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Should We Use Bridging Therapy during Switching Patients from Warfarin to Novel Oral Anticoagulants?

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CASE REPORT

ABSTRACT

Rivaroxaban is a new anticoagulant that was approved by the Food and Drug Administration in 2011 for stroke and systemic embolism prophylaxis in patients with nonvalvular atrial fibrillation. Several characteristics have made rivaroxaban an attractive alternative to warfarin: once-daily dosing, obviating the need for monitoring the international normalized ratio (INR), noninferiority to warfarin for preventing stroke in patients with atrial fibrillation, and comparatively lower risk of intracranial hemorrhage. Both The European Summary of Product Characteristics and the US Prescribing Information recommend to discontinue warfarin and to start rivaroxaban on the following day if the initial INR level is below 3.0, yet many clinics convert patient from warfarin to rivaroxaban when INR level is <2.0 due to increased risk of hemorrhage. Since there are no conventional coagulation measures to reliably demonstrate the level of anticoagulation in patients on rivaroxaban, there is an increased risk of adverse events, especially for patients with high ischemic burden. We report a case of acute ischemic stroke in a patient who switched from warfarin to rivaroxaban (20 mg once daily). A 68-year-old female patient with multiple co-morbidities was admitted to our clinic with ischemic stroke. After 1 week follow-up with parenteral anticoagulation in the neurology clinic, she was discharged with mild deficits and with dabigatran treatment (150 mg twice daily). Novel oral anticoagulants are attractive options for anticoagulation particularly in patients who are incompatible with warfarin therapy. On the other hand, physicians should be alert during switching patients from warfarin to novel oral anticoagulants.

Keywords: Warfarin, novel oral anticoagulants, switch, stroke

INTRODUCTION

Rivaroxaban is one of the newer oral anticoagulant used for primary and secondary prevention of atrial fibrillation (AF). Comparing with warfarin, there is a decreased risk of intracranial bleeding in patients on rivaroxaban therapy. Once-daily dosing and obviating the need for monitoring the international normalized ratio (INR) are other favorable characteristics which make rivaroxaban an alternative to warfarin. Although the manufacturer recommends converting warfarin therapy to rivaroxaban when patient's INR is <3.0, general practice is stopping wafarin and starting rivaroxaban therapy when INR is <2.0. In this case report, we present a patient having an ischemic stroke while switching her warfarin therapy to rivaroxaban.

CASE REPORT

The patient was a 68-years-old woman with a history of coronary artery disease, AF, hypertension, and congestive heart failure; she was transferred to our hospital. Her CHA_2DS_2-VASc score was 4. We started warfarin therapy (5 mg once daily) and monitored INR levels. But the patient was hospitalized in cardiology clinic on account of excessive INR levels several times. Due to the patient's inadequate compliance and labile INR levels, we switched her to rivaroxaban (20 mg once a day). When we started rivaroxaban, her INR was 2.2.

But 4 days after starting rivaroxaban, she presented to the emergency department with left upper extremity and left lower extremity weakness, left facial droop, and slurred speech. Her first vital signs were temperature 36.5°C, blood pressure 145/80 mmHg, heart rate 102 beats/minute, and oxygen saturation 96% on room air. On physical examination, the patient was alert and followed commands intermittently, extraocular movement was intact bilaterally, and pupils were equal and reactive bilaterally. Cranial nerve exam revealed left facial droop. Strength exam were 5/5 in right upper extremity and right lower extremities, 3/5 in left upper extremity, and 2/5 in left lower extremity. Patient was transported to computed tomography (CT) immediately. After her emergency CT scans, we ruled out of intracerebral hemorrhage and transferred her to the neurology clinic. According to her physical findings, neurologists diagnosed her as having ischemic stroke, which was most likely associated with inadequate anticoagulation.

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Her laboratory tests revealed white blood cell 11.10 K/µL, hemoglobin 12.9 g/dL, hematocrit 41.9%, platelet 270 bil/L, sodium 136 mmol/L, potassium 3.4 mmol/L, CO2 22 mmol/L, blood urea nitrogen 30 mg/dL, creatinine 0.78 mg/dL, prothrombin time 21.3 s, INR 1.8 IU, aPTT 38.7 s. Since it was not available in our ED department, we could not assess direct factor Xa activity and plasma rivaroxaban level. After first evaluation, she was transported to the neurology clinic. Three days later, we performed another cranial CT for further evaluation. Her CT scans showed hypodense areas in right insular cortex consistent with ischemia. In addition, a hypodense area was in right thalamic region compatible with chronic ischemia. We also performed carotid ultrasound, which demonstrated non-critical lesions in her carotid arteries. During her follow-up, her symptoms ameliorated, and we reinitiated anticoagulant therapy earlier than expected. Because of her negligence to warfarin therapy and having an ischemic stroke under rivaroxaban, we prescribed her dabigatran etexilate (150 mg twice a day). One week after presentation, she was discharged from the neurology clinic with mild neurological deficits.

DISCUSSION

Rivaroxaban (Xarelto) is a new anticoagulant that was approved by the FDA in 2011 for stroke and systemic embolism prophylaxis in patients with nonvalvular AF. Rivaroxaban is also indicated for treatment and prevention of pulmonary embolism and deep vein thrombosis (1, 2). Factor Xa inhibitor is a new anticoagulant drug class that emerged because of the fact that warfarin requires frequent monitoring, and has multiple drug and food interaction. Rivaroxaban was developed with the goal of predictable pharmacokinetics that eliminates the need for monitoring the INR (3-6). Several characteristics have made rivaroxaban an attractive alternative to warfarin: once-daily dosing, obviating the need for monitoring the INR, noninferiority to warfarin for preventing stroke in patients with AF, and lower risk of intracranial hemorrhage compared with warfarin (7, 8).

The highest INR permitted at the time of transition was 3.0 for starting rivaroxaban according to Rivaroxaban Once Daily Oral Direct Factor Xa Inhibition Compared with Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation (ROCKET AF). In addition, there was no signal in this trial that overlap was associated with an increased risk for bleeding. When switching patients with atrial fibrillation from warfarin to rivaroxaban, the US Prescribing Information recommends to discontinue warfarin and start rivaroxaban on the following day if the initial INR level <3.0 (Janssen Pharmaceuticals Inc.; 2014). The European Summary of Product Characteristics also supports this advice. Recent simulation models support these values in terms of efficacy and safety of switching warfarin to novel oral anticoagulants (9).

Although clinical trials like Rivaroxaban Once Daily Oral Direct Factor Xa Inhibition Compared with Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation (ROCKET AF) demonstrated noninferiority for rivaroxaban compared with warfarin, little is known about adverse events occurred during converting warfarin to novel oral anticoagulants. Moreover, relevant clinical data are not available in terms of the optimal time at which the risk of recurrent thromboembolism exceeds the risk of intracranial hemorrhage due to inadequate anticoagulation.

CONCLUSION

Physicians should be alert during switching warfarin to novel oral anticoagulants. There is a question which must be addressed that should we implement bridging therapy at least for patients with high ischemic burden who had ischemic stroke while converting warfarin to rivaroxaban like in our patient?

Informed Consent: Written informed consent was obtained from patients.

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REFERENCES

1. EINSTEIN Investigators. Oral rivaroxaban for symptomatic venous thromboembolism. N Engl J Med 2010; 363(26): 2499-510. [CrossRef]
2. Prandoni P. Anticoagulant treatment of pulmonary embolism: impact and implications of the EINSTEIN PE study. Eur J Haematol 2012; 89(4): 281-7. [CrossRef]
3. Kubitza D, Becka M, Voith B, Zuehlsdorf M, Wensing G. Safety, pharmacodynamics, and pharmacokinetics of single doses of BAY 59-7939, an oral, direct factor Xa inhibitor. Clin Pharmacol Ther. 2005; 78(4): 412-21. [CrossRef]
4. Perzborn E, Roehrig S, Straub A, Kubitza D, Mueck W, Laux V. Rivaroxaban: A New Oral Factor Xa Inhibitor. Arterioscler Thromb Vasc Bio 2010; 30(3): 376-81. [CrossRef]
5. Winstanley L, Chen R. New thrombin and factor Xa inhibitors for primary and secondary prevention of ischaemic stroke. CNS Neurol Disord Drug Targets 2013; 12(12): 242-51. [CrossRef]
6. Kakar P, Watson T, Lip GY. Rivaroxaban. Drugs Today (Barc) 2007; 43(3): 129-36. [CrossRef]
7. Turpie AG. New oral anticoagulants in atrial fibrillation. Eur Heart J 2008; 29(2): 155-65. [CrossRef]
8. Patel MR, Mahaffey KW, Garg J, Pan G, Singer DE, et al. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. N Engl J Med 2011; 365(10): 883-91. [CrossRef]
9. Burghaus R, Coboeken K, Gaub T, Niederalt C, Sensse A, Siegmund HU, et al. Computational investigation of potential dosing schedules for a switch of medication from warfarin to rivaroxaban-an oral, direct Factor Xa inhibitor. Frontiers in physiology 2013; 5: 417.