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POSTER ABSTRACTS

332.THROMBOSIS AND ANTICOAGULATION: CLINICAL AND EPIDEMIOLOGICAL

Efficacy and Safety of Antithrombin Supplementation in Neonates and Infants on a Continuous Heparin Infusion

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Introduction: Antithrombin (AT) is an inhibitor of several coagulation proteins, including FIIa and FXa. Heparins accelerate/potentiate the interaction between AT and these factors through a conformational change in AT. Plasma AT concentrations are low in neonates, lower in sick premature neonates, and reach adult levels by 6 to 12 months of age. The developmental differences in plasma AT levels are an important consideration when treating an infant with heparin, as the activity of heparin depends on the presence of AT as a cofactor. As a result, AT supplementation is often considered in this cohort, particularly in the setting of heparin resistance.

Objective: The objective of this study was to describe the use of AT supplementation at Boston Children's Hospital (BCH), a quaternary care, free-standing children's hospital, and investigate the safety and efficacy of AT supplementation in infants on a continuous heparin infusion.

Methods: This study was approved by the Institutional Review Board at BCH. Data were abstracted for infants who received AT supplementation while on a therapeutic heparin infusion in the neonatal, cardiac, and medical intensive care units between January 2016 and October 2022. Infants on extracorporeal membrane oxygenation and continuous renal replacement therapy were excluded. The primary outcome was attainment of therapeutic anticoagulation within 48 hours after an AT course, defined as at least one occurrence of a partial thromboplastin time (PTT) level between 60 and 85 seconds and/or anti-factor Xa (anti-FXa) activity between 0.35 and 0.7 units/mL. Clinically relevant bleeding was defined as moderate/clinically relevant non-major bleeding or severe/major bleeding, as determined by either the Neonatal Bleeding Assessment Tool for infants with post-menstrual age (PMA) < 44 weeks or the International Society on Thrombosis and Haemostasis criteria for infants with PMA > 44 weeks, respectively. Data were summarized using descriptive statistics.

Results: Over the 7-year period, 50 infants receiving 61 courses of AT supplementation were included. 12 patients received multiple AT doses within a course, resulting in the administration of 75 total AT doses. The median gestational age was 38 weeks (range 28-41 weeks), with a mean birth weight of 3.1 kg (range 0.8-4.5 kg). Median postnatal age at the time of the first AT dose was 19 days (range 3-341 days). The majority of heparin courses were indicated for thrombosis (49%) and post-operative cardiac surgery (40%). Median baseline AT activity was 37% (range 18-61%). The primary outcome was achieved in 90% AT courses. Of these, 73% were therapeutic only by PTT levels, 9% only by anti-FXa activity, and 18% by both. The benefit of AT administration was not sustained, as only 39% PTT levels and anti-FXa activity measured 48 hours after the AT course remained therapeutic.

41 infants had an AT level measured within 6 hours after the dose, and 61% (25/41) achieved a level between 80 and 120% of the calculated target. AT levels decreased over 48 hours, with an estimated half-life of 49 hours. 21% of AT courses had an increase in bleeding severity, with the majority being minor bleeds. Clinically relevant bleeding occurred after AT administration in only 8% (4/50) subjects.

The relationship between simultaneously measured PTT levels and anti-FXa activity was investigated in a secondary analysis. Of the 250 paired levels, only one pair was therapeutic for both values (**Figure 1**). Other than the single pair, in all other samples with a therapeutic anti-FXa, the simultaneously measured PTT was supratherapeutic. Three of the four patients with clinically relevant bleeding had at least one paired PTT level and anti-FXa activity available on the day of bleeding. Out of the seven paired samples, 86% of moderate bleeding occurred when the PTT level was supratherapeutic and the anti-FXa activity was subtherapeutic.

Discussion: AT supplementation in infants may briefly increase the therapeutic efficacy of heparin, dependent on the monitoring parameter used, as PTT levels and anti-FXa activity poorly correlate. Additionally, permitting the PTT to increase over a certain threshold may increase the risk of bleeding. Further studies are needed to provide recommendations on heparin infusion titrations, AT dosing, and the monitoring of PTT levels and/or anti-FXa activity in the neonatal/infant populations on a continuous heparin infusion.

Disclosures No relevant conflicts of interest to declare.

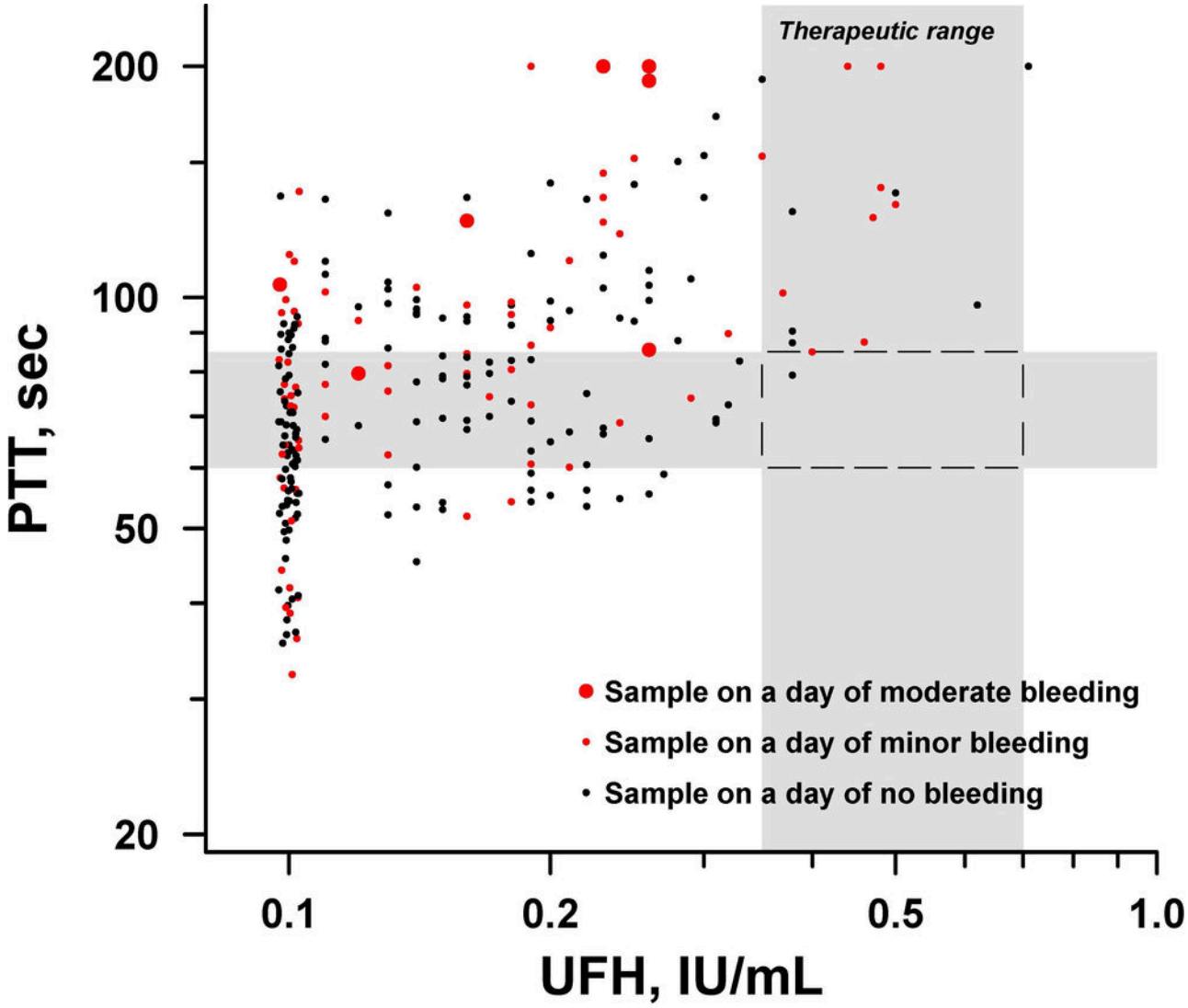

Figure 1. Relationship between simultaneously measured PIT levels and anti-FXa activity (UFH) and severity of bleeding. The gray areas represent therapeutic ranges for PTT and UFH.

Figure 1

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