Recombinant activated factor VII for uncontrolled bleeding postcardiac surgery

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A retrospective observational study to review the safety and efficacy of rFVIIa in persistent hemorrhage in post cardiac surgical patients.

Methods: **Patients who had bleeding of 3 ml/kg/h or more for 2 consecutive hours after cardiac surgery were arranged into two groups; control group, who received conventional treatment and rFVIIa group, who received conventional treatment and rFVIIa.**

Results: **There was no significant difference in demographic and surgical characteristics of both groups. The chest tube output significantly decreased in the rFVIIa group compared to the other group 4 hours after admission {1.4 (IQR: 1–2.2) ml/kg/h vs 3.9 (IQR: 3.1–5.6) ml/kg/h; $p = 0.004$} and continues to be significant till 9 hours after CSICU admission {0.6 (IQR: 0.4–1.1) ml/kg/h vs 1.9 (IQR: 1.2–2.2) ml/kg/h; $p = 0.04$}. The median number of blood products units transfused to rFVIIa group was significantly lower compared to control group in the period from 3–12 hours after CSICU admission. 13 (5.5%) patients in rFVIIa group had Thromboembolic adverse events (TAE) compared to 7 (2.4%) patients in other group $p = 0.27$. 8 patients in the rFVIIa group needed reexploration compared to 19 patients in the other group, $p = 0.01$. No significant difference was noticed between the 2 groups regarding: new onset renal failure, median number of mechanical ventilator days, pneumonia, mediastinitis, ICU and hospital lengths of stay, survival at 30 days and at discharge.**

Conclusion: **In this analysis, rFVIIa succefully reduced the chest tube bleeding and blood products transfused during severe post cardiac surgical bleeding. However, safety of rFVIIa remains unclear. Prospective controlled trials are still needed to confirm the role of rFVIIa.**

Keywords: Bleeding, Cardiac surgery, rFVIIa

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Introduction

Despite improvements in surgical skills and strategies, bleeding remains a problem in cardiac surgery. Bleeding is also a significant cause of morbidity and mortality, prolonged hospital stay, and increased cost [1,2]. Increased risk of postoperative complications as well as reduced short- and long-term survival is associated with the transfusion of red cells that have been stored for >2 weeks in patients undergoing cardiac surgery [3]. Other reports argue that for patients undergoing cardiac surgery, bleeding contributes to mortality through mechanisms unrelated to blood transfusion [4]. Efforts to minimize the use of limited resources such as blood products are essential and the most obvious and probably the most effective strategy is to improve surgical techniques and hemostatic management.

Recombinant activated factor VII (rFVIIa) is a potent prohemostatic agent currently approved for bleeding in patients with hemophilia or other congenital hemostasis and coagulation defects. Over the past years, the estimated number of patients treated with rFVIIa has grown rapidly, mainly for off-label indications, including excessive bleeding after trauma and cardiac operations [5–10].

The rFVIIa promotes hemostasis by enhancing the generation of thrombin on platelets. rFVII complexes with all available tissue factor to activate factor X directly and induce thrombin generation. This results in the formation of a tight and stable fibrin plug that is resistant to premature fibrinolysis [11].

The aim of our work is to present our experience of the use of rFVIIa in treating intractable hemorrhage postcardiac surgery in adult patients with respect to its efficacy and safety.

Abbreviations

rFVIIa	recombinant activated factor VII
CSICU	Cardiac Surgical Intensive Care Unit
TAE	Thromboembolic Adverse Events
CVA	Cerebrovascular accidents
MI	Myocardial infarction
PE	Pulmonary embolism
DVT	Deep venous thrombosis
ml/kg/h	milliliter/ kilogram/hour
IQR	Interquartile range
aPTT	activate partial thromboplastin time
ACT	activated Clotting time
INR	international normalized ratio
gm/l	gram/Liter
mcg/kg	microgram/ kilogram
CPB	cardiopulmonary bypass
FFP	fresh frozen plasma
Cryo	cryoprecipitate
ICU	intensive care unit
35.5 C	35.5 degree celsius
mg/dl	milligram/deciliter
RBCs	red blood corpuscles
TAFI	thrombin activation fibrinolysis inhibitor
PT	pro-thrombin time
RCT	Randomized Controlled Studies
FEIBA	Factor Eight Inhibitor Bypass Activity

Materials and methods

The study was conducted in the Cardiac Surgical Intensive Care Unit (CSICU), King Faisal Heart Center, King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia.

Patients

Retrospectively, the medical charts of all adult patients ($n = 4856$) who had cardiac surgery in the period between February 2004 and December 2013 were screened for the occurrence of postoperative bleeding in the intensive care unit (ICU). Patients who were younger than 18 years, those who had a primary coagulation defect, pregnant women, those who received rFVIIa in the operating room, those having surgery for the correction of congenital heart diseases, requiring a mechanical circulatory support device, or extracorporeal membrane oxygenation in the operating room were excluded ($n = 42$). All patients who had chest tube bleeding of $\geqslant 3$ mL/kg/h for $\geqslant 2$ consecutive hours postadmission to CSICU from the operating room ($n = 441$) were included in the study and arranged in two groups: control group [those who received conventional treatment; Fig. 1 boxes 2, 4, and 6 ($n = 207$)]; and the rFVIIa group [those who received conventional treatment and rFVIIa; Fig. 1 boxes 2, 4, 6, and 7 ($n = 234$)].

The study protocol was approved by King Faisal Research Center and Medical ethics committee. Being a retrospective chart review study, consent was waived by the ethical committee.

The patients' demographics, preoperative comorbidities, preoperative anticoagulation, priority of surgery, type of surgery, cardiopulmonary bypass time (CPB), aortic cross clamp time, and surgical re-exploration were collected. The European System for Cardiac Operative Risk Evaluation II score system was used to assess the severity for each patient [12].

Coagulation parameters (international normalized ratio, activated partial thromboplastin time, activated clotting time, and fibrinogen levels) and platelets count were measured on admission

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