Comparison of D-dimer values at peak and trough concentrations of direct oral anticoagulants: result of D-dimer testing is not affected by plasma drug concentration

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INTRODUCTION

Knowledge of the effect of direct oral anticoagulants (DOACs) concentration in plasma on D-dimer values has so far been insufficiently examined.

AIM

The aim of the study was to investigate whether peak *vs.* trough plasma concentration of DOACs (dabigatran, rivaroxaban and apixaban) affects D-dimer values.

METHOD

THE STUDY INCLUDED A TOTAL OF 218 PLASMA SAMPLES INCLUDING PEAK (N=109) AND TROUGH (N=109) DOACS LEVELS IN OUTPATIENTS TREATED WITH STANDARD DRUG DOSES (DABIGATRAN N=35, 2X150 MG/DAY, RIVAROXABAN N=37, 1X20 MG/DAY AND APIXABAN N=37, 2X5 MG/DAY) IN STEADY-STATE AND OBTAINED DURING THEIR REGULAR CLINICAL EXAMINATION. BLOOD SAMPLES WERE TAKEN ON THE SAME DAY TO OBTAIN BOTH TROUGH (IMMEDIATELY PRIOR THE NEXT DRUG DOSE) AND PEAK (TWO HOURS AFTER DRUG ADMINISTRATION) DOACS CONCENTRATIONS. RIVAROXABAN AND APIXABAN CONCENTRATIONS WERE DETERMINED USING CHROMOGENIC ANTI-FXA ASSAY (INNOVANCE HEPARIN, SIEMENS HEALTHINEERS, GERMANY) WITH DRUG SPECIFIC CALIBRATORS (HYPHEN BIOMED, FRANCE). DABIGATRAN WAS MEASURED USING INNOVANCE DTI ASSAY (SIEMENS HEALTHINEERS, GERMANY). D-DIMER CONCENTRATION WAS DETERMINED BY QUANTITATIVE PARTICLE-ENHANCED IMMUNOTURBIDIMETRIC ASSAY USING MONOCLONAL ANTIBODY (INNOVANCE D-DIMER, SIEMENS HEALTHINEERS, GERMANY). ALL MEASUREMENTS WERE PERFORMED ON BCSXP ANALYZER (SIEMENS HEALTHINEERS, GERMANY). STATISTICAL ANALYSIS WAS DONE USING WILCOXON TEST BY MEDCALC STATISTICAL SOFTWARE VERSION 11.5.1. THE STUDY WAS FUNDED BY THE CROATIAN SCIENCE FOUNDATION AS PART OF THE RESEARCH PROJECT IP-2016-06-8208.

RESULTS

As shown in Table 1, the concentrations of all three DOACs have shown statistically significant differences between peak and trough levels ($P < 0.001$). On the contrary, concentrations of D-dimer did not show significant differences in samples with peak and trough concentrations of all three DOACs drugs ($P = 0.852$, $P = 0.274$ and $P = 0.833$).

Table 1. Results of DOACs peak and trough concentrations and appropriate D-dimer values.

DOAC drug	Peak drug conc. (ng/mL) Median (95%CI) IQR	Trough drug conc. (ng/mL) Median (95%CI) IQR	D-dimer (mg/L FEU) at peak drug conc. Median (95%CI) IQR	D-dimer (mg/L FEU) at trough drug conc. Median (95%CI) IQR
Dabigatran N=35	154 (112-186) 97-248	70 (59-92) 50-119	0.35 (0.28-0.62) 0.27-0.77	0.37(0.26-0.62) 0.25-0.73
P	<0.001		0.852	
Rivaroxaban N=37	205 (175-235) 133-243	22 (11-51) 9-81	0.53 (0.40-0.67) 0.34-0.89	0.47 (0.40-0.62) 0.37-0.81
P	<0.001		0.274	
Apixaban N=37	184 (154-211) 142-234	109 (84-129) 71-139	0.53 (0.46-0.72) 0.37-0.76	0.55 (0.42-0.74) 0.37-0.81
P	<0.001		0.833	

IQR = interquartile range; P< 0.05 was considered statistically significant

CONCLUSIONS

CONCENTRATIONS OF ALL THREEE DOACS IN PLASMA DO NOT AFFECT D-DIMER VALUES. OUR RESULTS CLEARLY INDICATE THAT D-DIMER TESTING CAN BE PERFORMED AT ANY TIME POINT IN PATIENTS TREATED WITH ALL THREE DOACS WITHOUT EFFECT OF DRUG CONCENTRATION IN PLASMA ON THE D-DIMER TEST RESULT.

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