

Clinical Efficacy of Recombinant Activated Factor VII for Haemophilia Patients Requiring Dental Treatment

Mihaela Maria Ghinea¹, Zizi Niculescu², Stoian F³, Gabriela Lilios⁴

Constanta, Romania

Abstract

Introduction. Haemophilia is a group of sex-related recessive-transmission hereditary genetic disorders characterized biologically by quantitative deficit of either factor VIII or factor IX. Product NovoSeven (rFVIIa) is an important alternative treatment for any form of hemorrhage in haemophilia patients.

Material and method. This study surveys 7 haemophilia patients admitted in the Department of Haematology at the Emergency Clinical County Hospital Constanța for episodes of oral cavity hemorrhage (3 cases), or in preparation for dental interventions (dental extractions or other dental surgery interventions – 4 cases).

NovoSeven (rFVIIa) was administered in intravenous drip or bolus.

Results and discussions. Treatment response was considered efficient in all 7 cases. In the 3 cases admitted for prolonged bleeding following dental extraction, administration at 3-hour intervals for 24 hours was necessary in 2 cases, and for 36 hours in 1 case. In the 4 cases in preparation for dental extractions and dental surgery, one dose before and after the intervention was sufficient.

Prothrombine Time (PT) is useful in monitoring this treatment for haemophilia patients.

Conclusion. NovoSeven (rFVIIa) treatment is efficient in controlling hemorrhagic manifestations occurring after dental interventions in haemophilia patients and in the prophylaxy of post-dental extraction bleeding.

Introduction

Haemophilia is a group of sex-related recessive-transmission hereditary genetic disorders characterized biologically by quantitative deficit of either factor VIII (A haemophilia) or factor IX (B haemophilia).

Haemophilia occurs exclusively in men, while women are only carriers.

Instant hemorrhage in haemophilia is erroneously interpreted because the least form of hemorrhage, however insignificant, is based on a non-apparent traumatic factor [3]. The tendency to hemorrhage is not lost, but it continues during the entire life.

Hemorrhage intensity depends on residual factor VIII–respectively factor IX– concentration. The factor level specifies the disease type and gravity. Howell time and partial thromboplastine time are prolonged. Bleeding time, Quick time (clotting time), and thrombocyte levels are normal.

A serious form of hemorrhage may appear in an adult with less severe haemophilia during surgery or major trauma; this hemorrhage is a first symptom of the disorder.

rFVIIa (NovoSeven product) contains clotting factor VII obtained by recombinant DNA technology. This aspect excludes the possibility of disease transmission by means of contaminated blood.

rFVIIa is indicated as first-hand treatment for patients having developed inhibitors of clotting factors VIII or IX [5]. Haemophilia patients having these inhibitors run the risk of uncontrolled bleeding especially during surgery. NovoSeven product is an important alternative treatment of any kind of hemorrhage occurring in haemophiliac patients [1].

Material and method

This study surveys 7 haemophilia patients admitted in the Department of Haematology at the Emergency Clinical County Hospital Constanța for episodes of oral cavity hemorrhage (3 cases), or in preparation for dental interventions (dental extractions or other types of dental surgery – 4 cases).

The survey has extended retrospectively over a period of 2 years.

NovoSeven (rFVIIa) was administered in intravenous drip or bolus. Except for the case of

¹ MD, PhD, Associate Professor, Department of Internal Medicine, Faculty of Medicine, Ovidius University Constanța, Romania

² MD, PhD, Associate Professor, Department of Internal Medicine, Faculty of Medicine, Ovidius University Constanța, Romania

³ MD, Teaching Assistant, Department of Internal Medicine, Faculty of Medicine, Ovidius University Constanța, Romania

⁴ MD, PhD, Associate Professor, Department Physiology, Faculty of Medicine, Ovidius University Constanța, Romania

dental extraction preparation, when a dose of 60µg/kg/body was administered just before the intervention and another dose 2 hours after, in the other 3 cases the doses were administered at 3-hour intervals for 24-36 hours (until symptom amelioration).

The following parameters were observed:

- clinical evolution of hemorrhage;
- laboratory tests: prothrombine time (PT), activated partial thromboplastine time (aPTT);
- side effects of the treatment.

Results and discussions

1. Clinical evolution of hemorrhages

Controlling the hemorrhagic syndrome was a criterion of appreciation for the clinical efficiency of rFVIIa treatment. Treatment response was considered efficient in all 7 cases. In the 3 cases of extensive bleeding following dental extractions, rFVIIa administration was necessary at every 3 hours for a period of 24 hours (2 cases) and for a period of 36 hours (1 case).

Most studies argue that rFVIIa treatment response is more efficient when the product is administered soon after hemorrhage onset [2].

In the 4 cases in preparation for dental extraction and dental surgery, administration of one dose of rFVIIa before and one after the intervention was sufficient. No hemorrhage complication occurred in these cases.

Analyzing the clinical efficiency of rFVIIa in haemophiliac patients in relation to mode of administration and dosage, no significant difference between the modes of administration could be observed, but there is a better response in patients having received a higher total dose in a larger number of applications.

2. Paraclinical follow-up of rFVIIa treatment

For the paraclinical follow-up of rFVIIa treatment the following tests were made: thrombocyte level, prothrombine time (PT), and activated partial thromboplastine time (aPTT).

Selective Bibliography

1. Altisent C., Lozano M., Sol E. et al. Dental extraction using rFVIIa, *Haemophilia*, 2000; 6, 4: 408.
2. Fressinaud E., Sigaud-Fiks M., Boterff C. et al. Use of recombinant factor VIIa (NovoSeven) for dental extraction in a patient affected by platelet-type (pseudo-) von Willebrand disease, *Haemophilia*, 1998; 4: 299.

Tests of prothrombine time (PT), and activated partial thromboplastine time (aPTT) were made one hour after each rFVIIa administration. The two investigative parameters of hemostasis were correlated with clinical amelioration and showed as follows:

- PT was 5 seconds lower than initial level;
- aPTT was 15 seconds lower than initial level.

PT modification was better correlated with clinical response. Therefore, PT is useful in monitoring this treatment for haemophiliac patients.

3. Side effects of the treatment

rFVIIa treatment may cause adverse symptoms, such as cephalaea, pruriginous allergic reactions, blood-pressure alterations, nausea, vomit, pectoral angina, neurological complications, kidney function impairment [4]. No patient in this study was registered with side effects.

Conclusions

1. rFVIIa (NovoSeven) treatment is efficient in controlling hemorrhages occurring after dental interventions in haemophiliac patients.

2. rFVIIa administration has an important role in preventing bleeding in haemophiliac patients expecting dental interventions (especially dental extractions).

3. A dose of 60µg/kg/body of NovoSeven is administered 15-30 minutes before dental surgery to prevent bleeding in dental extraction. Repeated dose is administered only if post-extraction bleeding persists or is aggravated. Post-extraction administration was necessary for the surveyed lot.

4. As concerns mode of administration, rFVIIa therapeutic efficacy was similar in both intravenous drip and bolus. Better results were obtained for a higher total dosage.

5. PT, aPTT, and thrombocyte-level tests are useful in monitoring rFVIIa treatment for haemophiliac patients. As regards the correlation with clinic therapeutic response, PT is the most useful.

3. Ghinea Mihaela Maria, Tatiana Adam. *Hematologie practică*, Ed Muntenia 2002: 193-202.

4. Harrington B. Primary dental care of patients with haemophilia, *Haemophilia*, 2000; 6, suppl. 1: 7-12.

5. Rodriguez-Merchan EC, Lee CA. "Inhibitors in patients with haemophilia." Oxford: Blackwell Science, 2002: 69-87.

Correspondence too: MD, PhD Zizi Niculescu, Department of Internal Medicine, Faculty of Medicine, Ovidius University Constanța, Ilarie Voronca strret, no.7, cod 900684, Romania, e-mail: ziziniculescu@yahoo.co.uk