



COMPARISON OF PEAK AND TROUGH CONCENTRATIONS OF DABIGATRAN, RIVAROXABAN AND APIXABAN WITH THE PUBLISHED EXPECTED VALUES IN PATIENTS WITH NON VALVULAR ATRIAL FIBRILLATION

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INTRODUCTION Direct oral anticoagulants (DOACs), dabigatran, rivaroxaban and apixaban, have been increasingly used for the prevention and treatment of thromboembolic diseases in recent years. However, peak and trough concentrations of these DOACs in certain clinical indications are still insufficiently investigated. The aim of this study was to assess both peak and trough plasma concentrations of all three DOACs in patients treated for non valvular atrial fibrillation (NVAF) and to compare our own results with the first published expected values.

METHODS The study included plasma samples from patients treated for NVAF and taking dabigatran (N=37), rivaroxaban (N=28) and apixaban (N=36). 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 measured using chromogenic anti-FXa assay (Innovance anti-FXa, Siemens Healthineers, Germany) calibrated with specific calibrators for rivaroxaban and apixaban (Hyphen BioMed, France). Dabigatran was measured using commercial chromogenic method (Innovance DTI assay, Siemens Healthineers, Germany). All coagulation assays were performed on Behring Coagulation System XP (BCSXP) analyser (Siemens Healthineers, Germany). Statistical analysis was done using Mann-Whitney test by MedCalc Statistical Software version 11.5.1. The study was funded as an integral part of the Croatian Science Foundation research project IP-2016-06-8208.

RESULTS Table 1. Results for dabigatran, rivaroxaban and apixaban peak and trough concentrations in NVAF patients.

	N	Dosing regimen	Measured conc. (ng/mL) Median (95%CI) IQR	P	Published expected values* (ng/mL)	Within expected values	Below expected values	Above expected values
Dabigatran peak	37	150 mg twice a day	201 (136-239) 117-258	<0.001	175 117 - 275	27/37 0.73	6/37 0.16	4/37 0.11
Dabigatran trough	37		101 (59-139) 52-160		91 61 - 143	26/37 0.70	6/37 0.16	5/37 0.14
Rivaroxaban peak	28	20 mg once a day	171.5 (134-246) 122-277	<0.001	249 184 - 343	21/28 0.75	3/28 0.11	4/28 0.14
Rivaroxaban trough	28		35 (23-89) 19-103		44 12 - 137	22/28 0.79	2/28 0.07	4/28 0.14
Apixaban peak	36	5 mg twice a day	180 (164-203) 153-224	<0.001	171 91 - 321	28/36 0.78	5/36 0.14	3/36 0.08
Apixaban trough	36		89 (72-126) 56-135		103 41 - 230	28/36 0.78	4/36 0.11	4/36 0.11

*Gosselin RC et al . International Council for Standardization in Haematology (ICSH) Recommendations for Laboratory Measurement of Direct Oral Anticoagulants. Thromb Haemost 2018;118:437-50

CONCLUSIONS The study showed a good agreement of both peak and trough concentrations for dabigatran, rivaroxaban and apixaban with the published expected values in NVAF patients.