Bivalirudin Use in Pediatric Patients

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Background

- Bivalirudin is a direct thrombin inhibitor indicated for patients with known or suspected heparin induced thrombocytopenia in adult patients requiring percutaneous coronary interventions
- There is limited data to guide dosing of bivalirudin in pediatric patients

- Study objective: To describe our experience with bivalirudin in pediatric patients

Methods

- Retrospective chart review
- All pediatric patients younger than 18 years old who received bivalirudin at UMMC Children's Hospital from August 2016 to October 2019

Study Endpoints

- Time in therapeutic range (TTR) using Rosendaal method
  - –Duration of therapy, days within range, percent days within range
- Time to therapeutic range
- Incidence of major bleeding
  - – Bleeding in a critical area
  - – ≥ 20 mL/kg/day of red blood cells required
- Clotting complication
  - –Incidence of oxygenator/pump exchange and post-cannulation thrombosis
  - –Systemic thrombosis
- Incidence of serotonin release assay confirmed HIT
- Doses of bivalirudin
- Cost of bivalirudin therapy

Disclosure & Abbreviations

The authors of this presentation do not have any financial or personal relationships with any commercial entities to disclose that may have a direct or indirect impact on the subject matter of this presentation

TTR- time in therapeutic range; n- number, IQR- interquartile range; kg- kilograms; cm- centimeters; U- units; hr-hour; HIT- heparin induced thrombocytopenia; mL- milliliters; mg- milligrams

Results

Table 1. Baseline Characteristics

Characteristic	No of Patients=13
Male, n (%)	7 (53.8)
Median Age, months (IQR)	10 (0, 53.2)
Median Gestational Age, weeks (IQR)	38 (36, 38)
Median Weight, kg (IQR)	7.58 (4.73, 21.2)
Median Height, cm (IQR)	64 (55.5, 103.2)
Patients receiving ECMO, n (%)	5 (38.5)
Patients on LVAD, n (%)	3 (23.1)
Patients on CRRT, n (%)	2 (15.4)
Other, n (%)	5 (38.5)
Heparin use prior to bivalirudin, n (%)	12 (92.3)
Median dose of heparin prior to bivalirudin initiation, U/kg/hr (IQR)	30.5 (21.8, 37.2)

Table 2. Indications for Bivalirudin

Indication	n (%)
Suspected HIT	4 (30.8)
Heparin resistance	6 (46.2)
First line therapy	3 (23.1)

Table 3. Study Endpoints

Endpoint	No of Patients=13
Median duration of therapy, days (IQR)	18.1 (3.7, 48.2)
Median days within range, days (IQR)	10.6 (5.8, 79.7)
Median percent days within range, % (IQR)	60.6 (49.7, 69.4)
Time to therapeutic range, hrs (IQR)	4 (0, 12)
Median number of RBC transfusions per patient, n (IQR)	9 (1, 15)
Median RBC transfusions required, mL/kg (IQR)	15 (9, 15)
Incidence of major bleeding, n (%)	9 (69.2)
Number of patients with thrombotic events, n (%)	5 (38.5)
Incidence of serotonin release assay confirmed HIT, n (%)	0 (0)
Median starting dose, mg/kg/hr (IQR)	0.15 (0.1, 0.25)
Median dose, mg/kg/hr (IQR)	0.2 (0.16, 0.5)
Median maximum dose, mg/kg/hr (IQR)	0.48 (0.3, 0.9)

Table 4. Study Endpoints for Specific Patient Groups

	ECMO without CRRT	ECMO with CRRT	LVAD
Number of patients	3	2	3
Median duration of therapy, days (IQR)	14 (9.9, 26)	11.7 (8.4, 14.9)	119.3 (99.5, 178.2)
Median days within range, days (IQR)	8.9 (6.3, 13.9)	6.5 (4.4, 8.5)	49.9 (49.1, 66.3)
Median percent days within range, % (IQR)	63.6 (56.7, 63.7)	51.5 (48, 54.9)	60.6 (40.8, 65)
Time to therapeutic range, hrs (IQR)	4 (3,6)	6 (3, 10)	8 (0,17)
Median number of RBC transfusions per patient, n (IQR)	15 (13.5, 18)	18 (12, 24)	22 (14, 31)
Median RBC transfusions required, mL/kg (IQR)	15 (10, 15)	15 (15, 20)	8 (6, 15)
Incidence of major bleeding, n (%)	3 (100)	2 (100)	3 (100)
Number of patients requiring pump/LVAD exchange, n (%)	2 (66.7)	0 (0)	2 (66.7)
Number of patients with thrombotic events, n (%)	2 (66.7)	1 (50)	2 (66.7)
Median starting dose, mg/kg/hr (IQR)	0.2 (0.15, 0.35)	0.2 (0.18, 0.23)	0.125 (0.11, 0.14)
Median dose, mg/kg/hr (IQR)	0.5 (0.29, 0.59)	0.18 (0.13, 0.25)	0.8 (0.2, 1.9)
Median maximum dose, mg/kg/hr (IQR)	0.9 (0.6, 0.95)	0.33 (0.32, 0.34)	3 (1.74, 3.7)

Table 5. Cost Analysis

Cost	$949.44 per 250 mg/ 50 mL vial
Median days of therapy	18.1 days
Cost/day/patient	$949.44
Cost/course/patient	$17,184.86

Discussion

- 60% of the time aPTTs were within range
- Bivalirudin doses were higher in patients on LVADs
- Despite the number of thrombotic events and transfusions required, bivalirudin therapy was continued
- Further data is needed before conclusions on the safety and efficacy of bivalirudin in pediatric patients can be determined
- Limitations: Retrospective, descriptive statistics, lack of definition of heparin resistance
- Future directions: Compare with heparin, develop a guideline for the use of bivalirudin