Case Studies

Real-World Experience with Idarucizumab to Reverse Anticoagulant Effect in Dabigatran-Treated Patients: Report of 11 Cases from Taiwan

Li-Kai Tsai, MD, PhD,* Huey-Juan Lin, MD, MPH,† Su-Kiat Chua, MD, PhD,‡ Pen-Chih Liao, MD,§ Yuan-Po Yang, MD,‖ Ping-Chen Chou, MD,¶ Chun-Wei Lee, MD,# Mao-Jen Lin, MD, PhD,** Hsi-Ming Chen, MD,†† Jung-Tze Yeh, MS,‡‡ and Yi-Heng Li, MD, PhD§§

Background: This study aims to observe the effectiveness and safety of idarucizumab in dabigatran-treated patients with severe bleeding or requiring surgery in Taiwan. *Methods and Results:* In Taiwan, 11 dabigatran-treated patients developed severe bleeding, fracture that needed surgery, and acute ischemic stroke requiring thrombolysis. These patients were treated with idarucizumab and obtained adequate hemostasis. Our experiences reconfirmed the efficacy and safety of idarucizumab in Asian patients. *Conclusions:* Idarucizumab improves safety in dabigatran-treated patients. Continued education about the availability and appropriate use of idarucizumab is necessary in Asia. **Key Words:** Idarucizumab—dabigatran—anticoagulation reversal—bleeding—surgery—thrombolysis.

Introduction

Non–vitamin K antagonist oral anticoagulant (NOAC) has become the first-line therapy to prevent stroke in patients with non–valvular atrial fibrillation (AF).[1] Notably, the therapeutic efficacy and bleeding complications with anticoagulant treatment seem to be different between Asians and non-Asians. In the phase 3, randomized clinical trials of NOAC, Asian patients using warfarin had a higher risk of major bleeding events, including intracranial hemorrhage (ICH), than non-Asian patients with warfarin even though Asians were less intensely anticoagulated with warfarin.[2] In addition, NOACs are more effective and safer in Asians than in non-Asians in comparison with warfarin with more reduction in AF-related embolic events and the risk of major bleeding or ICH.[3] However, even under the treatment with the same dose of NOACs, Asian patients still have a higher risk of major bleeding than non-Asians.[2,3] Therefore, the effectiveness and safety of anticoagulants or reversal agents should not only be investigated in non-Asian populations but also need to be reconfirmed in the Asian group.

From the *Department of Neurology, National Taiwan University Hospital, Taipei, Taiwan; †Department of Neurology, Chi Mei Medical Center, Tainan, Taiwan; ‡Department of Internal Medicine, Shin Kong Wu Ho Su Memorial Hospital, Taipei, Taiwan; §Division of Cardiovascular Medical Center, Far Eastern Memorial Hospital, New Taipei City, Taiwan; ‖Cardiovascular Department, Changhua Christian Hospital, Changhua, Taiwan; ¶Department of Neurology, National Taiwan University Hospital Hsin Chu Branch, Hsinchu, Taiwan; #Department of Internal Medicine, Mackay Memorial Hospital Tamshui Branch, New Taipei City, Taiwan; **Department of Medicine, Taichung Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, Taichung, Taiwan; ††Department of Neurology, Ton Yen General Hospital, HsinChu, Taiwan; ‡‡Medical Department, Boehringer Ingelheim Taiwan Limited, Taipei, Taiwan; and §§Department of Internal Medicine, National Cheng Kung University Hospital and College of Medicine, Tainan, Taiwan.

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All authors contributed equally to this study.

Address correspondence to Yi-Heng Li, MD, PhD, Department of Internal Medicine, National Cheng Kung University Hospital, 138 Sheng Li Road, Tainan 704, Taiwan. E-mail: heng@mail.ncku.edu.tw.

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As with any anticoagulant, NOACs are still associated with bleeding complications. The annual risk of ICH in NOAC-treated patients ranged from .23% to .50% in phase 3 clinical trials.[4] Thus, the existence of effective reversal agents for NOACs becomes mandatory when patients suffer from life-threatening bleeding or need rapid reversal for emergent procedure or surgery. Idarucizumab is a humanized monoclonal antibody that rapidly reverses the dabigatran-induced anticoagulant effect.[5] The phase 3 clinical study, RE-VERSE AD, further demonstrated that idarucizumab 5 g intravenous infusion resulted in almost 100% reversal of the anticoagulant effect within 4 hours after the administration of the drug as assessed by the coagulation times in dabigatran-treated patients with severe bleeding or requiring emergent surgery or procedure.[6] In patients with severe bleeding, the median time to hemostasis after the administration of idarucizumab was 2.5 hours, whereas 93.4% of the patients that underwent emergent surgery experienced normal intraoperative hemostasis.[6] Recently, real-world experience using idarucizumab to reverse the anticoagulant effect of dabigatran has been published[7]; however, such an experience is rarely reported in Asian patients. Here, we report the real-world experience with idarucizumab in Taiwan (Table 1). Our experience carries important clinical implications for Asian patients who have a higher risk of bleeding with anticoagulant treatment.

Case Presentation

Group A: Spontaneous Bleeding

Case 1. A 78-Year-Old Woman with the Left Cerebellar Hemorrhage

A 78-year-old woman had a history of AF, hypertension, diabetes mellitus, and old ischemic stroke, who received dabigatran 110 mg twice daily over the last 1 year. She developed acute onset of dizziness and unsteady gait, and head computed tomography (CT) scan revealed a small hematoma (estimated hematoma volume: .2 mL) at the left cerebellum. On admission, the modified Rankin scale (mRS) score was 4. The creatinine clearance was 44 mL/min and activated partial thromboplastin time (aPTT) was 44.7 seconds. The last intake of dabigatran was about 5 hours before admission. Intravenous idarucizumab 5 g was given at 4 hour 24 minutes after admission and aPTT became 28.6 seconds. The patient's symptoms improved gradually in the following few days. Follow-up brain magnetic resonance imaging 3 days later showed no further expansion of the hematoma. The patient was discharged at day 10 with the mRS score of 3. No anticoagulant was reused at discharge.

Case 2. An 81-Year-Old Man with the Right Parieto-Occipital Hemorrhage

An 81-year-old man had a history of AF, hypertension, heart failure, and old cerebellar infarction. Dabigatran 110 mg twice daily was given to replace warfarin 2 years ago. This time, he was sent to the emergency department due to acute onset of left hemiparesis, hemianopsia, and drowsy consciousness. The last intake of dabigatran was about 7 hours before admission. The creatinine clearance was 76 mL/min and aPTT was 25.4 seconds. Head CT scan revealed ICH at the right parieto-occipital lobe. He did not receive surgical intervention. Intravenous idarucizumab 5 g was given at 1 hour 12 minutes after admission. The neurological condition was stable in the following days. Follow-up CT scan 6 days after admission revealed partial resolution of hematoma (estimated hematoma volume: from 87 mL to 79 mL). The patient was discharged 6 weeks later and can walk using quadricane (mRS score, 3). No anticoagulant was reused further.

Case 3. An 83-Year-Old Man with Massive Gastrointestinal (GI) Bleeding

An 83-year-old man had a history of AF and coronary artery disease. He received dabigatran treatment at 110 mg twice daily in replacement of warfarin 1 month ago. This time, he developed massive bloody stool, and his blood hemoglobin dropped from 10.6 to 6.8 g/dL. The last intake of dabigatran was about 5 hours before admission. The creatinine clearance was 106 mL/min and aPTT was more than 150 seconds. Following volume resuscitation and pack red blood cell transfusion, intravenous idarucizumab 5 g was given at 4 hours 19 minutes after admission. The aPTT reduced to 33.5 seconds and the bleeding stopped soon after idarucizumab treatment. A colonofibroscope showed diverticulitis in the ascending colon, which was the likely bleeding source. The patient was discharged 1 week later without further incident and was given clopidogrel rather than an anticoagulant.

Group B: Fall-Related Bleeding or Fracture

Case 4. A 77-Year-Old Man with Fall-Related Subdural Hematoma

A 77-year-old man had a history of AF and hypertension. He suffered from ischemic stroke 3 years ago and received warfarin treatment, which was replaced by dabigatran 110 mg twice daily for 1 year. He accidentally fell on the ground and developed left hemiparesis, slurred speech, and drowsy consciousness. The last intake of dabigatran was about 16 hours before admission. The creatinine clearance was 77 mL/min and aPTT was 31.5 seconds. Head CT scan showed the right subdural