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Weight-based enoxaparin dosing for venous thromboembolism prophylaxis in the obese trauma patient

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Abstract

BACKGROUND: Limited data exist regarding the efficacy of weight-based dosing of low–molecular weight heparin for venous thromboembolism (VTE) prophylaxis in obese trauma patients.

METHODS: Consecutive obese trauma patients were placed on a weight-based protocol for VTE prophylaxis (enoxaparin .5 mg/kg subcutaneously every 12 hours). Peak anti-Xa levels were drawn, and bilateral lower extremity duplex ultrasound was performed. The incidence of VTE and bleeding complications were recorded.

RESULTS: Eighty-six patients met the study criteria. Seventy-four patients achieved target prophylactic anti-Xa concentrations, with a mean level of .42 ± .01 IU/mL. Eighteen patients were found to have deep vein thrombosis. However, in 16 of these patients, deep vein thrombosis was diagnosed before weight-based low–molecular weight heparin initiation. No bleeding complications occurred, and no symptomatic pulmonary emboli were identified.

CONCLUSIONS: In obese trauma patients, weight-based enoxaparin is an efficacious regimen that provides adequate VTE prophylaxis, as measured by anti-Xa levels, and appears to be safe without bleeding complications.

Venous thromboembolism (VTE) is a major cause of morbidity and mortality among trauma and critically ill patients despite advances in anticoagulation therapy and is among the most preventable hospital-related complications.[1–5] Patients with traumatic injuries and obesity stand out among the highest risk groups, and traumatic injury and obesity are actually independent risk factors for the development of VTE.[1–7] Reported incidence varies widely in the literature, ranging from 3% to 58% after major trauma, depending on factors such as type of injury, patient demographic, surveillance method (venography vs today's gold standard, duplex ultrasound), and medication used, if any, for prophylaxis.[1,2,5]

In addition to traumatic injury, obesity places patients at high risk for VTE. Obesity was found to be associated with a relative risk of 2.50 for deep vein thrombosis (DVT) compared with nonobese patients and was also identified as a risk factor for recurrent VTE.[4,8] Low–molecular weight heparin (LMWH) is currently recommended for VTE prophylaxis in major trauma patients.[9] Because of the predictable pharmacodynamics of LMWH, dosing guidelines are

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currently standardized, and monitoring drug concentration is not recommended in most patient populations.[9–11] However, weight-based dosing may be prudent in obese patients.[9–12] Studies evaluating LWMH dosing in obese, trauma, and critically ill medical and surgical patients have found a strong negative correlation between weight and anti-Xa levels with fixed dosing and that weight-based dosing results in favorable anti-Xa activity.[7,11,13–18]

The purpose of our study was to determine if a weight-based dosing protocol for LMWH in obese trauma patients was efficacious and safe, as measured by peak anti-Xa levels, the incidence of VTE, and bleeding complications.

Methods

All adult ($\geq$18 years of age), obese (body mass index [BMI] $\geq$ 30 kg/m^2) patients with traumatic injuries admitted to our level I trauma center from January 2011 to July 2012 were considered for inclusion. Exclusion criteria were intracranial hemorrhage, pregnancy, active hemorrhage (as determined by the attending trauma surgeon), renal insufficiency (creatinine clearance $<$ 30 mL/min), need for epidural anesthesia, coagulopathy, heparin allergy or history of heparin-induced thrombocytopenia, thrombocytopenia (platelet count $<$50,000 or $>$50% drop from baseline), or indication for therapeutic anticoagulation before initiation of enoxaparin prophylaxis.

Eligible patients were placed on a weight-based enoxaparin dosing protocol for VTE prevention and prospectively followed. Patients were given enoxaparin .5 mg/kg subcutaneously every 12 hours, rounded to the nearest 10 mg without dose capping, on the basis of actual body weight on admission. Timing of chemoprophylaxis initiation was at the discretion of the trauma service clinicians, on the basis of traumatic injuries, the timing of operative procedures, and overall clinical condition. Sequential compression devices were applied in all patients unless contraindicated by lower extremity injuries. Bilateral lower extremity duplex ultrasound was performed on hospital days 2, 4, and 7 and weekly thereafter, per standard trauma service DVT screening protocol, or at any time during hospitalization if clinically suspected. Computed tomography of the chest was obtained on the basis of clinical suspicion for pulmonary embolism (PE).

All patients had peak anti-Xa levels drawn with venipuncture 4 hours after the 3rd or 4th dose of enoxaparin. To quantify the anti-Xa activity for enoxaparin, all blood samples were analyzed with the STA-Compact instrument (Diagnostica Stago, Parsippany, NJ), using the Diagnostica Stago heparin anti-Xa chromogenic assay.[19] The acceptable peak anti-Xa level for prophylaxis was considered to be .2 to .6 U/mL.[7,14] If the anti-Xa level was $<$.2 IU/mL, the total daily dose was increased by 20 mg, and if the anti-Xa level was $>$.6 IU/mL, the total daily dose was decreased by 20 mg, similar to the regimen implemented by Borkgren-Okonek et al.[16] Any dose changes were discussed and approved by the clinical team, and peak anti-Xa levels were redrawn accordingly. Chemoprophylaxis was discontinued if any bleeding complications (clinically identified active hemorrhage, transfusion of $\geq$2 U of packed red blood cells, drop in hematocrit of $\geq$5 points), thrombocytopenia (platelet count $<$50,000 or $>$50% drop from baseline), heparin-type allergy, or VTE requiring treatment occurred. Bleeding complications were identified as follows: An initial chart review was performed. If a dose of enoxaparin was missed after initiation of the weight-based protocol, this warranted a more detailed review of clinical notes and data in search of the aforementioned events that would indicate a bleeding complication. Patients were excluded from the study if the timing of the peak anti-Xa level was incorrectly drawn or ordered.

Data collected included age, gender, height, weight, BMI, serum creatinine at admission, platelet count at admission, enoxaparin dose, peak anti-Xa level, list of injuries, Injury Severity Score, length of hospital stay, and incidence of DVT and PE.

The primary outcome measure of the study was to determine whether a weight-based enoxaparin dosing protocol was efficacious, as measured by anti-Xa levels within target range. Secondary outcome measures were the incidence of DVT and symptomatic PE, as well as bleeding complications. All data are presented either as mean $\pm$ SEM or medians with interquartile ranges, as appropriate. Unpaired Student's t tests were used to compare normally distributed continuous variables. Continuous variables that were not normally distributed were compared using Wilcoxon's rank-sum tests. P values $<$.05 were considered significant. This study has been approved by the Intermountain Healthcare Institutional Review Board and is currently recruiting patients (Salt Lake City, UT).

Results

Of all patients who met study criteria, 86 had $\geq$1 peak anti-Xa level drawn and received $\geq$3 accurate weight-based doses of enoxaparin and thus were included in the analysis. Patients were predominantly men (70%), with a mean age of 52 $\pm$ 1.78 years. The median BMI and weight were 35.3 kg/m^2 (interquartile range, 9.8 kg/m^2) and 113.3 kg (interquartile range, 30.0 kg), respectively. Table 1 displays comprehensive patient characteristics. Target anti-Xa levels were achieved by 74 patients (86%) after the 3rd or 4th dose of enoxaparin, with a mean of .42 $\pm$ .01 IU/mL. No correlation between body weight and anti-Xa level was found (r^2 = $-$.01; Fig. 1).

Twelve patients were outside the target prophylactic anti-Xa range. Eight patients were above goal, with a mean anti-Xa level of .68 IU/mL, and 4 patients were below goal. When comparing the group above to that below the target anti-Xa range, there were no significant differences found in weight (107.9 $\pm$ 11.5 vs 104.1 $\pm$ 15.2 kg, P = .85) or BMI