Comparison of the DOAC Dipstick test from urine to the chromogenic substrate methods from plasma of patients treated with direct oral anticoagulants

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INTRODUCTION

At present, direct oral anticoagulants (DOACs) have become the leading therapeutic choice demonstrating considerable efficacy, safety, and convenience in thromboembolic settings, qualities closely related to DOAC presence in patient’s blood, identifying daily treatment adherence as a major factor of efficacy. The in vitro diagnostic DOAC Dipstick is an easy-to-use bedside test whose development was based on the rationale that DOACs are excreted in urine. Direct oral factor-Xa and thrombin inhibitors are detected on separate DOAC Dipstick pads, each containing immobilized reagents that specifically interact with the respective type of DOAC.

RESULTS

Biographic data shows no differences between the DIO and DTI groups (Table 1). All patients had a normal renal function and the urine color pad was observed as “normal” in these cases. Based on the plasma threshold of ≥30ng/mL in the DIO group (n=121), the factor Xa inhibitor pad was evaluated in 103/106 cases as correct positive (sensitivity: 97.1%, CI: 92.0-99.4%) and in 3/15 cases as true negative (specificity 20%). CI: 4.3-48.1%, low validity due to low number of DTI patients. The PPV, NPV and accuracy values were 89.5%, CI: 86.9-91.2%, 50%, CI:18.15-81.85%, and 87.6%, CI: 80.4-92.9%, respectively (Tables 1 and 2).

For the threshold of ≥20 ng/mL, sensitivity and accuracy were at 96.7 % and the PPV 100%. Specificity and NPV could not be calculated due to the absence of negative pad results (Table 3).

The results of correct and false visual evaluations of FXA pads at thresholds of ≥20 ng/mL and ≥20 ng/mL for patients treated with apixaban and rivaroxaban as well as results of sensitivity, specificity, NPV, PPV and accuracy are given on tables 2 and 3, respectively.

The number of negative results limit the reliability of the calculated specificity and NPV of subgroups. The agreement of the visual agreement of DOAC Dipstick test results between two observers was 123/123 for FXA and THR pads of the DII and DTI groups. The kappa value was calculated at (Table 4).

Table 1: Median age, sex distribution, indications, renal function, other medication, DOAC Dipstick test results between two observers was 123/123 for FXA and THR pads of the DII and DTI groups. The kappa value was calculated at (Table 4).

CONCLUSIONS

✓ DOAC Dipstick detects with high sensitivity and PPV plasma concentrations of DXI at ≥30 ng/mL, plasma.
✓ The sensitivity of DOAC Dipstick increases at lower DXI levels thus improving patients safety for medical decision making.
✓ Specificity and NPV values are not reliable due to the low number of negative DOAC Dipstick test results. One reason is the decreasing descript of Dabigatran compared to DXI at our medical center.
✓ The number of subgroups of DXI and dabigatran is also too low to enable generating robust data on Specificity and PPV for the reason given above.
✓ The inter-observer agreement supports earlier data on the strength of visual assessment of DOAC Dipstick.
✓ The authors believe that the aforementioned results demonstrate the comfort, efficacy and safety of the DOAC Dipstick device for anticoagulant treatment assessment in various clinical settings.

METHODS

It consisted of an observational cohort study. Herein presented the results of consecutively enrolled patients on DOAC treatment, followed-up at the Antithrombotic Clinic of Tenon, an academic hospital which forms part of the Assistance Publique Hôpitaux de Paris (AP-HP) Sorbonne Université. The study period was conducted from the 1st of December 2019 to the 31st of July 2021, including patients on active treatment or prevention of venous thromboembolism with DOACs. Dipstick test was performed from patients’ urine samples and subsequent visual evaluation of pads’ colors for oral direct factor Xa (DXI) and thrombin inhibitors (DTI) by trained staff. DOACs’ plasma concentration was assessed STA®-Liquid Anti-Xa and a STA®-Liquid Anti-Ⅱa chromogenic substrate assays. Threshold values of DOACs were compared at ≥20 ng/ml and ≥20 ng/ml to positive and negative results of DOAC Dipstick, because it was reported that lower concentrations of DOACs in plasma were detected at a higher sensitivity (1). The sensitivity, specificity, negative (NPV) and positive predictive values (PPV) were determined at both threshold levels. Specificity values and NPV were determined despite their low validity due to low number of available values from the DTI group. P-values were calculated by t-test statistics.