ABSTRACT

Characterization of bivalirudin use at a pediatric hospital

Edward Mueller, PharmD, Seth Campbell, PharmD, BCPPS, and Daniel Heble, Jr., PharmD, BCPPS

Purpose

Bivalirudin is a direct thrombin inhibitor currently FDA approved for use only in adult patients undergoing percutaneous coronary intervention and in the setting of heparin-induced thrombocytopenia. Current data are limited in the pediatric population but do support use for a variety of indications. Recently, increased utilization of bivalirudin has been observed at our pediatric institution. Due to this change in clinical practice and the significant cost disparity compared to traditional anticoagulant therapy, a medication use evaluation was completed. The primary objective was to characterize the use of bivalirudin at our institution to better understand potential future utilization and expenditure.

Methods

A retrospective chart review was completed of patients who received bivalirudin between June 30, 2015 and July 1, 2020. This protocol was approved by the health system's Institutional Review Board. Subjects were excluded if they had an order for bivalirudin, but never received the medication or if they received bivalirudin in the operating room or cardiac catheterization lab. Collected data included demographic measures (age, weight, height, gender, and location) and clinical measures (administration date/time, dose, order sentence and comments, administration titration rates, primary admission diagnosis, indication for bivalirudin use, previously used anticoagulant, concurrent medications, allergies, documented adverse reactions, administration of medications to relieve side effects, reason for discontinuation of bivalirudin, reason for inpatient administration). Collected data were analyzed to characterize use of bivalirudin in pediatric patients to observe trends in utilization at our institution over the five-year evaluation period.

Results

Sixty-four patients, encompassing 66 different patient encounters, met inclusion criteria during the observation period. The median age of patients was 1.02 years (range: 0.02 to 19.27 years) and the mean normalized initial infusion rate was 0.279 $\pm$ 0.119 mg/kg/hr. Bolus doses were observed in 12 patient encounters with few patients receiving multiple bolus doses. The median duration of bivalirudin administration was 10 days (range: 1-345 days). Goal partial thromboplastin time (PTT) ranges were variable with 60-90 seconds being the most commonly cited (n=40, 61%).

The most common indication for bivalirudin administration was deep vein thrombosis (n=24, 36%). Bivalirudin was utilized for anticoagulation in continuous renal replacement therapy (CRRT) (n=7, 11%), extracorporeal life support (ECLS) (n=15, 23%), and ventricular assist devices (VAD) (n=8, 12%). Other indications included heparin-induced thrombocytopenia (HIT), hepatic artery prophylaxis following liver transplantation, and intracardiac thrombus. Forty-five patients (68%) were transitioned from bivalirudin to a different antithrombotic agent. Additional indications for discontinuing bivalirudin included decompensation/death (n=11, 17%) and receiving a heart transplantation (n=7, 11%).

Forty-seven patients (71%) had documented antithrombotic therapy prior to the initiation of bivalirudin; continuous heparin infusion was the most frequent (n=38, 58%). Additionally, 29 patients received concomitant antithrombotic therapy with aspirin being the most common (n=20, 30%). Bleeding events were documented in 16 patients (24%).

Conclusion

The use of bivalirudin has increased over the past five years with the most considerable increase occurring in the final year of the observation period. Bivalirudin was utilized for a variety of indications and throughout the entire spectrum of pediatric patients. Goal PTT ranges were widely variable for patients included in the evaluation. Bleeding events were frequently observed; however, the observational design of the evaluation limits the ability to assign causality or control for specific patient factors.

Only three existing protocols at our institution incorporate bivalirudin therapy: hepatic artery thrombosis prophylaxis follow liver transplantation, VAD anticoagulation, and ECLS anticoagulation. Due to significant use beyond these indications, along with wide variability in monitoring and concerns for bleeding events, further protocol development and implementation is warranted. Due to the high cost of bivalirudin, defining criteria for use would be beneficial.