Optimal Dosing of Enoxaparin in Critically Ill Patients with VTE

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BACKGROUND

- Incidence of first venous thromboembolism (VTE) occurrence is estimated to be 100 per 100,000 people annually in the Unites States
- Mortality rates remain high in critically ill patients with VTE regardless of standard anticoagulation
- Enoxaparin is a low molecular weight heparin commonly used for treatment of VTE that can be monitored in special populations via anti-Xa levels for optimal dosing
- Emerging evidence suggests critically ill patients will not achieve therapeutic anti-Xa levels with standard enoxaparin dosing

Purpose: To examine whether standard enoxaparin dosing will achieve therapeutic anti-Xa levels in MICU patients with VTE

Hypothesis: Current standard dosing will not result in therapeutic anti-Xa levels consistently

METHODS

- **Design:** IRB-approved, retrospective, single-center cohort study
- **Time Frame:** January 2013- December 2019
- **Setting:** 350-bed Community Teaching Hospital
- **Inclusion Criteria:**
  - Adult (≥18 years old)
  - Critically ill
  - Receiving enoxaparin at the standard dose for VTE treatment
  - At least one peak anti-Xa level drawn at the correct time interval
- **Statistics:** Outcomes were analyzed with descriptive statistics.

OUTCOMES

- **Primary:** Proportion of patients who achieved therapeutic anti-Xa levels with standard dosing (1 mg/kg Q12H or 1.5 mg/kg Q24H)
- **Secondary:** Weight-based dose of enoxaparin required to achieve a therapeutic anti-Xa level, types of dose adjustments required, and the proportion requiring multiple dose-adjustments

RESULTS

Table 1. Baseline Characteristics

Total Patients	**n=53**
Age, years	63 (48 – 76)
Male gender	21 (39.6%)
Body Mass Index (BMI), kg/m^2	35 (28.7 – 39.3)
BUN, mg/dL	15 (9 – 22)
SCr, mg/dL	0.91 (0.71 – 1.13)
Race	
Caucasian	40 (75.5%)
African-American	12 (22.6%)
Unknown	1 (1.9%)
Indication for Enoxaparin	
Treatment for DVT	14 (26.4%)
Treatment for PE	37 (69.8%)
Treatment for both DVT and PE	2 (3.8%)

Table 2. Enoxaparin Dose Interventions and Patient Outcomes

Achievement of Therapeutic Anti-Xa Levels with Initial Dosing Regimen	
Patients receiving 1 mg/kg every 12 hours (n=41)	12 (29.3%)
Patients receiving 1.5 mg/kg every 24 hours (n=12)	2 (16.6%)
Anti-Xa Level at First Measurement	
Therapeutic	14 (26.4%)
Subtherapeutic	31 (58.5%)
Supratherapeutic	8 (15.1%)
Dose Adjustment after Initial Anti-Xa Result	**n=39**
Increase, mg/kg	1.31 (1.01 – 2.09)
Decrease, mg/kg	0.87 (0.76 – 0.88)
Anti-Xa Level at Second Measurement	
Therapeutic	2 (5.1%)
Subtherapeutic	12 (30.8%)
Supratherapeutic	2 (5.1%)
Dose Adjustment after Second Anti-Xa Result	**n=14**
Increased appropriately	2 (16.7%)
Decreased appropriately	1 (50%)
No dose adjustment made	6 (42.9%)
Anti-Xa Level at Third Measurement	
Therapeutic	5 (35.7%)
Subtherapeutic	2 (14.3%)
Supratherapeutic	1 (7.1%)

Table 2 (Continued). Enoxaparin Dose Interventions and Patient Outcomes

Dose Adjustment after Third Anti-Xa Result	**n=3**
Enoxaparin discontinued	2 (66.7%)
No dose adjustment made	1 (33.3%)
Patient Outcomes	
Total cumulative enoxaparin, mg	460 (290–720)
Need for blood transfusion	5 (9.4%)
Length of hospital stay, days	6 (3 – 9)
Inpatient mortality	1 (1.9%)

CONCLUSIONS

- Standard dosing of enoxaparin in the medical intensive care unit (MICU) did not result in therapeutic anti-Xa levels for a majority of patients.
- Patients receiving 1.5 mg/kg every 24 hours were less likely to achieve a therapeutic anti-Xa level than those receiving 1 mg/kg every 12 hours.
- With additional anti-Xa monitoring throughout a MICU stay, therapeutic levels are more likely to be obtained using appropriate dose adjustments.
- Increased use of anti-Xa levels to adjust enoxaparin dosing may lead to improved patient safety in patients with VTE.

Limitations: small sample size; retrospective, single-center design

Future Direction: Identify patient factors associated with the requirement for higher or lower enoxaparin dosing

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