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ORIGINAL ARTICLE

Tooth extraction in patients taking nonvitamin K antagonist oral anticoagulants

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Abstract *Background/purpose:* The nonvitamin K antagonist oral anticoagulants direct-thrombin inhibitor dabigatran and the Xa inhibitors rivaroxaban and apixaban are now being used clinically. The course of the patients on these anticoagulants who underwent tooth extraction was assessed.
Materials and methods: The medical charts of these patients were investigated. Tooth extraction was performed while maintaining conventional anticoagulant therapy.
Results: Twenty-three teeth were extracted in 19 patients, including two surgical extractions. Among the 19 patients, nine patients ingested rivaroxaban, six apixaban, and four dabigatran. One patient on rivaroxaban showed persistent postoperative bleeding following two surgical extractions. Mild oozing was observed in five patients (two on rivaroxaban and three on apixaban). There was no bleeding episode in the patients on dabigatran.
Conclusion: The patients on rivaroxaban with a prolonged prothrombin time value have a higher risk of bleeding, especially undergoing surgical extraction. Apixaban correlates to neither activated partial thromboplastin time nor prothrombin time values and the countermeasures should be employed based on the clinical findings.

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Introduction

Nonvitamin K antagonist oral anticoagulants (NVKAs) have been developed as an alternative to warfarin. The direct thrombin inhibitor dabigatran and the Xa inhibitors rivaroxaban and apixaban are now being used clinically.

In mega-studies on efficacy for stroke prevention of each drug [RE-LY (Randomized Evaluation of Long-Term Anticoagulation Therapy) study for dabigatran,[1] the ROCKET AF (Rivaroxaban Once Daily Oral Direct Factor Xa Inhibition Compared with Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation) study for rivaroxaban,[2] and the ARISTOTLE (Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation) study for apixaban[3]], each drug was compared with warfarin in atrial fibrillation (AF) patients and found to be not inferior for prevention of stroke (stroke incidence: dabigatran 1.53%/y vs. warfarin 1.69%/y; rivaroxaban 1.7%/y vs. warfarin 2.2%/y; apixaban 1.27%/y vs. warfarin 1.60%/y), with less hemorrhagic incidence (major bleeding: 110 mg of dabigatran, 2.71%/y vs. warfarin 3.36%/y; apixaban 2.13%/y vs. warfarin 3.09%/y; intracranial hemorrhage: rivaroxaban 0.5%/y vs. warfarin 0.7%/y).[1–3]

With regard to metabolism of dabigatran and rivaroxaban, 70% is excreted by the kidneys and 30% is metabolized by the liver, followed by excretion in the urine and feces,[4,5] while 30% of apixaban is excreted by the kidney and 70% metabolized by the liver. The peak plasma levels of dabigatran, rivaroxaban, and apixaban were measured after 3—4 hours. The half-life was 11—13 hours for dabigatran, 9—13 hours for rivaroxaban, and 8—15 hours for apixaban.[4,5]

The dose adjustments based on prothrombin time-international normalized ratio values, as with warfarin, are not necessary for these drugs. Therefore, NVKAs are increasingly being prescribed based on ease of use by both patients and physicians.

Continued treatment with dabigatran, rivaroxaban, or apixaban of patients undergoing tooth extraction is recommended because of a low rate of major bleeding.[6] However, there have been few reports of surgery-related hemorrhagic events and no uniform consensus exists regarding the management strategy. The purpose of this case series was to assess the course of patients on dabigatran, rivaroxaban, or apixaban who underwent tooth extraction. Additionally, a strategy for hemostatic management is discussed.

Materials and methods

Patients

The present study protocols were approved by the institutional review board and ethics committee of Kyushu University Hospital in compliance with the Helsinki Declaration. In the present study, the medical charts of patients were retrospectively reviewed to investigate the items below.

Tooth extraction was performed in patients on conventional dabigatran, rivaroxaban, or apixaban therapy between April 2013 and January 2015 at the Special Patient Oral Care Unit, Kyushu University Hospital.

The items investigated were patient characteristics (age and sex), dose of dabigatran, rivaroxaban, or apixaban, degree of anticoagulant effects [prothrombin time (PT) or activated partial thromboplastin time (APTT) value on the nearest day of tooth extraction], site and number of extracted teeth, type of tooth extraction (simple or surgical), time of extraction, and incidence of cases of postoperative hemorrhage. Furthermore, platelet count, blood urine nitrogen (BUN), creatinine, aspartate transaminase (AST), alanine transaminase (ALT), and alkaline phosphatase (ALP) were also recorded as laboratory data.

In patients at risk for infective endocarditis, amoxicillin was administered according to guidelines published by the Japanese Circulation Society in order to prevent infective endocarditis.[7] As analgesics, either loxoprofen sodium or acetaminophen was administered as needed.

Tooth extraction and local hemostatic management

Tooth extraction was performed while continuing to maintain doses of dabigatran, rivaroxaban, or apixaban. Local anesthesia was induced using 3% prilocaine (containing 0.054 IU of felypressin). Teeth were extracted in a minimally invasive manner using elevators and forceps, and inflamed granulation tissue was completely curetted. As for local hemostatic measures after tooth extraction, extraction wounds were packed with oxidized cellulose (Surgicel; Ethicon, Somerville, NJ, USA) or atelocollagen sponge (Telpulug, Terumo, Tokyo, Japan), and then horizontal mattress sutures using 4-0 silk were given. When hemostasis could not be achieved using these procedures, bleeding points in soft tissue were cauterized using electrocautery, when necessary. Each patient was asked to bite down on gauze for 30 minutes for compression, and hemostasis was confirmed. The wounds were protected by a surgical acrylic splint with periodontal pack when needed. Sutures were removed after 1 week. Tranexamic acid mouth wash was not used, as use of this agent is not approved in Japan. Likewise, fibrin glue was not used because this agent is not indicated for use during tooth extraction in Japan.

Results

Patient characteristics

The patients (19) included 17 men and two women, with ages ranging from 43 years to 86 years. Twenty-three teeth were extracted, including two surgical extractions (Table 1). Among the 19 patients, nine took rivaroxaban, six apixaban, and four dabigatran. Most of the teeth were extracted 4—9 hours after taking the anticoagulant. Two patients (Cases 15 and 17) received concomitant aspirin (100 mg/d). All patients receiving rivaroxaban indicated prolonged PT values, and most patients receiving dabigatran indicated prolonged APTT values. There were no patients with severe renal or liver dysfunction or thrombocytopenia.

One patient on rivaroxaban showed persistent postoperative bleeding, and mild oozing for short durations was observed in five patients (Table 1). Adequate hemostasis was achieved in all other patients postoperatively.