# Characterization of bivalirudin use at a pediatric hospital

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## Background

Bivalirudin acts as an anticoagulant through specific, reversible thrombin inhibition. Normally, thrombin circulates through the blood and is a key factor in the coagulation cascade. By binding to the catalytic and anionic exosite of thrombin, bivalirudin prevents the thrombin-mediated cleavage of fibrinogen to fibrin, which is essential for clot formation. Additional anticoagulant effects come from inhibition of factors V, VIII, and XIII.[1]

Bivalirudin is currently FDA approved for use 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 including the prevention of thrombosis in patients with heparin-induced thrombocytopenia (HIT) and those on extracorporeal life support (ECLS) or ventricular assist devices (VAD) as well as the treatment of thrombosis.[2,3,4,5] Recently, increased utilization of bivalirudin has been observed at Children's Mercy Hospital. Due to this change in clinical practice and the significant cost disparity compared to traditional anticoagulant therapy, a medication use evaluation was completed.

## Objectives

### Primary Objective:

To characterize the use of bivalirudin in pediatric patients

### Secondary Objective:

To determine a need to develop a protocol or identify use restrictions for bivalirudin at this institution in the future

## 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.

**Inclusion Criteria:**

- Any patient with an order for bivalirudin

**Exclusion Criteria:**

- Any patient with an order for bivalirudin, but never received the medication
- Any patient who received bivalirudin in the operating room or cardiac catheterization lab

**Collected data included:**

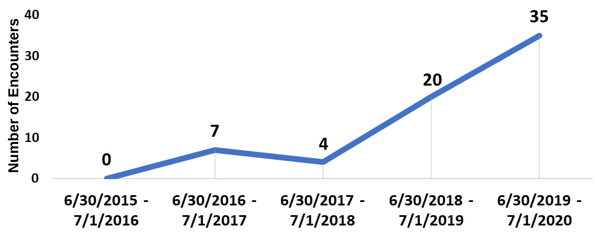
- Demographic measures – age, weight, height, and gender
- Clinical measures – administration date/time, dose, order sentence and comments, administration titration rates, primary admission diagnosis, indication for bivalirudin use, previously used anticoagulant, concurrent medications, allergies, documented adverse reactions, administration of medications to relieve side effects, reason for discontinuation of bivalirudin, reason for inpatient administration
- Location measures – nursing unit of administration, recommending service

## Results

### Table 1. Demographic summary

| Patient Characteristics (n = 64 patients) | |
|---|---|
| Unique Patient Encounters Receiving Infusion, n (%) | 66 (100) |
| Age (years), median (range) | 1.021 (0.019 - 19.266) |
| Weight (kg), median (range) | 8.6 (0.8 - 120) |
| Height (cm), median (range) | 65.5 (30.5 - 189.5) |
| Male, n (%) | 36 (54.5) |
| Encounters with Documented Bleeding Events, n (%) | 16 (24.2) |
| Primary Hospital Service | |
| Cardiac Intensive Care (CICU), n (%) | 29 (43.94) |
| Pediatric Intensive Care (PICU), n (%) | 28 (42.42) |
| Neonatal Intensive Care (NICU), n (%) | 8 (12.12) |
| Hematology/Oncology (Heme/Onc), n (%) | 1 (1.52) |

### Figure 1. Patient encounters that received bivalirudin by time period




### Table 2. Bivalirudin summary

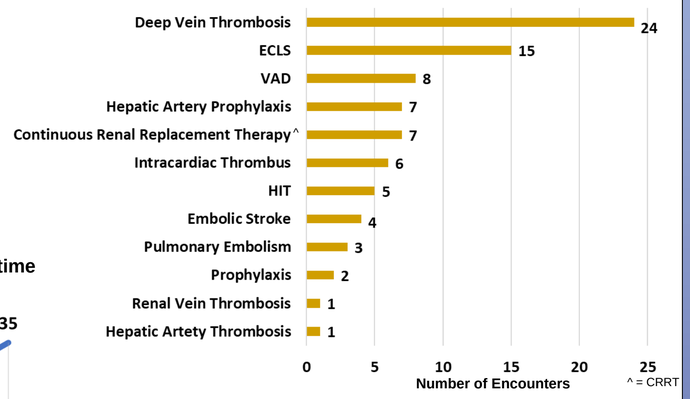
| Bivalirudin Administration Information | |
|---|---|
| Initial Infusion Rate (mg/kg/hr), mean ± standard deviation | 0.279 ± 0.119 |
| Total Number of Bolus Doses, n | 17 |
| Total Number of Patient Encounters Receiving Bolus, n (%) | 12 (18.2) |
| Bolus Dose (mg/kg), mean ± standard deviation | 0.264 ± 0.487 |
| Duration of Administration (days), median (range) | 10 (1 - 345) |
| Total Cost of Therapy (dollars), median (range)* | 4037.50 (102.00 - 130411.25) |

*based upon average wholesale price

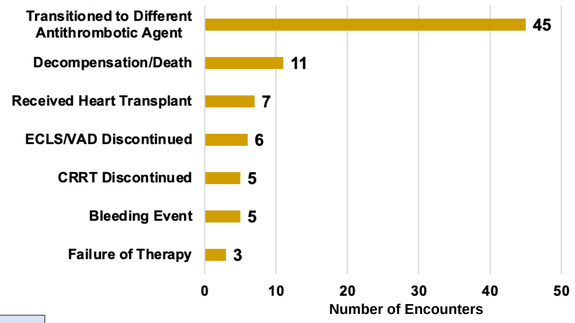
### Table 3. Relevant medication summary

| Medications Relevant to Bivalirudin Therapy | | | |
|---|---|---|---|
| | Antithrombotic Agents Prior To Bivalirudin Therapy | Antithrombotic Agents During Bivalirudin Therapy | Medications to Relieve Adverse Effects |
| Total Number of Encounters | 47 | 29 | 46 |
| Alteplase Infusion | 4 | 5 | |
| Antithrombin III | 14 | 5 | |
| Argatroban | 1 | 0 | |
| Aspirin | 4 | 20 | |
| Dipyridamole | 2 | 13 | |
| Enoxaparin | 11 | 1 | |
| Heparin Infusion | 38 | 2 | |
| Warfarin | 1 | 2 | |
| Aminocaproic Acid | | | 1 |
| Tranexamic Acid | | | 6 |
| Phytonadione | | | 19 |
| Coagulation Factor VIIa | | | 1 |
| Cryoprecipitate | | | 22 |
| Platelets | | | 30 |
| Fresh Frozen Plasma | | | 23 |

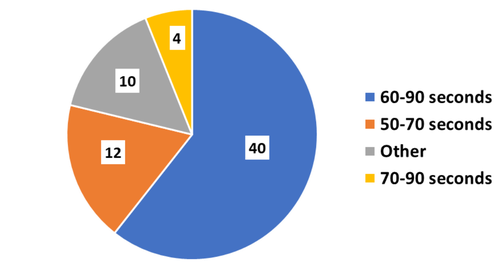
### Figure 2. Indication for bivalirudin administration




### Figure 3. Indication for bivalirudin discontinuation




### Figure 4. Percentage of Subject Encounters with Goal Partial Thromboplastin Time (PTT) range for bivalirudin therapy (n = 66)




## Discussion

- The use of bivalirudin at this institution has grown as demonstrated by the progressive increase in the number infusions over the past five years
- The scope of indications for bivalirudin administration remains broad with most subject encounters receiving bivalirudin for the treatment of deep vein thrombosis
- Bivalirudin was administered to subjects throughout the entire spectrum of pediatric patients from less than 7-days-old to greater than 19-years-old with varying duration of administration
- Most patients received antithrombotic therapy with heparin prior to bivalirudin administration
- Antiplatelet agents were most commonly used concomitantly with bivalirudin; additional concomitant antithrombotic agents included alteplase, enoxaparin, and heparin
- The predominant indication for bivalirudin discontinuation was transitioning to an alternative antithrombotic agent
- Goal PTT ranges remained highly variable throughout the study period

## Conclusion

- Bivalirudin use has expanded to a variety of indications throughout the entire spectrum of pediatric ages with differing infusion durations
- Bivalirudin is incorporated into only three currently existing protocols for hepatic artery thrombosis prophylaxis, anticoagulation in VAD, and anticoagulation in ECLS
- Current lack of consistency in monitoring parameters for therapy despite frequently observed bleeding events
- Further protocol development and implementation is warranted at our institution
- Due to the high expense of this medication, specific criteria for use should be considered

## References

1. Bivalirudin [package insert]. Celerity Pharmaceuticals, LLC., Rosemont, IL; https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/208374s000lbl.pdf. Accessed 23 July 2020.
2. Rutledge, J. M., Chakravarti, S., Massicotte, M. P., et al. Antithrombotic strategies in children receiving long-term Berlin Heart EXCOR ventricular assist device therapy. J Heart Lung Transpl. 2013;32(5):569-73.
3. Rayapudi, S., Torres Jr, A., Deshpande, G. G., et al. Bivalirudin for Anticoagulation in Children. Pediatric Blood Cancer. 2008;51:798-801.
4. Peiri, M., Agracheva, N., Bonavegilo, E., et al. Bivalirudin Versus Heparin as an Anticoagulant During Extracorporeal Membrane Oxygenation: a Case-Control Study. J Cardiothoracic Vasc An. 2013;27(1):30-4.
5. Hamzah M, Jarden AM, Ezetendu C, et al. Evaluation of Bivalirudin As an Alternative to Heparin for Systemic Anticoagulation in Pediatric Extracorporeal Membrane Oxygenation [published online ahead of print, 2020 May 13]. Pediatr Crit Care Med.

## Disclosures

The authors of this presentation have nothing to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation.