

Role of Recombinant Activated FVII in Severe Post-Partum Haemorrhage

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ABSTRACT

In Pakistan, improvement of health care structure and evolution of perinatal care, have led to momentous drop in pregnancy related deaths, however obstetrical haemorrhage maintains to be the principal cause of maternal mortality. The aim of this study was to probe the utilization of activated, and recombinant, Factor VII (rFVIIa) in cases of severe postpartum haemorrhage (PPH). This study was carried out at Unit 2 of Obstetrics & Gynaecology Department of Sir Ganga Ram Hospital (Fatima Jinnah Medical University), Lahore, over a period of 10 weeks, from 15/01/2023, to 31/03/2023. Fifteen females with severe PPH who were treated with rFVIIa were included in this study. The overall observed median and mean blood loss were 8639 mL and 11835 mL respectively. The management prior to rFVIIa involved trans-arterial embolization in five patients, while three of them had hysterectomy. One patient had one single dose, two of them had two doses, three of those patients had four doses, two patients had five plus doses, and a single patient had twenty plus doses of rFVIIa. The mean (\pm SD) of single dose was at 81.60 ± 16.25 μ g/kg. Fourteen of those females could survive, however one of them died due to complication. The cause of that death was uterine rupture, and the quantum of haemorrhage in that case of death, was 6428–43 810 mL. This may, therefore, lead us to conclude that, irrespective of the fact whether a patient would survive or otherwise, much depends upon her general health and proceeding rFVIIa infusion, rather than haemorrhage. Four of those females presented thromboembolic events post rFVIIa management deep vein thrombosis (DVT), DVT plus pulmonary embolism (PE), PE and acute myocardial infarction (MI). This study revealed that rFVIIa infusion had promising effects for severe PPH and markedly reduced the maternal mortality.

Keywords: Post-Partum Haemorrhage, Hystectomy, rFVIIa, thromboembolism

INTRODUCTION

In Pakistan, improvement of health care structure and evolution of perinatal care, have led to momentous drop in pregnancy related deaths, however obstetrical haemorrhage maintains to be the principal cause of maternal mortality.

The recognised guidelines in the management of critical bleedings in obstetrics field, state that severe intrapartum / post-partum haemorrhage would occur in approximately one case in three hundred pregnant female¹. It is recommended that the shock index (SI) is more than 1.5, while where the score of obstetric disseminated intravascular coagulation (DIC) occurs equal to, or more than 8, the patient should be deemed to have serious condition regarding haemorrhage in obstetrics. It may also be suggested that an emergency shifting of the patient be arranged to a tertiary care unit for undergoing of abrupt blood transfusion and DIC management². In case of haemostasis is not reached despite of managements like ligation / embolization of the supracervical, then complete hysterectomy would be suggested³.

rFVIIa is suggested for inclined bleedings in patients carrying haemophilia with inhibitors, Vonwillebrand disease, Glanzman thrombasthenia, and congenital factor FVII deficiency. Considering the fact that rFVIIa carries vigorous haemostatic outcome, it is anticipated to be a useful treatment for critical bleeding in obstetrics^{4,5}. rFVIIa is regularly used in patients carrying severe PPH since early 2000 for whom haemostasis is not obtained despite several attempts. Several studies have been conducted in more developed countries regarding haemorrhage in obstetrics, and the utility of rFVIIa has been defined. Different registry projects from more developed countries have presented hopeful outcomes regarding usefulness of rFVIIa against severe PPH, however rFVIIa escalates the probability of thromboembolism. It is therefore observed that any management with rFVIIa would require adequate procedures for safeguarding against hostile drug reactions⁶. FVIIa usage for PPH is not regularly practiced, and it is, therefore, not anticipated that adequate information regarding rFVIIa's actual usage would be taken. In order to contemplate this, data was gathered regarding usage of rFVIIa in managing patients with severe PPH. This study has gauged the effectiveness, safety, and suitable dosing regimens of rFVIIa. This study has further suggested usage of rFVIIa in certain situations in PPH.

MATERIAL AND METHOD

This study was carried out at Unit 2 of Obstetrics and Gynaecology Department of Sir Ganga Ram Hospital (Fatima Jinnah Medical University), Lahore, over a period of 10 weeks, from 15/01/2023, to 31/03/2023. Fifteen females with severe PPH who were treated with rFVIIa were included in this study. The overall observed median and mean blood loss were 8639 mL and 11835 mL respectively. The information regarding patient age, body weight, gestational week at delivery, extend of haemorrhage, PPH causes, management for PPH, blood product doses and concomitant drugs were collected. The primary intervention to control severe PPH saved many patients. As a secondary intervention, the correlations between pre-dose conditions and haemostatic effects were evaluated. Information on adverse drug reactions such as thromboembolism was noticed. After every such dose regarding reducing, stopping, unchanged, or worsening, the obstetricians evaluated haemostatic effects.

RESULT

Table 1 presents the characteristics of patients including age, body weight, gestation at delivery, parity, mode of delivery, and causes of PPH. Figure 1 shows the treatment of PPH before rFVIIa. Management prior to rFVIIa consisted of trans-arterial embolization in 05 patients and hysterectomy in 03.

Table 1: Characteristics of patients' management with rFVIIa and causes of PPH

	Mean \pm SD	Minimum	Medium	Maximum
Age (Years)	33.3 \pm 5.21	20	33	42
Body weight	60.3 \pm 9.56	31	60	87.2
Gestation at delivery	37.1 \pm 40.04	17	38	41
Parity n(%)				
Primipara	8			
Multipara	61			
Delivery Mode %				
Vaginal delivery	37			
Cesarean section	63			
Causes of PPH %				
Uterine atony	30			
Haematoma at the vaginal delivery	11			
Abruption placenta	10			
Placenta accreta	9			
Eclampsia	6			
Amiontic Fluid embolism	6			
Placenta Previa	5			

One patient had only one dose, two infused two doses, three infused four doses, two had five plus doses and only one patient had twenty plus doses of rFVIIa. The mean (\pm SD) single dose was observed to be $81.60 \pm 16.25 \mu\text{g/kg}$. Fourteen of those females survived, one of them passed away because of complication. The root cause of her death was uterine rupture, and around 5000 mL blood was lost.

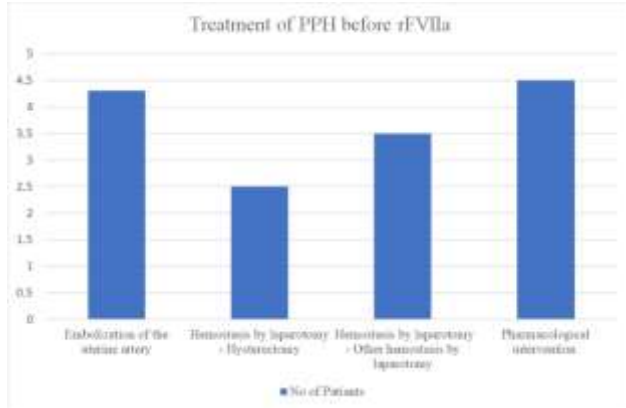


Fig 1: Treatment of PPH before rFVIIa

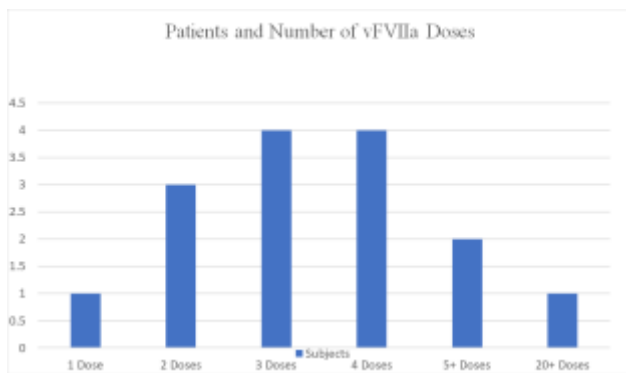


Fig 2: Patients and Number of vFVIIa Doses

DISCUSSION

This study showed a promising result and confirmed the objective that rFVIIa is useful tool in severe cases of PPH who are non-responsive to standard therapy. rFVIIa is established to be useful while using a standard dosage recommended Internationally. Meta-analysis that consisted of a total of two hundred and seventy-two females with PPH from global registries and presented that rFVIIa has been a helpful tool either impeding, or lessening haemorrhage in maximum females. In the present study, mortality estimation, that is associated with rFVIIa, was non-conclusive, which was primarily due to the lesser number of patients^{7,8}. No distinct trend was observed in the haemorrhage or any of its cause, in the deceased female.

It can, therefore, be construed that patient survival was more reliant on patient’s general state, both pre and post rFVIIa usage, instead of quantum of blood loss preceding rFVIIa usage. Nevertheless, hysterectomy, or IVR, is the recognised mode of choice where conditions so allow, it seems to be suitable to think about rFVIIa prior to those interventions, rely upon the generally observed condition of the patient. The present study indorsed the proposition that multiple factors, including the rectification of acidosis and hypothermia, and quantity of fibrinogen, may have bearing on enhancing the usefulness of rFVIIa. The present study, which is descriptive in nature, may be able to offer a recommendation for the management of PPH with rFVIIa. Furthermore, management through rFVIIa should be taken into

account prior to the performance of the aforementioned recognised interventions, in case patient’s generally prevailing condition is tremendously poor⁹. If management through rFVIIa is opted for severe PPH, and the generally prevailing state of the patient, her affordability, coupled with the available potential of the health care system, is advised to be kept kept under consideration. Based on the above-narrated facts, it would be inappropriate to strike a uniformly recognised selection criteria for the application of rFVIIa, exclusively treatment on the quantum of haemorrhage and management history. In order to avoid the incidence of thromboembolism owing to undiscerning application of rFVIIa, an enhanced knowledge about patient’s selection for the application of rFVIIa is advised to be considered. In this study, venous thromboembolism was observed in four of the studied females. There four females got diagnosed at an early stage, received treatments, and their adequate recovery was confirmed. It was also observed that thromboembolism impediments were limited, and results of this study insinuated that development of thromboembolism may well depend upon with the usage of certain drugs as well. It could, therefore, be concluded that application of rFVIIa, coupled with tranexamic acid, may be prone to venous thromboembolism. It is therefore suggested that increased application of tranexamic acid may well be avoided. Application of rFVIIa is not approved currently for the management of PPH in Pakistan.

Owing to the fact that, there is an excessively less digits of females with PPH, and who are managed with rFVIIa, and also, owing to the fact that PPH carries tendency of instantly developing in the course of pregnancy/delivery, and to further progressing speedily, it is immensely strenuous to carry out probable clinical studies¹⁰. Finally, based on both, the literature review, as well as own experience, the present study included some suggestion on the therapeutic role of rFVIIa in the management of PPH.

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