Bivalirudin Medication Use Evaluation and Cost Savings Initiative

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Abstract

Bivalirudin is a parenteral anticoagulant that elicits its effect through inhibition of both free and clot bound-thrombin. Inhibition of thrombin serves as a unique mechanism for anticoagulation when compared to heparin as thrombin serves as the final common pathway for the intrinsic and extrinsic coagulation cascades. Due to unclear benefit over heparin, concerns regarding reversibility, and most importantly cost its use as a parenteral anticoagulant varies by institution. A recent drug expenditure review within our institution noted a significant increase in the contribution bivalirudin had on the overall drug budget. In an effort to establish the rationale for the cost increase, a medication use evaluation was performed. While it was discovered that 625 out of 1364 days of bivalirudin therapy were potentially avoidable, an equally important discovery was the amount of waste that was associated with bivalirudin therapy. Calculating daily requirements for bivalirudin indicated that 60% of patients required less than 100 mg per day. Within this article, we describe a cost-savings initiative to reduce bivalirudin waste and the resulting cost-avoidance following implementation.

Keywords

anticoagulation, drug information, pharmacoeconomics, pharmacy administration, bivalirudin

The use of parenteral anticoagulants is common within the hospital setting for prophylaxis and treatment of various conditions. While heparin is the most frequently utilized intravenous anticoagulant, the use of bivalirudin has emerged as a viable option in certain clinical scenarios.¹ Specifically, it is approved for use in percutaneous transluminal coronary angioplasty, and percutaneous coronary intervention with the use of glycoprotein IIb/IIIa inhibitors.² In addition, it is frequently utilized, with significant supporting data, in patients with heparin-induced thrombocytopenia (HIT).^{3–6} Bivalirudin is a direct thrombin inhibitor and differs mechanistically from heparin as it inhibits the final common pathway in the intrinsic and extrinsic coagulation cascades. In addition, it has the unique ability to bind both free and clot-bound thrombin.

The routine utilization of bivalirudin at many hospitals has been limited, to this point, by the lack of a reversal agent, no proven benefit over heparin, and potentially, the cost over alternative agents. With bivalirudin being utilized and evaluated in more clinical scenarios, formulary issues may arise due to the cost discrepancy between bivalirudin and heparin.

Recently, a review of drug expenditures showed a large increase in the contribution bivalirudin had on the overall drug budget at our institution. It was noted that over a 2-year period, utilization had increased 4-fold with a 15-fold increase in the in-patient utilization (Figure 1). The following describes a subsequent cost savings initiative to optimize utilization of bivalirudin while reducing waste.

Figure 1. In-patient bivalirudin utilization: Bivalirudin annual purchasing.

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Table 1. Baseline Demographics.

Age, y	62 (22-92) ^a
Gender (male)	44 (78%)
History of significant bleed/bleeding disorder	7 (12%)
History of clotting/clotting disorder	14 (25%)
Indication for anticoagulation	
MCS	30 (54%)
Long-term devices (HeartMate II, HeartWare HVAD)	14 (47%) ^b
Temporary devices (intra-aortic balloon pump, ECMO, Tandem, CentriMag)	13 (43%) ^b
Syncardia	3 (10%) ^b
DVT/PE	8 (14%)
Atrial fibrillation	5 (9%)
Valve	4 (7%)
Other thrombus (PA, atrial)	4 (7%)
Acute coronary syndrome	2 (4%)
Other	3 (5%)
Indication for bivalirudin	
HIT (suspected or confirmed)	47 (84%)
Suspected pump thrombosis	5 (9%)
Other	4 (7%)
4T score	
0-3	37 (66%)
4-5	14 (25%)
6-8	5 (9%)
Days of heparin therapy prior to starting bivalirudin	8 days (1-26) ^a
Days of bivalirudin therapy	24.4 days (1-151+) ^a
Restarted on heparin after HIT negative	6 (18%) ^c

Note. Values reported in number (percent) unless otherwise indicated. MCS = mechanical circulatory support; ECMO = extracorporeal membrane oxygenation; DVT = deep vein thrombosis; PE = pulmonary embolism; PA = pulmonary artery; HIT = heparin-induced thrombocytopenia.

^aAverage with minimum-maximum range.

^bPercentages based on total of 30 MCS devices.

^c33 total patients were HIT negative.

Bivalirudin Utilization and Identifying Waste

We retrospectively reviewed bivalirudin use at our institution in hospitalized patients who received bivalirudin therapy for more than 24 hours over a 6-month period. A total of 56 patients meet the inclusion criteria for the analysis which equated to 1364 days of bivalirudin therapy (Table 1). Patients on mechanical circulatory support comprised the majority of bivalirudin use (54%), with the predominate indication being suspected or confirmed HIT (84%). The average duration of heparin therapy prior to starting bivalirudin was 8 days (range: 1-26 days), with bivalirudin being utilized for a median of 9.5 days and mode of 6 days (range: 1-151+). While our institution

does invoke a medication formulary, bivalirudin can be utilized without meeting specific criteria for use or preapproval.

Patients who were put on bivalirudin for suspected HIT were further evaluated for appropriateness by assessing heparin enzyme-linked immunosorbent assays and serotonin release assay testing. The results demonstrated that 46% (625 out of 1364 days) of bivalirudin utilization occurred after either a negative enzyme-linked immunosorbent assays or negative serotonin release assay test (Figure 2). While the authors identified this as a potential area for stewardship, assessment of patients receiving appropriate bivalirudin therapy suggested waste was potentially occurring. Reviews of individual patient requirements per day indicate that only 13% of patients were requiring 250 mg or more per day of bivalirudin to achieve and maintain therapeutic anticoagulation (Figure 3). Furthermore, our data indicated that 60% of patients were requiring less than 100 mg of bivalirudin per day.

Minimizing Waste

Within the package insert, bivalirudin is recommended to be diluted to a concentration of 5 mg/mL (250 mg in 50-mL solution) or 0.5 mg/mL (250 mg in 500-mL solution). Historically, our institution has prepared bivalirudin by mixing a vial (250 mg) with a 250-mg bag of solution (dextrose 5% or normal saline) to achieve a 1 mg/mL concentration.² We calculated drug waste per patient per day to evaluate the overall cost of the waste. Based on this simplistic approach, utilizing a 250-mg bag for a patient who is only requiring 100 mg per day represents potential waste of 60% of the vial cost (\$884.75 per vial based on 3Q14 Payment Allowance Limits for Medicare Part B) per day of drug.⁷ With 60% of all patients during the analysis requiring <100 mg per day, for the entire study duration (1364 days) there is a theoretical cost savings of ~\$434 000 over the 6-month study period.

Change in Preparation

Consideration into alternative bag sizes was based on ease of preparation, feasibility, and overall cost savings. A bag size of 100 mL was chosen for several reasons. First, in an effort to maintain the same drug concentration, this was the only realistic option. A 50-mL bag size was considered as well; however, it was felt that continuous infusion bag changes would become too cumbersome for nurses, especially for patients who were receiving >200 mg per day. Second, the average number of patients receiving bivalirudin per day during the analysis was 4.8. There were 150 days during the study analysis when 5 or more patients were receiving bivalirudin. Based on these points, we were able to prepare five 100-mL bags with the use of 2 vials.

Figure 2. Bivalirudin utilization flow diagram.
Note. Patients who received bivalirudin (n = 56) and the associated days of bivalirudin therapy (n = 1364 days). In all, 45 patients had heparin ELISA testing and 11 did not (representing 234 days of bivalirudin therapy). Of the patients who had heparin ELISA testing, an equal distribution of positive (n = 23) and negative results were seen (n = 22). Patients with a negative ELISA result represented 308 total days of bivalirudin therapy with 293 days occurring after a negative result. Confirmatory SRA testing was positive in 7 patients, negative in 11, and not completed in 5 patients with 228 days, 461 days, and 133 days of bivalirudin therapy, respectively. Patients with negative SRA result had 332 days of therapy following the negative result. ELISA = enzyme-linked immunosorbent assay; SRA = serotonin release assay.

Figure 3. Bivalirudin patients' daily dose requirements (total milligrams per day per patient).
Note. Bivalirudin requirements to achieve therapeutic anticoagulation were calculated based on total milligrams per day for each patient. Percentage of patients requiring specific bivalirudin amounts is reported.

Implementation and Education

Pharmacists and technicians were educated on the planned change in procedure as well as the rationale and potential cost savings. To reduce extra work on pharmacy technicians, we devised a standardized preparation (0800) and delivery time (0900) for bivalirudin. Nursing education was important to ensure understanding of a standardized delivery time to reduce medication errors. To ensure medications were administered with Alaris Guardrails (CareFusion, Becton, Dickinson and Company, Franklin, New Jersey) guardrails in place, patients who were actively on bivalirudin needed to have the infusion pumps restarted to update the alternative bag size. In an effort to make the transition easier and have better monitoring on waste, we devised a plan to have bivalirudin bags changed on a daily basis around 9:00 in the morning. This was important for several reasons; first, pharmacists implementing the change were available in the event confusion or questions arose; second, with a beyond use date of 24 hours from preparation, minimization of waste would be ensured if all bags were prepared and delivered to patients at the same time; and third, with preparation occurring at the same time, the overall impact on pharmacy operations would be minimized.

Figure 4. Demonstrated cost savings.

Note. Utilizing actual monthly patient requirements post implementation, actual cost of the 100-mg bag is reported compared with the calculated cost of meeting this same patient requirement with the 250-mg bag.

Cost Savings

Following implementation, we tracked the daily use of bivalirudin and calculated expected savings based on 100-mg bag versus 250-mg bag cost. Based on the information gathered over an entire year, the estimated savings by implementing a 100-mg bag of bivalirudin were ~\$800 000 (Figure 4). Despite tracking utilization on a daily basis, the overall cost savings may be slightly overestimated based on work flow. Specifically, medication waste could still be encountered if five 100-mg bags of bivalirudin were prepared but only 4 patients were receiving the medication. In addition, if patients were receiving more than 250 mg per day of bivalirudin, there could be potential waste of medication depending on the amount prepared during a given day. While we believe, in the right situation, this is a viable cost savings initiative, it is important to discuss potential hidden costs

associated. Pharmacists were required to provide education to the pharmacy staff as well as nursing staff immediately preceding implementation; however, ongoing education is an expectation within our institution. With respect to preparation and delivery, we argue that this actually may help the overall process as technicians can prepare and deliver all bags at the same time instead of performing tasks as requested by the nursing staff. Nursing education was completed at shift change and thus does not result in any additional costs from their standpoint.

Important Considerations

While the data presented indicate cost savings by a smaller bag size, there are several points that need to be considered. First, the average dosing for patients within this study was markedly lower than expected for a normal patient.

The specific reason for this is unclear but likely the result of the medication being utilized in patients with advanced heart failure who may present with hepatic congestion and cardiac cachexia, both of which may reduce coagulation factors leading to falsely elevated coagulation assays. Second, the benefit of smaller bags is dependent on overall census of patients on bivalirudin. The cost savings is negated if only one patient is receiving bivalirudin. Third, while our study utilized the premise of sending daily bags at a specific time (to help minimize confusion when initiating the process), overall logistics need to be considered, refined, and implemented to ensure extra medications are not wasted.

Conclusion

During this medication use evaluation, we discovered tremendous bivalirudin waste due to low individual dosing requirements. We were able to demonstrate cost avoidance through decreasing overall bag size; however, overall logistics need to be established to ensure optimization of utilization. Future projects should evaluate extending the beyond use date of reconstituted bivalirudin bags based on stability and sterility to further enhance logistics of bivalirudin administration.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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