

Analysis of adherence to therapy comparing DOAC Dipstick test with plasma concentration of rivaroxaban and apixaban in outpatients with venous thromboembolic disease

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Introduction

The efficacy and safety of rivaroxaban and apixaban in patients with venous thromboembolic disease (VTE) is closely related with their presence in patient's blood, identifying daily treatment adherence as a major factor of efficacy. In real life practice the frequent phenomenon of uncertainty of drug intake leads to misuse such as multiple taking or dosage skipping. This may impact the benefit of the antithrombotic treatment particularly in fragile patients and those at very high risk of VTE recurrence. Objective documentation of drug compliance might be a tool for patients' education and improvement of treatment adherence. This is usually achieved by measurement of the specific anti-factor Xa activity. This determination has significant limitations, requiring blood take, time-consuming sample preparation and costly laboratory equipment. The availability of an easy to perform, user-friendly and sensitive assay which could even allow self-assessment could lead to adherence improvement to the antithrombotic treatment based on personalized educational strategies.

The *in vitro* medical device DOAC Dipstick (DOASENSE GmbH) was developed based on the rationale that DOACs are excreted into the urine, thus being easily detectable. It gives qualitative results regarding the absence or presence of DOACs in a patient's urine sample for both direct oral factor Xa inhibitor and oral thrombin inhibitors. This single-use assay has a turnaround time of 10 minutes, and results can be determined by simple visual identification of specific colors with the naked eye¹.

Aim

Primary objective: to validate the use of the DOAC Dipstick device in the evaluation of the presence of rivaroxaban or apixaban in the urine of out-patients receiving these drugs for secondary prevention of VTE

Secondary objective: To test the sensitivity and specificity of the DOAC Dipstick device to detect rivaroxaban or apixaban in patients urine by comparison to the DOAC concentration in patients' plasma measured with specific chromogenic assays.

Materials and Methods

This is an ongoing observational cohort study. We present the results of the consecutively enrolled patients with documented VTE followed at the outpatient care unit of the Antithrombotic Clinic of the APHP.6 (Tenon and Saint Antoine University hospitals) as of the 1st of December 2019 to date. The subjects were on active antithrombotic treatment with rivaroxaban or apixaban for secondary prevention of VTE and fulfill the required inclusion and exclusion criteria for eligibility for participation.

The DOAC Dipstick test strips were incubated shortly in patients' urine samples. Then, after 10 min the colors of the factor Xa and thrombin inhibitor pads were adjudicated by comparison with a color scale on the test tube's label by the treating physician according to the description in the instructions for use. All participants were routinely assessed for anti-factor Xa activity in plasma using the specific chromogenic assays. Renal function was assessed by determination of serum creatinine according to the Cockcroft–Gault equation.

Results

The study population consisted of 41 patients with a female to male ratio of 15/26 and a median age of 55 ± 14 years old. Of these patients, 17% (n=7) were treated for deep vein thrombosis (DVT), 7% (n=3) for pulmonary embolism (PE), 46.3% (n=19) for recurrent thromboembolic disease, 26.8% (n=11) for cancer-associated venous thrombosis, 2% (n=1) for cerebral venous thrombosis. The anticoagulant treatment consisted of rivaroxaban for 75.6% (n=31) of these patients and apixaban for 24.4% (n= 10) of patients. The anti-factor Xa levels ranged from 20 to 418 UI /mL (median value 131.36 ± 113.95). The factor Xa inhibitor was detected in 40/41 cases (97.5%) as true positive and in 1 case (2%) as false negative after comparison with plasma anti-Xa levels at 152 IU/ mL measured after 4 hours of oral intake.

Conclusion

The test results demonstrate a very good sensitivity to detect oral factor Xa inhibitor intake, confirming previously published data¹. It is a simple, rapid and non invasive test with a useful interpretation using a predefined color scale. It is an easily repeatable test at any time without technical equipment, allowing the identification of the anticoagulant type even in non-communicating patients. This ongoing study will provide more data in order to validate in real-life the use of this device as an easy-to-use, accurate tool in assessing widely prescribed Direct Oral Anticoagulants for treatment of VTE.

Reference

¹Harenberg J, Beyer-Westendorf J, Crowther M, Douxfils J, Elalamy I, Verhamme P, Bauersachs R, Hetjens S, Weiss C; Working Group Members. Accuracy of a Rapid Diagnostic Test for the Presence of Direct Oral Factor Xa or Thrombin Inhibitors in Urine-A Multicenter Trial. *Thromb Haemost.* 2020 Jan;120(1):132-140.