Evaluation of anti-Xa levels in morbidly obese patients receiving enoxaparin treatment dosing

James Henderson, PharmD; Brianna Alexander, PharmD, BCPS; Paul Plec插入kowski, PharmD, BCPS; Michelle Schoonover, PharmD, BCPS
Duke University Hospital; Durham, North Carolina

Background

• Obesity greatly impacts the pharmacokinetics of many medications including enoxaparin. Enoxaparin is a hydrophilic medication that concentrates in the blood and lean tissue. In obese patients, the higher ratio of fat to lean tissue may lead to higher concentrations of enoxaparin in the blood, when dosing based on total body weight (TBW).

• Using traditional dosing of 1 mg/kg every 12h (TBW) may lead to supratherapeutic levels in these patients. The 2012 CHEST guidelines suggest monitoring therapy with anti-Xa levels for obese patients but no definition of obesity is given.

• While studies show that dose reductions of enoxaparin more commonly achieved therapeutic anti-Xa levels, their sample sizes were relatively small, and none of the studies could identify a relationship between supratherapeutic anti-Xa levels and incidence of major bleeding.

Objectives

Primary Objective

• To determine whether an enoxaparin dose <0.9mg/kg total body weight (TBW) every 12h will result in a higher percentage of therapeutic initial anti-Xa levels in morbidly obese patients compared to dosing≥0.9mg/kg (TBW) every 12h.

Secondary Objectives

• Determine proportion of patients with supratherapeutic initial anti-Xa level
• Determine proportion of patients with subtherapeutic initial anti-Xa level
• Determine average initial anti-Xa level
• Determine the average weight-based enoxaparin dose
• Identify the number of dose adjustments needed to achieve a therapeutic anti-Xa level
• Identify the incidence of major bleeding as defined by the International Society on Thrombosis and Hemostasis

Methods

Study Design

• IRB-approved, single-center, retrospective cohort study

• Morbidly obese patients defined as patients with a BMI >40kg/m² who were hospitalized within the Duke University Health System at Duke University Hospital, Duke Regional Hospital, or Duke Raleigh Hospital between July 1st 2013 and September 30th 2016.

Table 1: Inclusion and Exclusion Criteria

<table>
<thead>
<tr>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospitalized adult patients over 18 years old</td>
<td>Patients with a CrCl (Cockcroft-Gault) &lt;30mL/min while on enoxaparin</td>
</tr>
<tr>
<td>being treated with enoxaparin for any recognized indication requiring treatment doses</td>
<td>Morbidly obese patients defined as patients with a BMI &gt;40kg/m²</td>
</tr>
<tr>
<td>Morbidly obese patients defined as patients with a BMI &gt;40kg/m²</td>
<td>Patients who are receiving once daily dosing of enoxaparin</td>
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<tr>
<td>Anti-Xa level drawn within 2.5-5.5 hours after at least 3 consecutive identical doses of enoxaparin; with no more than one syringe of a different dose given prior to the consecutive identical doses</td>
<td>Patients receiving enoxaparin for VTE prophylaxis</td>
</tr>
<tr>
<td>Anti-Xa level drawn within 2.5-5.5 hours after at least 3 consecutive identical doses of enoxaparin; with no more than one syringe of a different dose given prior to the consecutive identical doses</td>
<td>Pregnant Patients</td>
</tr>
</tbody>
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Primary Endpoint

• The percentage of morbidly obese patients with a therapeutic initial anti-Xa level (goal 0.6-1.0 u/ml) who are initiated on enoxaparin at <0.9mg/kg (TBW) every 12h versus ≥0.9mg/kg (TBW) every 12h

Secondary Endpoints

• Percentage of supratherapeutic initial anti-Xa levels (>1.0 u/ml)
• Percentage of subtherapeutic initial anti-Xa levels (<0.6 u/ml)
• Average weight-based dose of enoxaparin
• Average initial anti-Xa level
• Average time in days from enoxaparin initiation to therapeutic anti-Xa level
• Average number of dose adjustments (increases or decreases) needed to achieve therapeutic anti-Xa level

Data Collection and Analysis

Statistical Analysis

• For primary analysis, patients will be divided into two groups, patients receiving enoxaparin dose <0.9mg/kg TBW every 12h and patients receiving ≥0.9mg/kg TBW every 12h.

• Continuous variables, such as anti-Xa level, will be summarized with mean/medians, standard deviation and ranges. Depending on whether the continuous variables are normally or non-normally distributed, two-sample t test or Wilcoxon-Mann-Whitney test respectively, will be used to compare <0.9 mg/kg TBW group and ≥0.9 mg/kg TBW group.

• Categorical variables (e.g. documented incidence of therapeutic initial anti-Xa levels) will be summarized with frequency counts and percentages.

• A 25% difference in initial therapeutic anti-Xa level between the treatment groups based on previous studies. Using an alpha=0.05, power=0.8, and a two-sided Fisher exact test it is estimated that we will require a sample size per group of 60 patients.

References


Disclosures: Authors have no conflicts of interests regarding personal or financial relationships with commercial entities that may have influenced the content or subject matter of this presentation.