Successful Hemostasis with Extended Half-life Recombinant Factor VIII in Circumcision

Uzun Etkili Rekombinan Faktör VIII ile Başarılı Sünnet Operasyonu

To the Editor,

Intensified coagulation factor replacement is essential for surgical procedures in people with hemophilia A (HA). It is indicated during surgery and in the postoperative period [1,2]. The efficacy and the safety of PEGylated recombinant human full-length coagulation factor VIII (BAX 855) in prophylaxis and treatment of bleeding episodes have already been reported and its half-life in the circulation was proven to be 1.5 times longer compared to standard half-life FVIII (SHL-FVIII) [3]. Circumcision is a common surgical intervention in approximately half of the world [4,5]. In this report, we aimed to present our experience with extended half-life recombinant FVIII (EHL-rFVIII)-BAX 855 treatment for circumcision in two severe cases of HA.

The first patient was diagnosed at the age of 3 months with severe HA (factor VIII = 0.001 IU/mL=0.1%) with no family history. He started primary prophylaxis twice a week at the age of 17 months; however, his prophylaxis regimen had to be changed to 3 times a week at the age of 5 years old due to frequent bleeding of the elbows. He was enrolled in an EHL-rFVIII clinical trial at 5.5 years old, and the prophylaxis was continued twice a week for 3 years with no bleeding. The second patient was diagnosed at the age of 8 months with severe HA (factor VIII=0.003 IU/mL=0.3%); he had a family history. He began primary prophylaxis twice a week at the age of 15 months. He was enrolled in an EHL-rFVIII clinical trial at 5.5 years old, and prophylaxis was continued twice a week for 3 years with no bleeding. Both patients had no adverse events and no inhibitors during this period. The two patients were circumcised at 8 years old in a pediatric urology clinic. Both patients were hospitalized on the day of circumcision. One patient had phimosis and was hospitalized for 3 days; the other patient was hospitalized for 1 day. Both patients were circumcised under...
local anesthesia using a diathermic knife. Hemostasis control was achieved by tranexamic acid and EHL-rFVIII. Both patients were under prophylaxis at a dose of 45 IU/kg/day twice a week. The circumcisions were performed on the prophylaxis day, and 2 extra EHL-rFVIII doses (50 IU/kg/dose) were used during the prophylaxis regimen. Factor FVIII level was assessed by chromogenic assay on the first day of the circumcision. Factor VIII level was under 0.030 IU/mL for both patients at the beginning and 1.252 IU/mL (125.2%) and 2.180 IU/mL (218%) at 30 min, respectively. Both patients had regular wound healing. No unexpected bleeding or wound infections were recorded. They returned to their routine lives within 7 days.

Circumcision is a cultural and traditional surgical intervention, and many patients want to be circumcised around the world. In previously published series, it was reported that circumcision could be performed with minimal complication rates by using a diathermic knife. In this routine clinical practice, tranexamic acid and SHL-FVIII products have been used for hemostasis with decreasing doses between 4 and 14 days until wound healing occurs, depending on the severity of hemophilia [6,7]. In another protocol in which circumcision was performed under general anesthesia, fibrin glue application with 2–3 days of factor supplementation was found to be sufficient [8]. As we report here, just two extra doses of EHL-rFVIII were needed on postoperative days 1 and 2 for our patients who underwent circumcision. Our experiences with these two patients demonstrate that PEGylated rFVIII is well tolerated and efficacious for bleeding prophylaxis before circumcision.

There are limited data on EHL-rFVIII products in surgical interventions in the literature [9,10,11]. The first such prospective study reported 15 surgical interventions with PEGylated EHL-rFVIII and hemostatic efficacy was excellent for all subjects in both the intraoperative and perioperative period. Additionally, all interventions were scored as excellent postoperatively, except for one dental procedure that was graded as good. In addition, no related adverse events, including thrombosis and inhibitors, were recorded [9]. To the best of our knowledge, this is the first report of our experiences with these two patients that PEGylated rFVIII is well tolerated and efficacious for bleeding prophylaxis before circumcision.

In conclusion, EHL-rFVIII was safe and effective for circumcision in cases of severe HA. Decreasing the amount and frequency of factor support seems to be possible according to this report.

Keywords: Hemophilia, Surgery, Circumcision, BAX 855

Anahtar Sözcükler: Hemofili, Cerrahi, Sünnet, BAX 855

Informed Consent: Informed consent has been received.

Authorship Contributions

Surgical and Medical Practices: B.Z., B.K., M.İ.Ö.; Concept: B.Z., B.K., M.İ.Ö.; Design: B.Z., B.K.; Data Collection or Processing: B.Z., B.K., M.İ.Ö.; Analysis or Interpretation: B.Z., B.K.; Literature Search: B.Z., B.K.; Writing: B.Z., B.K.

Conflict of Interest: The authors declare that they have no conflicts of interest with regard to this research.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Ingerslev J, Hvid I. Surgery in hemophilia. The general view: patient selection, timing, and preoperative assessment. Semin Hematol 2006;43:23–26.
2. Srivastava A, Brewer AK, Mauser-Bunschoten EP, Key NS, Kitchen S, Llinas A, Ludlam CA, Mahliangu JN, Mulder K, Poon MC, Street A; Treatment Guidelines Working Group on Behalf of the World Federation of Hemophilia. Guidelines for the management of hemophilia. Haemophilia 2013;19:e1-e47.
3. Konkle BA, Stasysshyn O, Chowdary P, Bevan DH, Mant T, Shima M, Engl W, Dyck-Jones J, Fuellinger M, Patrone L, Ewenstein B, Abbeuhl B. Pegylated, full-length, recombinant factor VIII for prophylactic and on-demand treatment of severe hemophilia A. Blood 2015;126:1078-1085.
4. Rizvi SAH, Naqvi SAA, Hussain M, Hasan AS. Religious circumcision: a Muslim view. BJU Int 1999;83(Suppl.1):13–16.
5. Kavaklı K, Kurugol Z, Goksens D, Nisi I. Should hemophiliac patients be circumcised? Pediatr Hematol Oncol 2000;17:149–153.
6. Zulfikar B, Karaman MI, Ovail F. Circumcision in Hemophilia. An Overview. Treatment of Hemophilia. Montreal, World Federation of Hemophilia, 2003.
7. Karaman MI, Zulfikar B, Öztürk MI, Koca O, Akyüz M, Bezgal F. Circumcision in bleeding disorders: improvement of our cost effective method with diathermic knife. Urol J 2014;11:1406-1410.
8. Avanoglu A, Celik A, Ulman I, Özcan C, Kavaklı K, Nişli G, Gökdemir A. Safer circumcision in patients with hemophilia: the use of fibrin glue for local hemostasis. BJU Int 1999;83:91-94.
9. Hampton K, Chowdary P, Dunkley S, Ehrenforth S, Jacobsen L, Nef A, Santagostino E, Sathar J, Takemoto CM, Négrier C. First report on the safety and efficacy of an extended half-life glyco PEGylated recombinant FVIII for major surgery in severe haemophilia A. Haemophilia 2017;23:689-696.
10. Mahliangu JN, Ragni M, Gupta N, Rangarajan S, Klamroth R, Oldenburg B, Nogami K, Young G, Cristiano LM, Dong Y, Allen G, Pierce GF, Robinson B. Long-acting recombinant factor VIII Fc fusion protein (rFVIIIFc) for perioperative haemostatic management in severe haemophilia A. Thromb Haemost 2016;116:1-8.
11. Brand B, Gruppo R, Wynn TT, Griskevicius L, Lopez Fernandez MF, Chapman M, Dvorak T, Pavlova BG, Abbeuhl B. Efficacy and safety of pegylated full-length recombinant factor VIII with extended half-life for perioperative haemostasis in haemophilia A patients. Haemophilia 2016;22:e251-e258.