Presentation of the patient with low peak dabigatran levels in plasma suggests the importance of quantitative measurement of DOAC drugs in clinical decision making and treatment

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INTRODUCTION

In special clinical conditions quantitative measurement of direct oral anticoagulants (DOACs) in plasma, should be performed to help clinical decision making and treatment.

AIM

To present a case report of a patient treated with dabigatran in whom low peak drug concentrations in plasma suggested inadequate anticoagulation.

METHOD

A 88 YEARS OLD MALE WAS HOSPITALIZED DUE TO RECURRENT SYMPTOMS OF CEREBRAL ISCHEMIA FOR LAST FEW DAYS AND BRAIN ISCHEMIA WAS CONFIRMED ON CT SCAN. BEFORE HOSPITALIZATION, THE PATIENT WAS TAKING DABIGATRAN (110 MG TWICE DAILY) DUE TO PERSISTENT ATRIAL FIBRILLATION.

DABIGATRAN WAS MEASURED BY INNOVANCE DTI ASSAY AND RIVAROXABAN WAS MEASURED BY ANTI-FXA ASSAY ON BCSXP ANALYZER (SIEMENS HEALTHINEERS, GERMANY). THE STUDY WAS FUNDED BY THE CROATIAN SCIENCE FOUNDATION AS A PART OF THE RESEARCH PROJECT IP-2016-06-8208.

RESULTS

Peak (two hours after the last dose) concentrations of dabigatran measured at three consecutive days were 35, 16 and 19 ng/mL, whereas trough (before the next dose) concentrations were 34, <5 and 14 ng/mL, respectively. Low peak dabigatran concentrations obtained in three consecutive measurements suggested anticoagulation undertreatment that might result with embolic complications. This observation led to the decision to replace dabigatran therapy with rivaroxaban (1x20 mg/day). Measurement of rivaroxaban plasma levels after the second day of administration has shown both peak and trough rivaroxaban concentrations within expected therapeutic values i.e., 215 and 30 ng/mL, respectively. No new ischemic symptoms occurred and the patient was discharged home with rivaroxaban therapy. Results of laboratory testing are presented in Table 1.

Table 1. The results of laboratory testing in a patient treated with dabigatran followed by replacement therapy with rivaroxaban.

	Drug	Dabigatran*	Dabigatran*	Dabigatran*	Rivaroxaban**
Dabigatran (ng/mL)	Peak	35	16	19	/
	Trough	34	<5	14	/
Rivaroxaban (ng/mL)	Peak	/	/	/	215
	Trough	/	/	/	30
Fibrinogen (g/L)	Peak	2.8	/	/	4.2
	Trough	2.6	/	/	4.0
PT (% act.)	Peak	49	52	51	126
	Trough	49	49	51	131
INR	Peak	1.4	1.4	1.4	0.9
	Trough	1.4	1.4	1.4	0.9
aPTT (s)	Peak	45	38	33	26
	Trough	38	38	30	25
TT (s)	Peak	145	30	33	15
	Trough	108	30	28	14
D-dimer (mg/L FEU)	Peak	/	0.35	0.36	/
	Trough	/	0.34	0.30	/
creatinine (µmol/L)		74	/	73	/
eGfR (CKD-EPI (mL/min/1,73m2)		78	/	79	/
hemoglobin (g/L)		133	/	150	/

PT – prothrombin time; INR – international normalized ratio; aPTT – activated partial thromboplastin time; TT – thrombin time; CKD-EPI – Chronic Kidney Disease - Epidemiology Collaboration; * measurements performed during the three consecutive days on dabigatran therapy; **measurements performed two days after replacing dabigatran with rivaroxaban therapy

CONCLUSIONS

Persistently low peak dabigatran concentrations could contribute to inadequate anticoagulation and consequent embolic complications in our patient. This case report strongly suggests the importance of quantitative measurement of DOACs levels in plasma in selected clinical conditions confirming as an effective approach in clinical decision making and treatment.

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