The Use of Idarucizumab for Dabigatran Reversal in Clinical Practice: A Case Series

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ABSTRACT

Purpose: To describe the use of idarucizumab (Praxbind, Boehringer Ingelheim) in routine clinical practice at a large urban academic medical center.

Summary: Seven total doses of idarucizumab were administered to six unique patients from October 31, 2015, to October 31, 2016. The reversal agent was used in conjunction with local bleeding control measures, blood product transfusions, and acid-suppressive therapy. In 86% of cases, idarucizumab administration resulted in a successful cessation of bleeding by clinical assessment. Two patients expired due to coexisting conditions. Idarucizumab was administered to patients with normal baseline coagulation tests in 43% of cases. No adverse reactions related to idarucizumab were reported.

Conclusions: Idarucizumab administration resulted in successful resolution of bleeding by clinical assessment. The therapy for acute bleeding with use of dabigatran (Pradaxa, Boehringer Ingelheim) remains supportive care, in addition to idarucizumab in cases of severe or uncontrolled bleeding. Development of institution-specific protocols and better guidance for using baseline coagulation tests are needed.

Keywords: anticoagulants, idarucizumab, dabigatran, hemorrhage, reversal

INTRODUCTION

Dabigatran (Pradaxa, Boehringer Ingelheim) is the first oral direct thrombin inhibitor approved by the Food and Drug Administration (FDA) for stroke prevention in atrial fibrillation (AF) and the treatment of venous thromboembolism (VTE). Unlike the vitamin K receptor antagonist warfarin, dabigatran therapy has a quicker onset and offset of action, does not require routine monitoring of coagulation parameters, and presents less potential for drug–drug and drug–diet interactions. Dabigatran, at a dose of 150 mg twice daily, has demonstrated better efficacy in stroke prevention in AF with similar rates of major bleeding compared with warfarin in the RE-LY trial. A major concern with newer oral agents, including dabigatran, was a lack of a specific reversal agent to be administered in case of severe and life-threatening bleeding. This lack of an effective reversal agent has remained a challenge to these agents’ widespread utilization. Prior to the approval of a reversal agent, the therapy for major bleeding while on dabigatran consisted of discontinuation of the agent, local bleeding control measures, blood transfusions, activated charcoal (in cases of recent ingestion), and hemostatic therapy (plasma, vitamin K, factor concentrates, cryoprecipitate, platelets). However, one study suggests that prothrombin complex concentrates may be ineffective for reversing the effects of dabigatran. In addition, dabigatran is the only direct oral anticoagulant agent that is significantly cleared by hemodialysis.

In October 2015, the FDA approved idarucizumab (Praxbind, Boehringer Ingelheim) as the first specific reversal agent for dabigatran, indicated for patients with life-threatening or uncontrolled bleeding, as well as in cases where rapid reversal is needed for urgent and emergent procedures. Idarucizumab is a humanized monoclonal antibody fragment that binds the thrombin-binding site of dabigatran with high affinity, effectively neutralizing its anticoagulant effects. Because the agent binds dabigatran with high specificity, it presents an attractive therapeutic option that can reverse the effects of dabigatran without directly affecting natural anticoagulation processes. In the full cohort analysis of a major phase 3 clinical trial that led to its approval (REVERSE-AD), idarucizumab successfully reversed dilute thrombin time (dTT) and ecarin clotting time (ECT) within one hour of administration in all patients with elevated coagulation tests at baseline.

Despite the rapid reversal of thrombin as demonstrated by coagulation parameters, the clinical outcomes were less clear and included a mortality rate of 13.5% in the severe bleeding arm, similar to the mortality demonstrated in pre-idarucizumab outcomes studies. In addition, the clinical real-world experience with idarucizumab is largely limited to isolated case reports and one case series of 11 patients in Europe. The tests used to assess idarucizumab efficacy are not routinely available in a clinical setting, where clinicians will often decide to administer idarucizumab based on history and a clinical situation as recommended by multiple consensus statements.

Finally, only 18% of patients in REVERSE-AD had a creatinine clearance (CrCl) of less than 30 mL/min, while the RE-LY trial excluded patients with renal insufficiency. This population may commonly necessitate the use of idarucizumab in cases of bleeding due to overlooked dose reductions (a 75-mg, twice-daily dabigatran dose is recommended for AF patients with CrCl of 15–30 mL/min) or acute kidney injury (AKI), which would limit the body’s ability to eliminate the medication in a timely manner.

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manner. Patients with poor kidney function would also require special considerations for restarting anticoagulation after the bleeding episode, ensuring that dabigatran is appropriately dosed based on the patient’s degree of renal impairment.

From October 31, 2015, to October 31, 2016, our institution treated six patients requiring the use of idarucizumab for reversal of severe bleeding due to dabigatran. This resulted in seven total episodes of idarucizumab administration (one patient was readmitted, requiring another reversal), which are presented here. All emergency department (ED) and inpatient orders for idarucizumab in the study date range were identified using Crystal Reports (SAP SE, Walldorf, Germany). Charts of all patients with a documented idarucizumab administration in the electronic medical record were retrospectively reviewed. Study approval was granted by the institutional review board at the Albert Einstein College of Medicine.

CASE REPORTS

Case 1
An 82-year-old woman with a past medical history significant for stage IV chronic kidney disease (CKD) and AF presented to the ED after two days of bloody stools. For two years prior to this admission the patient was taking dabigatran 75 mg twice daily, which is an appropriately adjusted dose for this degree of renal impairment; however, dabigatran therapy in patients with stage IV CKD requires frequent CrCl monitoring. Upon examination, the patient was found to be in AKI, with a serum creatinine (Scr) of 3.60 mg/dL—a marked increase from the baseline of 2.0 mg/dL. While the patient was hemodynamically stable, her hemoglobin (Hb) was decreased at 7.0 g/dL, with her partial thromboplastin time (PTT) at 41.4 seconds (reference 26.1–33.8 seconds at our institution) and interna-

tion profile included PT of 11.4 seconds, INR of 1.1, and PTT of 27.9 seconds. The ED course consisted of fluid resuscitation, pantoprazole infusion, transfusion of three units of packed red blood cells, and administration of a 5-g dose of idarucizumab. Following the administration and transfusions, the patient’s hemoglobin returned to 9.4 g/dL, PTT decreased to 21.0 seconds, PT decreased to 10.1 seconds, and BP improved to 110/66 mm Hg. Three days later, the patient had started passing nonbloody stools and tolerating a diet, while her hemoglobin and vital signs remained stable. She was discharged with a clinic follow-up appointment to discuss reinstitution of anticoagulation and outpatient colon cancer surveillance. The patient was reinstituted on dabigatran 150 mg twice daily during the follow-up clinic visit a week after discharge, which was appropriate for the calculated CrCl of 54.4 mL/min in the clinic.

Case 2
One month later the patient from case 1 presented with weakness and black and tarry diarrhea. Upon examination, she was found to be hypotensive (blood pressure [BP], 80/39 mm Hg), anemic (Hb, 6.2 g/dL), and with further deterioration of renal function with Scr of 4.00 mg/dL. The patient’s baseline coagulation profile included PT of 17.3 seconds, INR of 1.7, and PTT of 43.6 seconds. The ED course consisted of fluid resuscitation, pantoprazole infusion, transfusion of two units of packed red blood cells, and administration of a 5-g dose of idarucizumab. Subsequently, the patient’s clinical improvement was noted. Her hemoglobin returned to 8 g/dL and her BP returned to 144/60 mm Hg the following day. An esophagogastroduodenoscopy (EGD) was performed, revealing multiple small nonbleeding duodenal ulcers and one large crated duodenal ulcer without visible vessel. The patient was continued on pantoprazole infusion and intravenous hydration. Once the AKI resolved and no further bleeding was noted, the patient was discharged with a clinic follow-up appointment to discuss reinstitution of anticoagulation. Anticoagulation was held for four months until a follow-up EGD was performed on an outpatient basis, revealing a healed ulcer and moderate stenosis at genu of bulb and descending duodenum. Dabigatran was restarted at a dose of 75 mg twice daily (adjusted for renal dysfunction) due to the patient’s high risk of stroke (CHA2DS2-VASc score 4). No further admissions for bleeding were noted.

Case 3
An 82-year-old, 103-kg woman with a past medical history significant for AF, mild mitral valve stenosis, and colon cancer presented to the ED with rectal bleeding and generalized weakness. The patient had been taking dabigatran 150 mg twice daily for the past four years. The patient underwent a colon resection surgery one week prior to presentation. A few days post-surgery, she reported bright red blood with occasional black discharge in her stool. Bleeding after colonic anastomosis is not uncommon and can often be complicated by anticoagulant medications. Upon examination, the patient was found to be hypotensive (BP, 98/53 mm Hg), tachycardic (heart rate, 135 beats per minute), and anemic (Hb, 6.0 g/dL). The calculated CrCl was 37.8 mL/min. The patient’s baseline coagulation profile included PT of 11.4 seconds, INR of 1.1, and PTT of 27.9 seconds. The ED course consisted of fluid resuscitation, pantoprazole infusion, transfusion of three units of packed red blood cells, and administration of a 5-g dose of idarucizumab. Following the administration and transfusions, the patient’s hemoglobin returned to 9.4 g/dL, PTT decreased to 21.0 seconds, PT decreased to 10.1 seconds, and BP improved to 110/66 mm Hg. Three days later, the patient had started passing nonbloody stools and tolerating a diet, while her hemoglobin and vital signs remained stable. She was discharged with a clinic follow-up appointment to discuss reinstitution of anticoagulation and outpatient colon cancer surveillance. The patient was reinstituted on dabigatran 150 mg twice daily during the follow-up clinic visit a week after discharge, which was appropriate for the calculated CrCl of 54.4 mL/min in the clinic.

Case 4
A 79-year-old man with a past medical history significant for moderate mitral valve regurgitation, AF, CKD stage III, and recent automated implantable cardioverter defibrillator placement presented after two weeks of confusion, lethargy, and weakness. Of note, patients with a history of heart valve disorders were excluded from the RE-LY trial, although the definitions of heart valve disorders varied among direct oral anticoagulant trials, leading some clinicians to use these agents in patients with mild and moderate mitral valve regurgita-

tion. Upon presentation, the patient was hypertensive (BP,
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181/77 mm Hg) and anemic (Hb, 8.5 g/dL). A computed tomography (CT) scan of the head demonstrated an intracranial mass with surrounding edema and hemorrhage. The patient’s baseline coagulation profile included PT, 13 seconds; INR, 1.3; and PTT, 32.6 seconds. The patient was taking dabigatran 75 mg twice daily and had an estimated CrCl of 45.4 mL/min. The patient was administered a 5-g dose of idarucizumab to reverse dabigatran. Twenty-four hours after the idarucizumab infusion, the coagulation profile demonstrated a PT of 12.9 seconds, an INR of 1.3, and PTT of 24.9 seconds. The neurosurgery team performed an elective left temporal craniotomy, which the patient tolerated without complications. The patient was discharged to a rehabilitation facility without anticoagulants due to the risk of repeated intracranial bleeding.

Case 5

A 64-year-old woman from a nursing home with a past medical history significant for dementia, chronic obstructive pulmonary disease, congestive heart failure, and AF presented to the ED with altered mental status. The ED team initially administered fluids and antibiotics for suspected sepsis. Upon examination, she was found to be hypotensive (BP, 70/49 mm Hg) and hypoglycemic (blood glucose, 39 mg/dL). The team administered dextrose 50% and intravenous fluids and started her on vasopressors. Her initial lab values revealed severe anemia with Hb of 6 g/dL and a baseline coagulation profile that included PT of 28.7 seconds, INR of 2.8, and PTT of 200.0 seconds. The patient’s medical record revealed a regimen of dabigatran 150 mg twice daily at home. The calculated CrCl was 35.8 mL/min, with an SCR of 1.95 mg/dL elevated from 0.51 mg/dL a week earlier. The vascular surgery team diagnosed the patient with a left upper extremity compartment syndrome requiring an emergent fasciectomy and hematoma evacuation. Prior to the procedure, she received four units of packed red blood cells, two units of fresh frozen plasma, 20 units of cryoprecipitate (in the setting of a large transfusion while fibrinogen level was pending), two units of platelets, and a 5-g dose of idarucizumab to reverse dabigatran. The patient underwent the procedure without complications, but received an additional six units of packed red blood cells and two units of platelets postoperatively, followed by a transfer to the surgical ICU for observation. Twenty-four hours after the idarucizumab infusion, the patient’s hemoglobin returned to 9.1 g/dL, while the coagulation profile revealed a PT of 10.4 seconds, INR of 1.0, and PTT of 42.9 seconds. During the ICU stay, the patient developed sepsis with methicillin-resistant Staphylococcus aureus isolated in the sputum cultures. She remained hypotensive on vasopressors, with persistent decreases in hematocrit despite transfusions. Rebound increases in coagulation markers were not observed throughout the patient’s stay. As prognosis continued to worsen, the patient was terminaly extubated and expired shortly after.

Case 6

A 53-year-old man with a history of ethanol abuse, asthma, and AF was brought in by ambulance after an unresponsive episode with foaming at the mouth. The patient’s caregiver reported that he was taking dabigatran 150 mg twice a day for stroke prevention in AF. At presentation, the patient’s PTT was 38.6, INR was 1.4, and PT was 13.9. The patient’s CrCl was calculated to be 71 mL/min. In the ED, the patient experienced multiple grand mal seizure episodes, during which he was noted to bite his tongue. After the seizures were controlled with lorazepam and fosphenytoin, the patient was noted to be bleeding from the mouth, resulting in airway compromise in the setting of tongue swelling. The patient was intubated, and his mouth was packed with gauze in an attempt to control the bleeding. The ear, nose, and throat surgical team attempted to suture the tongue but was unable to close all lacerations due to the endotracheal tube placement, resulting in continued bleeding. The decision was then made to administer a 5-g dose of idarucizumab in an attempt to control the bleeding. Four hours later, all signs of active bleeding resolved. Follow-up PTT was drawn the next day, with the result of 32.2 seconds. A week after the initial presentation, dabigatran was restarted at the previous dose of 150 mg twice daily in the hospital, and the patient was discharged two days later.

Case 7

An 82-year-old woman with a past medical history of AF, a permanent pacemaker, and a previous episode of stroke presented to the ED with one day of right groin pain and nausea. On exam she was noted to have a distended and diffusely tender abdomen, with bilateral groin hernias. A CT scan revealed a perforated small bowel obstruction and a hemorrhagic right inguinal hernia. The patient was started on antibiotics and prepared for an emergent exploratory laparotomy, small bowel resection, and reduction and repair of right femoral hernia. Because the patient was taking dabigatran 150 mg twice daily at home, the team administered idarucizumab for dabigatran reversal before the procedure. The baseline Hb was normal at 13.9 g/dL, but no baseline coagulation profile was ordered. The patient’s calculated CrCl was 53.9 mL/min. Postoperatively, the patient was transferred to the surgical ICU, where the patient’s PTT was 29.7 seconds four hours after idarucizumab infusion. The patient’s postoperative course was protracted due to slow return of bowel function. The team postponed resuming dabigatran until the patient was able to tolerate oral feeds. However, the patient continued to worsen and expired on postoperative day 6 due to a cardiac arrest following an episode of bilious vomiting requiring nasogastric decompression.

DISCUSSION

We herein describe six patients receiving a total of seven doses of idarucizumab in the ED of a large urban academic medical center (Table 1). To our knowledge, this is the largest case series of idarucizumab use in clinical practice at a single institution in the United States to date, which adds to the current case literature on the real-world experience with this agent. A series of 11 cases was published from multiple institutions in Europe, with varying indications for idarucizumab use that included postoperative bleeding, emergency high-bleeding-risk surgery, lumbar puncture, intracranial bleeding, and thrombolyis. In contrast, all of our patients required emergent reversal of anticoagulation for cessation of bleeding. Our patients had a median age of 80.5 years (range, 53–82 years), and four out of six patients (67%) were female. All patients were on dabigatran therapy for AF. In five of the seven cases, the patient was suc-
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Table 1 Case Summaries

<table>
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<tr>
<th>Case 1*</th>
<th>Case 2*</th>
<th>Case 3</th>
<th>Case 4</th>
<th>Case 5</th>
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<td>Discharged</td>
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</table>

* Cases 1 and 2 represent the same patient.
† Creatinine clearance estimates were not calculated in patients with acute kidney injury because the Cockcroft-Gault formula requires a stable serum creatinine level.28

AKI = acute kidney injury; BID = twice daily; CrCl = creatinine clearance, estimated using Cockcroft-Gault equation; Hg = hemoglobin; INR = international normalized ratio; N/A = not available; PTT = partial thromboplastin time.

cessfully discharged from the hospital after the resolution of bleeding. Two patients receiving idarucizumab expired prior to discharge from causes likely unrelated to the initial bleeding episode (sepsis and cardiac arrest). Idarucizumab was used in conjunction with fluid resuscitation, blood product transfusions, local bleeding control measures, and acid-suppression therapy when the bleeding site was gastrointestinal.

The cases described here represent a cross-section of real-world use of idarucizumab in a clinical setting. At this institution, a specific protocol for dabigatran reversal was lacking, resulting in deviation from management practices described in the REVERSE-AD trial. In cases 2 and 7, pre- or post-administration coagulation tests were not ordered, with clinicians instead relying on hemodynamic measures and clinical assessment to confirm anticoagulant reversal. This practice could result in potentially missed rebound increases in anticoagulation, which could warrant an additional dose if coupled with clinically significant bleeding. In one case, idarucizumab was administered in a patient whose bleeding severity did not meet the criteria used in REVERSE-AD. In addition, while 26% of patients in the REVERSE-AD trial were administered idarucizumab with normal baseline PTT values, this proportion of patients was larger at our institution (43%). The development of institution-specific guidelines and clinical pathways is needed to ensure that clinicians’ approach to patients is standardized and evidence-based.

This case series confirms that idarucizumab is effective in restoring coagulation parameters in patients presenting with elevated PTT. However, ultimately the clinical outcomes of patients can be influenced by many factors, such as hospital-acquired infections and other coexisting conditions. In addition, the size of anatomical bleeding lesions and potentially missed sources of blood loss may result in negative patient outcomes despite timely reversal of anticoagulation.15 None of the deaths in our patients occurred within the first 96 hours of presentation to the ED, and none seem to be related to the initial bleeding episode.

Indications, Dosing, and Renal Function

In our institution, idarucizumab was used for management of uncontrolled bleeding in all seven cases. In addition, in two cases (29%) idarucizumab was used immediately before surgical procedures for the management of bleeding, which included hemorrhagic hernia repair and intracranial surgery. In case 1, idarucizumab was administered in a patient with a stable hemoglobin and without hemodynamic instability, which did not meet the “overt, uncontrollable, or life-threatening bleeding” indication used in the clinical trial. In compliance with the prescribing information, idarucizumab orders consisted of two 2.5-g doses administered no more than 15 minutes apart. Our physician order-entry system ensured that the order was entered and administered correctly in all instances.

In three of our seven cases (43%) requiring the use of idarucizumab, the patient presented with an acutely worsened renal function, while in five of seven cases (71%) the CrCl upon admission was less than 50 mL/min. These cases highlight the importance of closely monitoring renal function in patients with moderate-to-severe chronic kidney disease on dabigatran because 85% of unchanged bioavailable drug is cleared by the kidneys.26 Only two patients presenting with bleeding in the setting of an acute kidney injury are reported in the case literature,17,18 in addition to the 43% of patients in REVERSE-AD presenting with a CrCl of less than 50 mL/min. There are no current recommendations for adjusting idarucizumab dose in patients with renal impairment, who may exhibit higher concentrations of dabigatran upon presentation.19 In these patients, the potential rebound effect may require redosing or hemodialysis. None of the patients in our institution received a second dose of idarucizumab. Administration of additional doses is described in only one case report, where a patient on hemodialysis demonstrated persistently elevated coagulation parameters.18 In accordance with the REVERSE-AD protocol, a second dose should be administered only in a patient with clinical signs of continued bleeding.5
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Monitoring Coagulation Parameters

The decision to administer idarucizumab in our patients was made without baseline ECT/dTT values but rather based on history of intake, clinical presentation, and assessment of bleeding severity. This is similar to the enrollment practices of the REVERSE-AD trial, where clinicians selected candidates for idarucizumab without access to dTT or ECT values. At our institution, only PT, INR, and PTT values are routinely available, while dTT is available as a send-out test to a central laboratory. PTT values upon presentation did not appear to influence the decision to administer idarucizumab because, in three encounters (43%), the patient’s initial PTT was within normal limits, while in one encounter (14%) the baseline PTT was not ordered at all. A history of idarucizumab use with an uncontrolled or life-threatening bleed or a need for preoperative reversal was a sufficient indication for ordering idarucizumab.

The utility of currently available baseline coagulation tests is questionable. Waiting for results of coagulation tests in an acutely bleeding patient may delay life-saving therapy and result in adverse outcomes. Forty-two patients in REVERSE-AD (8.3%) received idarucizumab with normal baseline dTT and ECT values, but they were excluded from the efficacy analysis. The trial results suggest that idarucizumab can be given safely in patients with normal baseline coagulation parameters, while a study in healthy volunteers confirmed that idarucizumab does not carry a procoagulant risk. Some suggest that dTT can be used to assess the degree of reversal more accurately than PTT; however, our patients were all assessed for cessation of bleeding clinically.

Rebound dabigatran concentrations 24 hours after idarucizumab infusion have been reported in 114 patients (23%) in REVERSE-AD, in addition to multiple case reports describing rebound increases in PTT. So far, only one case describes clinically significant bleeding resulting from the increased coagulation parameters requiring an administration of a second dose of idarucizumab. None of the patients at our institution experienced rebound coagulation parameters, but one patient (case 7) continued to exhibit decreases in hematocrit despite sustained reversal of anticoagulation as demonstrated by PTT. The patient did not receive repeat doses of idarucizumab. The prescribing information for idarucizumab recommends redosing only if clinically significant bleeding persists but does not provide guidance on the use of coagulation tests.

Pharmacoeconomic Considerations

A challenge that health systems will face is the high cost of idarucizumab that may potentially be wasted if administered to patients with normal baseline dabigatran levels (average wholesale price, $4,200 per dose). Because REVERSE-AD evaluated only pharmacokinetic reversal of dabigatran and excluded patients with normal ECT/dTT values at baseline from the efficacy analysis, we cannot conclude whether idarucizumab will have any efficacy in patients with normal baseline PTT. If idarucizumab provides no efficacy in these patients, it may suggest that at least 43% of the doses administered at our institution have been unnecessary. Studies evaluating clinical outcomes of patients treated with idarucizumab are needed, particularly evaluating clinical outcomes in patients with normal values on the standard coagulation tests.

The tests used in REVERSE-AD as markers for dabigatran concentration require sending samples to a central laboratory and thus would not be available to guide administration decisions. Development of point-of-care testing to evaluate dabigatran concentrations would help ensure administration of idarucizumab only to patients who will likely benefit from it. Before such tests are developed, idarucizumab should be administered to all patients presenting with severe, uncontrolled bleeding and a history of recent (less than 24 hours) dabigatran intake despite high medication costs.

Reinitiating Anticoagulation

After an admission for a bleeding episode, clinicians are often reluctant to discharge the patient on dabigatran. Only one of our patients was restarted on dabigatran therapy as an inpatient, while in three instances reinitiation was deferred to an outpatient follow-up. In a patient who presented with an intracranial hematoma, the decision was made to avoid anticoagulation therapy altogether. Although none of these patients developed thrombotic or embolic events prior to reinitiation, it is important to note that there is always a risk of thrombus or embolus when patients are off their anticoagulant medications. While idarucizumab does not cause a prothrombotic state due to its specificity to dabigatran, the patients’ underlying AF predisposes them to embolic morbidity and mortality as assessed by the CHA2DS2-VASc score. It is recommended that clinicians carefully evaluate the risk of thrombosis in these patients and reinitiate the agent if risk of thrombosis outweighs risk of bleeding. A study by Glund et al. demonstrated that restarting dabigatran in healthy volunteers 24 hours after reversal achieved levels of anticoagulation similar to those prior to reversal, which suggests that dabigatran can be reinitiated with no loss of efficacy. However, because many patients will present with renal dysfunction, it is crucial to ensure that the dose is adjusted to the patient’s level of renal impairment. It is also important to note that the data on novel oral anticoagulant use in patients with chronic kidney disease (especially with a CrCl less than 30 mL/min) is limited; therefore, clinicians should strongly consider using warfarin in this population because of the ability to monitor the degree of anticoagulation by INR.

CONCLUSION

In a large urban academic medical center, idarucizumab was used to reverse acute bleeding from dabigatran in seven cases during a one-year period. The standard coagulation markers at baseline did not appear to influence the decision to administer the reversal agent, with a large proportion of patients receiving idarucizumab without elevated PTT. Six of seven cases (86%) had a clinical resolution of bleeding with no adverse events reported, while two patients (29%) expired prior to discharge. This case series did not include patients with dabigatran-associated bleeding who did not receive idarucizumab; as such, comparative studies are needed to better understand the real-world efficacy of idarucizumab. The therapy for the reversal of major bleeding due to dabigatran remains discontinuation of the agent, local bleeding control measures, activated charcoal if the patient presents within two hours of ingestion, blood transfusions where appropriate, and idarucizumab in cases where the bleeding is severe or uncontrolled.
Reinitiating anticoagulation after reversal remains a challenge, with great attention given to the patient’s renal function. Further guidance on using coagulation tests to guide idarucizumab administration is needed. Institutions should develop clinical pathways and administration protocols for treating patients presenting with dabigatran-related bleeding.

REFERENCES


