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BRIEF REPORT – OPEN ACCESS



# Management of Patients with Factor VII Deficiency in Surgery: A Single-center Experience

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ABSTRACT

Factor VII deficiency is a rare condition characterized by a broad spectrum of clinical phenotypes, from asymptomatic status to severe, life-threatening bleeding, such as central nervous system or gastrointestinal bleeding. Factor VII deficiency is usually diagnosed after a bleeding attack or as a result of screening tests performed in cases with a family history. Importantly, bleeding may also occur in patients with a factor level of 20% to 50%. This report describes the approach to management before, during, and after surgery used in 5 patients with varying factor levels. The use of recombinant factor VIIa (15–30 µg kg) was required in 3 of the patients. No bleeding or thromboembolism was observed in any of the 5 patients.

**Keywords:** FVII deficiency, recombinant factor VIIa, surgery

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## INTRODUCTION

Hereditary factor VII deficiency is the most common of the rare bleeding diseases with autosomal recessive inheritance. The prevalence is approximately 1/500,000. Coagulation factor VII (FVII) is a K vitamin-dependent serine protease produced by the liver. Its role in coagulation begins with its interaction with tissue factor. Only small amounts of FVIIa are required to trigger clotting. The FVII plasma half-life is 2.5–5 hours (1, 2). Hereditary FVII deficiency is characterized by a broad spectrum of clinical phenotypes, from asymptomatic status to severe, life-threatening bleeding, such as central nervous system or gastrointestinal bleeding. While patients with a FVII level of <2% may present with severe bleeding, patients with a factor of >20% are often asymptomatic. The International Society on Thrombosis and Haemostasis has reclassified FVII deficiency as severe: FVII <10%, risk of spontaneous major bleeding; moderate: FVII 10% to 20%, risk of mild spontaneous or triggered bleeding; and mild: FVII 20% to 50%, mostly asymptomatic disease. However, bleeding may also occur in patients with a factor level between 20% to 50% (2, 3).

Hereditary FVII deficiency is usually diagnosed after a bleeding attack or with screening tests in cases with a family history. However, FVII deficiency may also be detected as an incidental finding, particularly in asymptomatic cases. Patients with isolated prothrombin time prolongation can be diagnosed with the condition if the FVII level remains low after dilution correction (2–4).

Several therapeutic options are currently available for the treatment of hereditary FVII deficiency: i) recombinant activated factor VII (rFVII), ii) factor VII derived from plasma, iii) fresh frozen plasma, and iv) prothrombin complex concentrates. However, bleeding risk prediction and treatment options can be difficult in cases of acute spontaneous bleeding episodes or surgery. The 2 most important challenges are bleeding and thromboembolism due to replacement therapy. These problems lead to prolonged hospitalizations and greater costs. Evaluation of the risks and benefits is complex. As it is a rare disease, cooperation between the hematology and surgical teams is very important.

This report is presented to share and discuss the management of patients with hereditary FVII deficiency before, during and after surgery as performed in our clinic.

## MATERIALS and METHODS

The records of patients diagnosed with factor VII deficiency who were followed up by the Trakya University Faculty of Medicine Department of Hematology during the period of 2017–2020 were reviewed. The patient data in the hospital information system and patient files indicated that 5 patients had a history of surgery. The preoperative, perioperative, and postoperative data and demographic details, as well as the treatment and side effects were analyzed.

**Table 1.** Demographic information and clinical findings of the patients

| | Demographic details and clinical findings | | | | |
|---|---|---|---|---|---|
| | **Case 1** | **Case 2** | **Case 3** | **Case 4** | **Case 5** |
| Age (years) / Gender | 23/Female | 48/Female | 29/Male | 31/Male | 20/Male |
| PT (sec) | 21.9 | 24.9 | 28.9 | 15.4 | 15.4 |
| Mixing PT (sec) | 13.6 | 13.5 | 13.5 | 13 | 13.7 |
| FVII level (%) | 9 | 1.9 | 2 | 47 | 26.4 |
| Symptomatic bleeding history | Nose bleed | - | Nose bleed at circumcision | - | - |
| Bleeding during circumcision | - | - | Yes | No | No |
| History of rFVII use | + | - | - | - | - |
| History of tranexamic acid use | + | - | + | - | - |
| Surgery | Cesarean section | Carpal tunnel syndrome | Rhinoplasty | Cholecystectomy | Nasal angiofibroma |
| Hospitalization (days) | 3 | 3 | 5 | 2 | 7 |
| rFVII use (15–30 µg/kg) (days) | 1 | 2 | 3 | None | None |
| Total dosage of rFVII (mg) | 4 | 10 | 12 | None | None |
| Average daily dosage of rFVII (mg) | 4 | 5 | 4 | None | None |
| Fresh frozen plasma (mL/kg) | None | None | None | None | 10 |
| Postsurgical bleeding | None | None | None | None | None |
| Thromboembolism after surgery | None | None | None | None | None |

PT: Prothrombin time; rFVII: Recombinant activated factor VII

## RESULTS

Five patients with FVII deficiency had a surgical operation. The average age was 30.2 years (range: 20–48 years). Two patients were female. Three patients were classified as severe deficiency and 2 patients were classified as mild deficiency according to the International Society on Thrombosis and Haemostasis classification system. There was only 1 patient with a history of previous rFVII use. One of the 3 male patients had a history of extended bleeding after circumcision. One patient was followed up without treatment based on the FVII level. Fresh frozen plasma was administered to 1 patient as a result of epistaxis that did not regress with local treatment and a decrease in hemoglobin level, despite a factor VII level that was >20%. Three patients required rFVII (15–30 µg/kg) during surgery due to the factor level and severity of deficiency. The first doses were administered in the operating room just before the surgical procedure. Because of the plasma half-life, rFVII was administered at 3–4-hour intervals, taking into consideration the increased risk of bleeding based on the severity of the surgery and the procedures required for the surgical field during patient follow-up. The perioperative and postoperative measures were carefully planned prior to surgery by the clinician in consultation with the patient. No bleeding or thromboembolism was observed in the patients following replacement treatment. The average daily dose of rFVII was 4 mg for an average of 2 days. The average length of hospitalization in the group was 4 days, and 3.6 days for patients who received FVII therapy (Table 1).

## DISCUSSION

Unless replacement therapy is used, surgery for patients with FVII deficiency includes a risk of intraoperative or postoperative bleeding. The general approach is to provide maintenance therapy to patients who will undergo surgery, those with FVII activity of <10% to 15%, and those with a history of recurrent bleeding. Successful results with the use of recombinant activated FVII (rFVIIa, NovoSeven; Novo Nordisk Health Care AG, Zurich, Switzerland) have been reported in many cases, but there is no clear optimal treatment regimen. The common approach is to administer rFVII at a dose of 15–30 µg/kg at 4-hour intervals (5, 6).

Though rare, a deficiency of FVII may cause life-threatening bleeding in the perioperative and postoperative periods. The risk for patients who are not yet diagnosed may be quite significant. The treatment and follow-up of patients after diagnosis is also particularly important, given the risk of bleeding and side effect profiles that may occur after surgery. Patients should be evaluated preoperatively and the surgical team and the anesthesia team must be informed about a hereditary FVII deficiency. If rFVII administration is required, the first dose should be given immediately before surgery in the operating room. The expected duration of the surgery should be communicated, and the dose frequency should be adjusted according to the FVII half-life. Possible causes of bleeding that could occur in the surgical field in the postoperative period should also be part of a multidisciplinary planning discussion, as well as factors that could cause a thromboembolism.

In our center, 15–30 µg/kg rFVII treatment was planned for administration in the operating room just before the surgical procedure. Then, rFVII administration was continued based on the plasma half-life, the procedure, and the risk of bleeding and the procedures to be applied to the surgical field during follow-up. The average duration of treatment for the 3 patients who received rFVII was 2 days. The average daily dose of rFVII was 4 mg. One patient was monitored without treatment because the

factor VII level was >20%. Fresh frozen plasma was given to 1 patient following epistaxis that did not regress with local treatment and a decrease in hemoglobin level, although the factor VII level was >20%. No bleeding was observed in the postoperative period, and venous thromboembolism did not develop in any patient during long-term follow-up. The average length of hospitalization was 3.6 days for the patients who received rFVII therapy. No side effects were observed.

We believe that it is valuable to share reports of case management, particularly for rare hereditary diseases, such as factor VII deficiency. The scarcity of cases in the literature and the heterogeneity of FVII deficiency are important contributors to the lack of a standard approach. The diversity of prophylaxis approaches, the use of rFVIIa in severe deficiency, and the complications that could occur should be kept in mind and carefully managed.

**Informed Consent:** Written informed consent was obtained from patients who participated in this study.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept – UD, EGÜ; Design – UD, EGÜ; Supervision – EGÜ; Data Collection and/or Processing – VB, SKG; Analysis and/or Interpretation – UD; Literature Search – HOK, UD; Writing – UD; Critical Reviews – AMD.

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