Unlabeled Use of rFVIIa in Post Cardiac Surgery in Infants with Congenital Heart Disease: Pilot Study in One Institution

MANAL M. TBEILEH, M.D. 1; GAMAL GOUDA, M.D. 2; OSAMA ABO ALFOTOH, M.D. 3; SAMY YOUSEF, M.D. 1 and MERVAT KHALIL, M.D. 4

The Departments of Pediatrics, PICU-Chest Disease Hospital 1, Emergency, Mubarak Al-Kabee Hospital 2, Anesthesiology, PICU-Chest Disease Hospital 3 and Neonatology, NICU-Maternity Hospital 4, Kuwait

Abstract

Background: Recombinant activated factor VII (rFVIIa) has been used as a “rescue” for patients with coagulopathies. Usage in normal persons had been implicated in bleedings after major surgeries like cardiac bypass surgeries. Only recently, few case reports were published to use rFVIIa in pediatric age group and even less in pediatric patients especially in younger ages with congenital heart diseases.

Purpose: To report our experience in using rFVIIa as a “rescue” drug to control bleeding in infants who had cardiac bypass surgeries for congenital heart disease.

Data Source: Medical records of ten pediatric patients who underwent cardiac bypass surgeries to repair various congenital heart diseases were randomly studied. The study is a Retrospective Pilot study.

Results: Post cardiac bypass bleeding was not controlled effectively by rFVIIa alone in infant patients.

Conclusion: Further studies are needed to clarify the role of rFVIIa in controlling bleeding.

Key Words: Recombinant factor VIIa – Pediatrics – Congenital heart disease – Cardiac bypass surgery.

Introduction

RECOMBINANT factor VIIa (rFVIIa) is a hemo-static agent indicated for the treatment and prevention of bleeding in patients with factor VII deficiency or congenital factor XI deficiency or hemophilia with inhibitors to coagulation factors VIII or IX [1]. Recombinant FVIIa achieves hemostasis by binding to tissue factor (TF) and activated platelets at sites of tissue injury or vascular disruption; this activates factor X and IX, resulting in thrombin generation and initiation of a fibrin clot. A TF-independent mechanism may also contribute to hemostasis, in which rFVIIa is able to directly activate factor X on the surface of activated platelets or monocytes, independently of TF, leading to thrombin generation. Because of its effectiveness in clot formation, there has been increasing use of rFVIIa for the treatment and prevention of bleeding in nonhemophiliac patients.

The scientific literature is expanding, with reports and clinical studies describing the successful use of rFVIIa in patients with almost every type of clinical bleeding, including trauma, cardiac surgery, liver failure, intracranial hemorrhage, surgical bleeding, and severe coagulopathy. Optimal timing, dosage, and efficacy of rFVIIa treatment for these diverse indications remains uncertain, and reports of serious thromboembolic complications raise concern about the safety of this drug in nonhemophiliac patients [2,3]. Few studies have looked at the use of rFVIIa in pediatric nonhemophiliac patients [4], thus we sought to describe the clinical practice of off-label rFVIIa use in a tertiary pediatric hospital.

Abbreviations:

APTT : Activated partial thromboplastin time.
ASO : Arterial switch operation.
AVSD : Atrioventricular septal defect.
CoA : Coarctation of aorta.
Cryo : Cryoprecipitate.
TA : Truncus arteriosus.
TGA : Transposition of great arteries.
TOF : Tetralogy of Fallot.
PICU : Pediatric intensive care medicine.
PT : Prothrombin time.
rFVIIa : Recombinant activated factor 7.
VSD : Ventricular septal defect.
NICU : Neonatal intensive care unit.
PICU : Pediatric intensive care medicine.

Correspondence to: Dr. Manal Tbeileh, E-mail: manjam4@yahoo.com
Material and Methods

Our goal was to report our institutional experience with recombinant factor VIIa for the treatment of bleeding in non hemophiliac children who underwent cardiac surgery for congenital heart disease.

The study is a retrospective pilot study of ten patients who underwent cardiac bypass surgery for congenital heart diseases and received rFVIIa to control bleeding during post-operative period.

A retrospective study of ten patients randomly chosen and reviewed their charts who underwent bypass cardiac surgery for repair of congenital heart diseases of different kinds, all of whom received activated recombinant factor VII to control chest drainage post-operatively. Dose ranges from 5.0 to 110 microgram per Kg body weight.

Ten infants (7 females and 3 males) were studied whose ages ranged from 2 months to 10 months, Table (1). Four cases were repair of AVSD, three cases VSD closure, one case repair of TOF, one case TA type 1 repair and one case ASO for TGA. The patients were following 3 criteria: rFVIIa treatment course <6 hours (up to 3 doses), survival for at least 24 hours after the last dose of rFVIIa, and treatment for bleeding, not prophylaxis, or prevention of bleeding. “Treatment” will be identified as Blood-product administration before rFVIIa treatment.

Data collection:

Coagulation status Prothrombin time (PT), activated partial thromboplastin time (PTT), platelet count, hematocrit was collected, within 4 hours before and after the rFVIIa dose. If the patient received more than 1 dose, the impact of rFVIIa on bleeding indices will be determined by collecting the first available laboratory values after the treatment course was initiated. A patient will be deemed to have a separate treatment course if doses were separated by >24 hours. Blood-product administration will be defined as the cumulative total volume of packed red blood cells (PRBCs), platelets, fresh-frozen plasma (FFP), and cryoprecipitate that were given 24 hours after the administration of rFVIIa. Chest tube drainage before and after giving rFVIIa are compared as a direct effect of giving rFVIIa. Data was analyzed using Microsoft Business Intelligence Analysis (Power Pivot).

All patients underwent from PICU-chest disease. Hospital Kuwait during 2011.

Results

Patients were received in PICU after surgery and were given rFVIIa to control chest tube drainage. The drainage decreased after 1st dose but did not improve after 2nd dose, Fig. (1). The longer the Bypass time the more drainage was there.

The need for PRBC, FFP and Cryo reduced after 1st and 2nd dose of rFVIIa, Figs. (2-4), but there was no significant increase in hematocrit, Fig. (5).

Platelets counts trend was dropping after the second dose of rFVIIa, as shown in Fig. (5). Platelet transfusion, hence was needed to control bleeding after 2nd dose, Fig. (4).

Table (1): Details of patients studied.

<table>
<thead>
<tr>
<th>Gender</th>
<th>Diagnosis</th>
<th>Age in months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>TOF repair</td>
<td>6</td>
</tr>
<tr>
<td>Female</td>
<td>AVSD repair</td>
<td>10</td>
</tr>
<tr>
<td>Female</td>
<td>VSD closure, debanding</td>
<td>6</td>
</tr>
<tr>
<td>Male</td>
<td>AVSD repair</td>
<td>5</td>
</tr>
<tr>
<td>Male</td>
<td>TA repair</td>
<td>4</td>
</tr>
<tr>
<td>Female</td>
<td>VSD closure</td>
<td>5</td>
</tr>
<tr>
<td>Female</td>
<td>VSD repair</td>
<td>4</td>
</tr>
<tr>
<td>Female</td>
<td>CoA repair</td>
<td>4</td>
</tr>
<tr>
<td>Female</td>
<td>AVSD repair</td>
<td>2</td>
</tr>
<tr>
<td>Male</td>
<td>ASO</td>
<td>2</td>
</tr>
</tbody>
</table>

Fig. (1): Chest tube drain tracking after 1st and 2nd dose of rFVIIa.

Fig. (2): Transfused PRBC tracking after 1st and 2nd dose of rFVIIa.
Discussion

In our pilot study, the drain was not well controlled with rFVIIa treatment and also did not decrease the need for Platelets transfusion. This could be explained by the less case number, the heterogenity of the diagnoses and the longer the bypass time.

The chest tube drainage was decreasing after the first dose but not the second dose; this raise the doubts about the benefits of repeating rFVIIa dosing. Platelets were dropping during the treatment period and also this raise the doubt whether this drop was related to the rFVIIa treatment or due to consumptive thrombocytopenia. This relation effect cannot be studied fully in this study.

Although rFVIIa is generally well tolerated, there are concerns regarding the risks of thromboembolic events. No thromboembolic events happened during the treatment and no mortality among the studied cases.

The optimal dose of rFVIIa in cardiac surgery remains unclear. Studies in other specialities have demonstrated a significant reduction in blood loss with doses of 20 to 80 gg/kg when used prophylactically on healthy patients [2-7].

Postoperative hemorrhage is a common complication in cardiac surgery, and it is associated with a considerable increase in morbidity, mortality, and cost. Recombinant activated factor VII (rFVIIa) is an emerging hemostatic agent, increasingly used in cardiac surgery. Recombinant FVIIa as a “rescue” therapy is used in hemorrhage refractory to other treatments. Its efficacy has been measured predominantly by studying subsequent blood loss as determined by chest tube drainage and transfusion requirements and it seems that rFVIIa is a potent hemostatic agent, particularly when used as a rescue therapy. However it has rarely been studied in isolation as most case reports or studies was dealing with patients who have received significant volumes of blood products prior to treatment.

Conclusion:

The potency of recombinant factor VIIa is doubtful as a pro-hemostatic agent as well as a “rescue” drug for the cessation of life-threatening refractory hemorrhage associated with cardiac surgery in infants.
Recommendations:

Although off-label use of rFVIIa has been reported in cardiac surgery, this has been published predominantly as case reports or series. The use of rFVIIa in patients experiencing refractory postoperative hemorrhage seems promising and relatively safe in pediatric and adult patients. However, further research is required to definitively establish its clinical utility in the postoperative cardiac infant patients.

References


