,15]. In our series, rFVIIa was administered intraoperatively, mean time 6 hours 40 minutes (range 3–17 hours).

Timing recommendations suggest rFVIIa use for persistent diffuse bleeding despite uterotonics and massive transfusion, prior to last-resort hysterectomy, or when embolization fails or is unavailable [6,9]. rFVIIa may be administered prophylactically before embolization or ligation, or curatively as last resort before hysterectomy.

Conclusion

Although rFVIIa shows promising efficacy and safety in obstetric hemorrhage, randomized controlled trials are needed to confirm these results, identify optimal dosing, and assess potential early use to avoid hysterectomy. In life-threatening therapeutic deadlocks, rFVIIa may complement existing strategies in severe PPH management.

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