JPPT | Case Report

A Distinctive Approach to Venous Thromboembolism Treatment in a Pediatric, Hemodialysis Patient: A Case Report

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Enoxaparin is a low molecular weight heparin (LMWH) that is the mainstay for treatment of pediatric patients with a venous thromboembolism, which provides better compliance compared with the use of unfractionated heparin (UFH) in long-term anticoagulation. Although data are limited in pediatric patients with renal insufficiency, enoxaparin can be used in this population. Data related to its use in hemodialysis (HD) pediatric patients is almost non-existent. A major concern for enoxaparin use in patients with renal insufficiency or for those on HD is bleeding. A few studies in adults showed an increased risk of bleeding, but the risk was similar to that of UFH when the two were compared. This case report describes the use of enoxaparin in an 8-year-old female who is on hemodialysis, without any bleeding or clotting complications. Although systematic trials are needed to support the safety and efficacy of LMWH in pediatric patients with renal dysfunction or on HD, this case will provide limited information for enoxaparin use in this population.

ABBREVIATIONS CrCL, creatinine clearance; HD, hemodialysis; IRB, institutional review board; LMWH, low molecular weight heparin; SVC, superior vena cava; UFH, unfractionated heparin; VTE, venous thromboembolism

KEYWORDS Enoxaparin; pediatric; renal dialysis; venous thromboembolism

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Introduction

Enoxaparin is a low molecular weight heparin (LMWH) that is the mainstay for anticoagulant treatment of pediatric patients with a venous thromboembolism (VTE) because of its more predictable pharmacokinetics and longer half-life when compared with those of unfractionated heparin (UFH). Enoxaparin is eliminated through the kidneys, and it may accumulate when combined with nephrotoxic medications in patients with acute or chronic kidney injury or those on hemodialysis (HD). For a pediatric patient who has a VTE and is on HD, anticoagulation options are limited. Although UFH would typically be the best option for a patient on HD, subcutaneous heparin does not have a treatment indication in pediatric patients, and the dosing regimen would need to be administered 3 times a day, which presents compliance concerns in terms of long-term anticoagulation.

Literature citing enoxaparin dosing and monitoring is limited in the pediatric population for children who have renal insufficiency and who are lacking in terms of HD. The anecdotal consensus is to use enoxaparin for chronic VTE treatment in patients with renal insufficiency. To ascertain information about LMWH prescribing patterns in children with renal insufficiency, a survey was conducted among hematologists through the Hemophilia and Thrombosis Research Society of North America.[1] Seventy-seven percent of physicians felt that LMWH could be prescribed safely in a patient with renal insufficiency as long as anti-Xa concentrations were monitored. To our knowledge, in terms of anticoagulation in pediatric patients on HD, data are non-existent.

Anticoagulation treatment duration can often vary among patients and disease-state characteristics. According to the American College of Chest Physicians Evidence-Based Clinical Practice Guidelines in Neonates and Children,[2] the recommended treatment duration for a central venous access device–associated thrombus is between 6 weeks and 3 months. In the interest of providing additional information to support the body of literature, we present a case study of enoxaparin use in an 8-year-old female who was undergoing HD and who was admitted for a superior vena cava (SVC) thrombus secondary to a HD catheter. This study has gone through the local institutional review board (IRB) process and has been determined not to constitute "human research."

Case

An 8-year-old Caucasian female weighing 20 kg presented to the University of New Mexico Hospital with intermittent periorbital edema. Past medical history was significant for vertebral defects, anal atresia,

cardiac defects, tracheo-esophageal fistula, renal anomalies, and limb abnormalities syndrome and end-stage renal disease on chronic HD. Echocardiogram revealed an HD catheter thrombosis of the VTE, and the pediatric hematology team was consulted for management of the periorbital edema. On admission, the patient underwent removal of the HD catheter and angioplasty/fibrin sheath disruption of the SVC, in which a clot was seen. A heparin drip was started 24 hours after the procedure at a rate of 20 units/kg/hr with a goal activated partial thromboplastin time of 50 to 59 seconds. The heparin drip was titrated based on the institution protocol to a target activated partial thromboplastin time concentration ranging from 48 to 63 seconds. After 4 days of heparin, enoxaparin 20 mg (1 mg/kg) administered subcutaneously every 24 hours was begun, with a goal anti-Xa of 0.5 to 1 units/mL. The heparin drip was stopped at the time of the first dose of enoxaparin, and the first anti-Xa was drawn 4 hours after the second dose. Per hematology, a reevaluation by Doppler was scheduled after 6 weeks of enoxaparin therapy.

The patient was receiving high-flux dialysis 3 to 4 times per week without heparin for anticoagulation in the circuit. Enoxaparin was dosed once daily throughout the 6-week treatment duration and was timed for afternoon so that it would be administered after each dialysis session. The first anti-Xa concentration was subtherapeutic, at 0.44 units/mL. Using enoxaparin prescribing information, the dose was subsequently increased by 10% to 22 mg (1.1 mg/kg) subcutaneously every 24 hours. The increase in enoxaparin dose resulted in an anti-Xa concentration of 0.53 units/mL.[3] Anti-Xa concentrations were checked after each dialysis session, and repeat values were all therapeutic, ranging from 0.52 to 0.58 units/mL. Following discharged, home doses of enoxaparin were drawn up by the local compounding pharmacy to prevent potential dosing error and were sent home with the family for administration. Based on medical record notes and laboratory values, the patient did not display signs or symptoms of bleeding or recurrent thrombosis. The 6-week repeat echocardiogram was negative for an SVC thrombus, and enoxaparin was discontinued.

Discussion

Low molecular weight heparin is a potential VTE treatment option in patients with renal insufficiency and HD, although literature to support this is limited, and there is a potential for increased bleeding risk. In our patient case, enoxaparin was used as an anticoagulation option for a HD catheter–induced thrombus. Based on adult data on enoxaparin with a creatinine clearance (CrCL) of <30 mL/min should have an empiric dose adjustment to 1 mg/kg daily.[3] In a pharmacokinetic study of enoxaparin in pediatric patients published by Moffett et al,[4] a 30% reduction in starting dose was recommended in patients with a CrCL of <30 mL/min. Given the limited available information, and by taking a more conservative approach, the dose was reduced to 1 mg/kg daily, which was a 50% reduction. This reduction ended up being appropriate because we only needed to make one 10% adjustment up on the dose to gain therapeutic concentrations.

A meta-analysis by Lim et al[5] showed that anti-Xa concentrations in adult patients receiving enoxaparin treatment, with a CrCL of <30 mL/min, had concentrations ranging from 1.27 to 1.58 units/mL after a minimum of 3 doses. Along with increased anti-Xa concentrations, they showed an increase in major bleeding in patients with a CrCL of <30 mL/min compared with in those with a CrCL of >30 mL/min (5.0% vs 2.4%; OR, 2.25 [95% CI, 1.19 to 4.27]; p = 0.013). Data are scarce for the use of LMWH in pediatric patients on HD; therefore, data in adult patients can be used. Atiq et al[6] conducted a systematic review to investigate accumulation of prophylactic LMWH in adults with renal dysfunction. Although enoxaparin was shown, based on anti-Xa concentrations, to accumulate in instances of renal dysfunction, patients who were on HD did not accumulate enoxaparin. For patients on HD, anti-Xa concentrations drawn 4 hours post–prophylactic enoxaparin dose were 0.38 units/mL at week 1 and 0.40 units/mL at week 4. These anti-Xa levels were slightly elevated for prophylactic dosing, but they also showed that enoxaparin was removed by HD. The study did not mention details about the type of HD circuit. It is important to note that although LMWH is generally not cleared through HD, it is a possibility with high-flux HD.

The risk of bleeding is a major concern with enoxaparin use in patients with renal dysfunction or in those who are undergoing HD. A single-center, retrospective chart review conducted by Gerlach et al[7] showed a potential bleeding risk for adults who are taking enoxaparin and have renal insufficiency. Total bleeding complications occurred in 22% of patients with normal renal function, compared with a rate of 51% in patients with renal dysfunction (p < 0.01). Major bleeds were also different, occurring in 2% and 30%, respectively (p < 0.01), in patients with normal renal function and those with renal dysfunction. Although a greater bleeding risk was shown in the renal dysfunction group, it was a small study, which made it difficult to establish causality between enoxaparin and bleeding risk in renal patients. Additional studies[8,9] in adults have shown that enoxaparin has similar rates of bleeding when compared to UFH for HD patients. Pon et al[8] found a major bleeding rate in adults on chronic HD of 6.1% vs 11% in enoxaparin compared to UFH (p = 0.4). Although the data show that the incidence of bleeding is similar between LMWH and UFH patients, the studies were conducted in the adult population, which makes it difficult to translate the findings to the pediatric population.

Conclusions

Based on this case report of a pediatric patient on HD and on the published data, we were able to use enoxaparin as VTE treatment while monitoring our patient throughout her course using anti-Xa concentrations. A treatment dose of 1 mg/kg administered subcutaneously every 24 hours was sufficient to achieve appropriate anti-Xa concentrations. Per the chart review, our patient did not experience any bleeding episodes or develop new SVC clots while undergoing treatment, which was confirmed on echocardiogram. For this patient, 6 weeks of therapy was sufficient, but it is important to consider that duration of therapy could have been extended if the clot was still present on ultrasound. As a result of dosing variability for pediatric patients, having an outpatient pharmacy draw up the doses would provide more accurate dosing and reduce the risk of errors in instances of home use. Enoxaparin provided an alternative to UFH for long-term anticoagulation in our patient, which is more practical in terms of administration. Although it proved to be beneficial in our case, larger prospective studies will be needed to acquire more information and to establish it use in anticoagulation guidelines in the pediatric population.

Article Information

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