Unfractionated Heparin Dosing for Treatment of Venous Thromboembolism in Patients Weighing Greater than 100 Kilograms

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Background: Unfractionated heparin (UFH) remains the first-line treatment of venous thromboembolism (VTE) in obese patients, but dosing in these patients is challenging due to decreased vasculature in adipose tissue, resulting in variable volumes of distribution. A 2013 study at the University of Virginia Health System (UVA) found that patients who weighed >100 kg required an UFH rate that was significantly less than the standard 18 units/kg/h to achieve a therapeutic activated thromboplastin time (aPTT) within 24 hours. As a result, the UVA dosing nomogram was changed such that patients weighing >100 kg received a standard 80 units/kg bolus followed by a decreased infusion rate of 16 units/kg/h. Patients weighing >125 kg appeared to require even less UFH; however, results were inconclusive due to the small sample size.

Methods: This single-center, retrospective observational study evaluated patients weighing >100 kg who received UFH for suspected or proven VTE from January 1, 2013 to November 30, 2015. Patients were classified into weight groups of 100-124.9 kg, 125-149.9 kg, and ≥150 kg. The primary objective was to identify optimal initial dosing of UFH in patients treated for suspected or proven VTE weighing ≥ 125 kg. The secondary objectives included validation of the change in heparin nomogram for patients weighing ≥ 100 kg, assessment of the effects of initial bolus dosing on patients weighing ≥ 100 kg, and evaluation safety in regard to adverse bleeding and clotting events in supratherapeutic and subtherapeutic patients.

Results: Of the 120 patients evaluated weighing ≥125 kg, 79 (66%) achieved a therapeutic aPTT within 24 hours of therapy initiation. The median therapeutic UFH infusion rate for all patients was 14.0 units/kg/h [11.9-16.2] and the median time to achieve a therapeutic aPTT was 19.0 hours [12.0-30.8]. The median initial bolus was 79.9 units/kg [77.7-80.2] followed by a median initial infusion rate of 16.0 units/kg/h [12.0-17.9]. Patients who weighed <150 kg (n=79) and ≥150 kg (n=41) required 14.7 units/kg/h [12.6-16.5] and 12.5 units/kg/h [11.0-15.1], respectively, to achieve a therapeutic aPTT. Of the 48 patients evaluated weighing 100-124.9 kg who received the new 16 units/kg/h initial infusion, 35 (73%) achieved a therapeutic aPTT within 24 hours of therapy initiation. The median time to achieve a therapeutic aPTT was 19.5 hours [13.0-26.0]. The median initial aPTT was 103.25 [61.9-181.1], and 30 (63%) patients had a supratherapeutic first aPTT. No patients had VTE recurrence and there was only one major bleeding event.

Conclusions: Our results suggest that patients who weigh >125 kg require less UFH than patients who weigh <125 kg. Furthermore, patients who weigh ≥150 kg require an even lower infusion rate to achieve a therapeutic aPTT. These findings suggest a need for additional weight categories with specific infusion rate recommendations in order to achieve a therapeutic aPTT within 24 hours. We also found that an increased percentage of patients weighing 100-124.9 kg are therapeutic within 24 hours with the nomogram change. However, a majority of these patients experience supratherapeutic first PTTs and therefore may require a decreased initial bolus.