Therapeutic Enoxaparin Dosing in Obese Patients

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Background: Enoxaparin is a low molecular weight heparin that is FDA approved to treat acute venous thromboembolism (VTE); however, there is limited guidance on dosing in obese patients. The package insert does not provide any specific recommendation on therapeutic dosing of enoxaparin in obese patients but states that for patients with a body mass index (BMI) > 30 kg/m^2, safety and efficacy for prophylaxis has not been determined. Additionally, the 2016 CHEST guidelines do not make any recommendations on treatment dosing for VTE in obese patients, but there have been some clinical trials that have analyzed therapeutic enoxaparin dosing in obese patients. These studies have found that a reduced dose may be appropriate for treatment of VTE in patients with a BMI $\geq$ 40 kg/m^2.

At SSM Health St. Mary's Hospital-St. Louis (SM-SL), the policy states for treatment of VTE the dose of enoxaparin should be 1 mg/kg based on actual body weight (ABW) administered subcutaneously every 12 hours or 1.5 mg/kg once daily. If the ABW is > 190 kg, it is recommended to monitor anti-Xa and adjust accordingly. Anti-Xa levels are a send-out lab for SM-SL so they are not practical to monitor during therapy. SM-SL's policy recommends using unfractionated heparin if anti-Xa levels cannot be monitored. The purpose of this study is to describe the dose of enoxaparin used in morbidly obese patients requiring VTE treatment at SM-SL.

Methods: This will be a retrospective, single-center, chart review of patients admitted at SM-SL. Adult patients hospitalized from January 1, 2016 through August 31, 2020 with a BMI $\geq$ 40 kg/m^2 and who received at least 2 doses of therapeutic enoxaparin will be included. Pregnant patients and those receiving dialysis will be excluded from the study. In addition to baseline demographics, the following information will be collected: enoxaparin dose, indication for enoxaparin, creatinine clearance, concomitant pharmacotherapy that increases bleeding risk and/or thromboembolic risk (i.e. warfarin, aspirin, systemic steroids, DOACs, NSAIDs, P2Y12 inhibitors, estrogens, progestins), medical conditions that increase bleeding risk and/or thromboembolic risk (i.e. Factor V deficiency, antiphospholipid antibody syndrome, malignancy), and baseline labs (i.e. hemoglobin, platelets, and baseline serum creatinine). The primary endpoint will be dose of enoxaparin received. Secondary outcomes will be bleeding events (major and minor bleeding), thromboembolic events, and anti-Xa levels when available. This study has been approved by the Institutional Review Board.

Results: There were 158 patients who met inclusion criteria and were evaluated in this study. The mean dose (mg/kg) of enoxaparin used was 0.98 $\pm$ 0.08. Bleeding events occurred in 19 (12%) of the patients with the majority of those being minor (10.1%). No thromboembolic events were reported for any patients, and there were no anti-Xa levels available.

Conclusions: Based on the results from this study, the average dose of enoxaparin used in obese patients (BMI $\geq$ 40 kg/m^2) with VTE at SM-SL is 0.98 mg/kg. Bleeding events occurred in 12% of

the patients. Future studies are needed to evaluate the relationship between dose of enoxaparin used and bleeding and thromboembolic events. Studies should also investigate whether once or twice daily dosing is more appropriate in patients with a BMI $\geq$ 40 kg/m^2 with renal dysfunction.