Comparison of visual versus reader results of the point of care test of direct oral anticoagulants from urine samples

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INTRODUCTION

Direct oral anticoagulants (DOAC) are increasingly used for anticoagulation. In emergency situations, a quick and safe method to detect or exclude the presence of DOACs may guide clinical decision-making. Because DOACs are excreted via the kidney, they can be detected in the urine with the point of care test DOAC Dipstick. DOAC concentrations are manifold higher in urine compared to plasma, which is important for normal ranges.

AIM

To identify concentrations of DOACs providing 100% negative (DOAC absent) or 100% positive (DOAC present) results for each of the two methods of determination (i.e. naked eye or photometric reader (DOASENSE Reader, CE-labelled).

METHOD

Samples of artificial urine (n=324) were spiked with concentrations of DOACs ranging from 0 ng/mL to 325 ng/mL.

Visual method (figure 1): 3 examiners independently identified in triplicate the colours of the pads of DOAC Dipstick for positive or negative for factor Xa inhibitors (DXI: apixaban, edoxaban, rivaroxaban) and thrombin inhibitor (DTI) dabigatran on the respective test pads of DOAC Dipstick by comparison with the colour label on the test tube

Reader method (figure 2): 4 photometric readers were used to identify the colours of the FXA pad and THR pad

Concentrations of DOACs represent the limits in urine samples for negative and positive results

Documentation: Negative and positive results of the respective concentration ranges of DOAC are documented for both methods for the comparison.

REFERENCES

1. Harenberg J, et al. Thromb Haemost. 2020;120(1):132-140
2. Harenberg J, et al. Semin Thromb Hemost 2019;45(3):275-284

RESULTS

Figure 1: Schematic representation of three DOAC Dipsticks with negative and positive results for DXI (factor Xa inhibitors) and DTI (thrombin inhibitors) on the area "DOAC Analysis" and of the control pads (not included into the study).

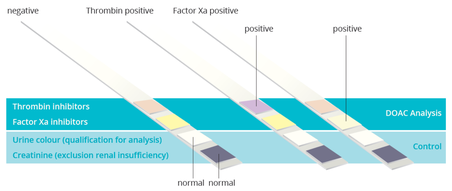

Figure 1: Schematic representation of DOAC Dipsticks divided into areas "DOAC Analysis" and "Control"

Figure 2: Photo of DOASENSE Reader together with DOAC Dipstick box and tube and sticks.

Figure 2: Photo of DOASENSE Reader with four DOAC Dipsticks. The tube with the label contains 12 strips and is conserved in the box.

Table 1

The results of DXI and DTI are categorized as "NEGATIVE" or "negative or positive" or "POSITIVE" (column 1 to 7, line 1 and 2).

- ✓ Column 8 and 9 show the number of samples analysed.
- ✓ Column 2, 3, 6, 7, line 3 and 4 show the concentrations limits at which 100% of results are NEGATIVE or POSITIVE.
- ✓ Column 4 and 5 line 3 and 4 indicate intermediate concentration ranges at which results of visual or reader analysis may be negative or positive.
- ✓ Concentration limits differ slightly between methods in a clinically not relevant range.

Methods	Visual	Reader	Visual	Reader	Visual	Reader	Visual	Reader
Results	NEGATIVE		negative or positive		POSITIVE		Total	
DXI ng/ml	<100	<100	100-200	100-275	>200	>275	452	452
DTI ng/ml	<50	<75	50-125	75-300	>125	>300	428	428

Legend: The three categories of results of visual and reader analysis. Differences of concentrations are clinically not relevant.

Table 2

The results of visual and reader analysis are shown for samples containing concentrations below or above or in between the limits given in table 1 for DXI an DTI as % of total number analysed.

- ➢ Most results of DXI and DTI are observed in the concentration range POSITIVE and few results in the two other concentration ranges.
- ➢ Using the limits of concentrations given in table 1:
- ➢ no differences between methods are observed in the POSITIVE range.
- ➢ maximal 2% different results between methods are observed in the two other ranges of concentrations for DXI and DTI.

Methods	Visual	Reader	Visual	Reader	Visual	Reader	Visual	Reader
Results	NEGATIVE		negative or positive		POSITIVE		Total	
DXI	3,3%	3,3%	3,8%	5,3%	92,9%	91,4%	452	452
DTI	0,5%	0,5%	0,7%	2,8%	98,8%	96,7%	428	428

Legend: Comparison of the results of visual versus reader analysis of DXI and DTI pads of DOAC Dipsticks in the three categories of evaluation (NEGATIVE, intermediate, POSITIVE) given in % of samples analysed.

CONCLUSIONS

Visual and reader analysis are in agreement for urinary concentrations to allow to exclude or to identify the presence of DOACs in urine.

- **No differences of visual and reader analysis for the range of NEGATIVE results of DXI and DTI.**
- **Most concentrations of DOACs in urine are high and therefore POSITIVE.**
- **Few results are in the intermediate concentration range of DOACs in urine.**
- **Results do not differ between methods at low concentrations of DOACs in urine.**
- **Results differ between methods to less than 2% at intermediate and high concentration of DXI and DTI in urine.**
- **Both methods can be used to determine accurately the absence and presence of DOACs in urine.**

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CONFLICT OF INTEREST

JH, FL: Managing director DOASENSE
RB, JBW, CW: consultancy fee DOASENSE; JD, IE, MC, PV, SH: none