Comparison of the sensitivity and specificity of rivaroxaban, apixaban and dabigatran concentrations measured in urine samples by the DOAC Dipstick with the cut-off plasma concentration of 30 ng/ml

INTRODUCTION

The qualitative determination of direct oral anticoagulants (DOACs) has been shown to be sensitive and specific when managing stroke and when deciding on treatment for acute hip fracture in relatively small clinical studies. Treatment of major haemorrhage, thrombolysis or ischemic stroke, and the timing of acute hip fracture repair in patients on DOAC therapy has been guided by a cut-off plasma DOAC level of ≥ 30 ng/mL.

AIM

The aim of the current study was to determine whether DOAC Dipstick test in urine can be used to exclude clinically relevant plasma concentrations. To do this, we compared direct oral factor Xa inhibitors (DXI) and thrombin inhibitor (DTI) in urine by the qualitative DOAC Dipstick test with the plasma concentrations of DOACs at a threshold of ≥ 30 ng/ml from patients taking DOACs.

RESULTS

Table 1: Plasma concentrations of DOACs according to positive and negative results of DOAC Dipstick from urine samples of patients

| DOAC  | Threshold (ng/mL) | AUC ROC (95% CI) | Sensitivity % (95% CI) | Specificity % (95% CI) | PPV % (95% CI) | NPV % (95% CI) | p-value
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<tr>
<td>DXI</td>
<td>≥ 30</td>
<td>0.859</td>
<td>(93.6–100)</td>
<td>21.4</td>
<td>(8.3–41.0)</td>
<td>71.8</td>
<td>(60.5–81.4)</td>
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<td>&lt;0.001</td>
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<td>DTI</td>
<td></td>
<td>0.814</td>
<td>(87.2–100)</td>
<td>5.9</td>
<td>(0.2–28.7)</td>
<td>62.8</td>
<td>(46.7–77.0)</td>
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<td>DXI</td>
<td>≥ 14</td>
<td>0.994</td>
<td>(981.1–1.0)</td>
<td>85.7</td>
<td>(42.1–99.6)</td>
<td>98.7</td>
<td>(93.1–100)</td>
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<td>&lt;0.001</td>
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<td>DTI</td>
<td>≥ 19</td>
<td>n.a.</td>
<td>(91.8–100)</td>
<td>100</td>
<td>(2.5–100)</td>
<td>100</td>
<td>(91.8–100)</td>
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Table 2: Area under the curve (AUC) according to the receiver operating curve (ROC) analysis and statistical parameters for DXI (n=84) and DTI (n=44) at thresholds of ≥ 30 ng/mL and thresholds of ≥ 14 ng/mL and ≥ 19 ng/mL in plasma. AUC = area under the curve, ROC = receiver operating curve, CI = confidence interval, PPV = positive predictive value, NPV = negative predictive value

CONCLUSIONS

- The DOAC Dipstick determines the presence and absence of rivaroxaban, apixaban and dabigatran in urine with at least >95% correctness when compared with the cut-off value of ≥ 30 ng/mL in plasma.
- The assessment of DXI and DTI concentrations at this cut-off value by visually inspecting the DOAC Dipstick pads and by using the DOASENSE Reader were close to 100% agreement.
- Further studies are currently evaluating these findings in additional patient groups.

METHODS

- We evaluated 131 of 132 plasma and urine samples taken from patients with neurologic and cardiovascular diseases and who were taking DOACs at Sestre Milosrdnice University Hospital Center at Zagreb. Participants were treated with rivaroxaban (n=53), apixaban (n=34) and dabigatran (n=44). Plasma and urine samples were taken before intake of DOAC to determine trough DOAC concentrations.
- The colours of DOAC Dipstick pads were visually evaluated to determine the presence or absence of DOACs by two trained medical professionals and by a DOASENSE reader. DOAC concentrations in plasma were measured by specific chromogenic substrate assays.
- Logistic regression analyses with the binary outcome DOAC present or absent was performed together with receiver operating curve (ROC) analyses in order to find best fitting thresholds for plasma concentrations for FXA and THR pads. A ROC analysis determines specified thresholds by the maximum value of the sum of sensitivity and specificity.

REFERENCE