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Original Contribution

Effect of Subcutaneous Unfractionated Heparin Prophylaxis on Activated Partial Thromboplastin Time: A Retrospective Evaluation☆,☆☆,★,★★,☆☆☆

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Abstract
Study Objective: Characterize the incidence of elevated aPTT results in patients treated with prophylactic, subcutaneous unfractionated heparin (UFH).
Design: Retrospective, cohort analysis.
Setting: Single-center, university hospital.
Measurements: Evaluation of 257 patients with activated partial thromboplastin time (aPTT) testing both prior to and following subcutaneous (SC) unfractionated heparin (UFH) therapy.

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Main Results: Evaluated patients received UFH 5000 units every 8 hours. Baseline aPTT values were within the normal range (mean ± SD, 32.0 ± 8.5 seconds). After initiation of UFH, aPTT values increased (mean ± SD, 37.6 ± 15.2 seconds). After 24 hours of SC UFH, mean aPTT values (mean ± SD, 38.6 ± 15.5) exceeded the normal laboratory range (23.3–35.7 seconds). An elevated aPTT result after UFH was associated with baseline aPTT, length of therapy, and weight-based UFH dose. A significant association was not identified between aPTT elevation and age, race, sex, history of liver disease, type of admission, or transfusion of blood products.
Conclusions: Treatment with UFH resulted in a small, but significant, increase in aPTT.

1. Introduction

The estimated annual incidence of venous thromboembolism (VTE), including pulmonary embolism (PE) and deep vein thrombosis (DVT), is 17 cases per 100,000 patients in the general population; however, the incidence of VTE is increased over 260-fold in hospitalized patients [1–2]. The risk of VTE also increases with age (especially age greater than 70 years), comorbid conditions (malignancy, history of VTE, pregnancy, congestive heart failure), reduced mobility, and recent surgery or trauma [3,4]. Based on this information, the American College of Chest Physicians (CHEST) recommends pharmacologic prophylaxis using subcutaneous (SC) unfractionated heparin (UFH) or low molecular weight heparins (LMWH) [1]. Since the twice daily (BID) LMWH regimen often utilized for surgical VTE prevention is contraindicated in patients with indwelling neuraxial catheters due to an increased risk of epidural hematoma development [5], SC UFH is often chosen for VTE prophylaxis in patients with indwelling neuraxial catheters.

Neuraxial catheters have been repeatedly shown to improve postoperative pain and patient outcomes following major abdominal and thoracic surgery [6–7]. However, this patient population is also at high risk for VTE and requires pharmacologic prophylaxis [1]. While large case series have reported utilization of SC UFH with indwelling neuraxial catheters without complications [8], the landmark study supporting the use of BID SC UFH for VTE prevention also reported statistically significant increases in activated partial thromboplastin time (aPTT) ($P < .001$) following SC UFH administration [9]. Unfortunately, the exact aPTT values were not published. Additionally, thrice daily dosing (TID) of SC UFH, which is preferred by many surgeons for postoperative VTE prophylaxis, was not examined. Subsequent publications have commented on the unknown effect TID dosing may have on aPTT [5].

We hypothesized that SC UFH administered TID will only slightly prolong aPTT to values that remain in our institution's normal laboratory range (23.3–35.7 seconds), which would help evaluate the safety of TID SC UFH with concomitant neuraxial catheter use. The primary objective of this study was to determine the incidence of elevated aPTT results in hospitalized patients treated with 5000 units TID SC UFH for VTE prophylaxis. Secondary objectives were to evaluate the impact of body mass index (BMI) on aPTT values and incidence of VTE in patients receiving prophylactic UFH.

2. Materials and Methods

This retrospective, single-center, institutional review board-approved study was conducted on a cohort of medical and surgical patients admitted to a large academic medical center between July 2011 and January 2012. Subjects included were age 18 and older that received doses of SC UFH for VTE prophylaxis and had aPTT testing performed both prior to and during SC UFH therapy. Exclusion criteria encompassed patients without documented height or weight and patients who received therapeutic intravenous UFH at any point during the specified admission.

Patient charts and information stored in a clinical data warehouse were reviewed to obtain all pertinent data. Data were collected and confirmed by 3 investigators. Collected demographic information included age, gender, race, height, weight, and length of stay. Data regarding UFH administration included dose, frequency, number of days of heparin therapy, and aPTT laboratory values. Pertinent ICD-9 diagnosis codes for liver dysfunction, bleeding complications or coagulopathies, and procedure codes related to administration of blood products during the admission were also examined. Incidence of VTE was also evaluated using ICD-9 diagnosis codes. Concomitant antiplatelet use was not assessed; however, patients with ICD-9 diagnosis codes for long-term anticoagulation with a vitamin K antagonist were excluded.

The baseline aPTT was defined as the aPTT value immediately preceding initiation of UFH therapy. All subsequent aPTTs drawn during active UFH therapy were included in the comparative analysis, with statistical adjustment for repeated measures in the same patient. The time between the baseline aPTT and subsequent aPTT values were measured in number of hours.

2.1. Statistical Analysis

Prior to data collection, a power analysis was conducted and determined that a sample size of 200 patients would be required for a power of 80% to detect a difference of 3 seconds between the baseline and treatment aPTT values. Descriptive statistics were determined for unique study subjects. Since multiple aPTT measures were recorded on each subject, univariate associations between aPTT and each variable in the data were examined using linear mixed models with a random