

A clinical outcomes comparison between direct thrombin inhibitors (DTIs) for the management of heparin-induced thrombocytopenia (HIT) in patients receiving hemodialysis.

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Abstract

Background: The thromboembolic risk associated with untreated HIT Type II can lead to severe life and/or limb threatening thromboembolic complications in more than 50% of patients. In order to prevent thromboembolic events in HIT, patients are managed with alternative anticoagulants, such as lepirudin and argatroban.

Patients receiving hemodialysis routinely require heparin for anticoagulation in order to maintain the patency of the vascular access and the circuit for continuous or intermittent renal replacement therapy. Suspected HIT has been reported to occur in 3.9% of patients receiving chronic dialysis, with positive HIT antibodies being found in up to 12% of these patients. Despite the need, there is little data to guide the use of direct thrombin inhibitors (DTIs) in patients receiving hemodialysis for the medical management of HIT. This research will fill a gap in current research by providing a unique comparison of the clinical outcomes associated with DTI use in patients with HIT and receiving hemodialysis. In addition, this research will provide an assessment of the pharmacodynamic relationship of activated partial thromboplastin time (aPTT) and associated the clinical outcomes of the different DTIs. Finally, this research will provide an evaluation of route administration and dosage for DTIs and the related clinical outcomes.

Purpose: To compare the clinical outcomes of DTI use in hemodialysis patients with HIT/HITTS in the real-world setting.

Objectives: The primary objective is to compare the triple composite endpoint (thrombosis, bleeding, and mortality) between DTIs including an evaluation of the pharmacodynamic response (aPTT) in patients receiving dialysis that are diagnosed with HIT/HITTS and are managed with a direct thrombin inhibitor. The secondary objective is to compare the clinical outcomes of the DTIs in patients receiving hemodialysis that are diagnosed with HIT/HITTS as a function of route of administration and dosage.

Methods: A retrospective outcome evaluation will be performed using the institution's electronic data repository. All patients receiving hemodialysis and argatroban, bivalirudin, or lepirudin between January 1, 1995 and July 31, 2007 will be included. Diagnosis of HIT will be determined by exposure to heparin in the prior 100 days or documented heparin allergy and one or more of the following: 1. Platelet count of less than 150,000/mm³ 2. Decline in platelets of greater than 50% from baseline 3. Documented ICD-9 diagnosis code for HIT. Incarcerated individuals, mentally challenged individuals, pregnant women, and patients less than 18 years of age will be excluded. The proposed data analysis for the primary outcome will be a comparison of the triple composite endpoint (thrombosis, bleeding, and mortality) between the three DTIs including an evaluation of the association between aPTT and the clinical endpoints. The secondary objective will be a comparison of

the triple composite endpoint of the DTIs between high versus low dosages and different routes of administration.

Significance: The results will contribute to the accomplishment of medication safety goals included in Objective 1.2 from the ASHP 2015 Health-System Initiative and the proposed joint Commission 2008 National Patient Safety Goal 3E. The results of this investigation will be used to define and create institutional guidelines for DTI use to support our pursuit of future funding of subsequent investigations into selection of the optimal agent for the management of HIT.