Exclusion of relevant concentrations of direct oral anticoagulants in blood by DOAC Dipstick – proposal of a diagnostic algorithm for improvement of clinical decision-making in emergencies

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INTRODUCTION

Rapid and accurate determination of direct oral anticoagulants (DOACs) is still a major medical need in urgent clinical situations.

AIM

The aim of this study was to identify the feasibility of algorithm for rapid exclusion of clinically significant concentration of DOACs (≥ 30 ng/mL) by data from inpatients from cardiology and neurology departments.

METHOD

128 paired plasma and urine samples at trough levels from patients treated for non-valvular atrial fibrillation or venous thromboembolism factor Xa inhibitor (DXI) (apixaban, n=31, rivaroxaban, n=53) direct thrombin inhibitor (DTI) (dabigatran, n=44) Plasma DOACs concentrations - Innovance anti-FXa assay for rivaroxaban and apixaban and Innovance DTI assay for dabigatran on BCSXP analyzer (Siemens Healthineers, Germany). Urine DOAC qualitative test - DOAC Dipstick test (DOASENSE GmbH, Heidelberg, Germany) Statistics: receiver operating curve (ROC) analysis – diagnostic accuracy kappa statistics - comparison between DOAC Dipstick test results and plasma concentrations of DOACs

RESULTS

ROC analysis revealed threshold values of plasma concentrations for DXI ≥14 ng/mL and ≥19 ng/mL for DTI for detection of DXI and DTI by DOAC Dipstick, respectively. At cut-off value ≥19 ng/mL for DTI there was no false negative or false positive results (kappa value=1.0). For DXI at cut-off ≥14 ng/mL one false positive result was obtained, κ=0.92 (95 % CI 0.74–1.00).

Table 1. Parameters of diagnostic accuracy obtained by receiver operating curve analysis (Margetic et al, 2022)

<table>
<thead>
<tr>
<th>DOAC</th>
<th>Threshold (ng/mL)</th>
<th>AUC (95 % CI)</th>
<th>Sensitivity (%) (95 % CI)</th>
<th>Specificity (%) (95 % CI)</th>
<th>PPV (%) (95 % CI)</th>
<th>NPV (%) (95 % CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DXI</td>
<td>≥14</td>
<td>0.994 (0.981–1.0)</td>
<td>100 (95.3–100)</td>
<td>85.7 (42.1–99.6)</td>
<td>98.7 (93.1–100)</td>
<td>100 (54.1–100)</td>
</tr>
<tr>
<td>DTI</td>
<td>≥19</td>
<td>NA</td>
<td>100 (91.8–100)</td>
<td>100 (2.5–100)</td>
<td>100 (91.8–100)</td>
<td>100 (2.5–100)</td>
</tr>
</tbody>
</table>

AUC = area under the curve, CI = confidence interval, PPV = positive predictive value, NPV = negative predictive value, NA = not applicable.

Figure 1. Suggested algorithm for emergency care of patients treated with DOACs for exclusion clinically relevant concentration of DOACs (≥ 30 ng/mL)

CONCLUSIONS

Application of an algorithm for exclusion of relevant plasma concentrations by DOAC Dipstick can be proposed by testing first DOACs in urine and if positive followed by quantitative DOAC assays if clinically required. Clinical verification of the proposed algorithm is needed.

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REFERENCES

Margetic et al. DOAC Dipstick testing can reliably exclude the presence of clinically relevant DOAC concentrations in circulation. Thromb Haemost 2022. in press. DOI:10.1055/a-1753-2748

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