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A New Method for Determining Concentrations of Direct Oral Anticoagulants

Bloemen, Saartje; Zwaveling, Suzanne; Douxfils, Jonathan; Peters, T.; Wagenvoord, Rob; Hemker, Hendrick Coenraad; Mullier, François; de Laat, Bas; Roest, Mark; Kremers, Romy

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PB 1199 | A New Method for Determining Concentrations of Direct Oral Anticoagulants

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<u>S. Bloemen</u>^{1,2}, S. Zwaveling^{1,2}, J. Douxfils³, T. Peters^{1,2}, R. Wagenvoord^{1,2}, H.C. Hemker^{1,2}, F. Mullier^{3,4}, B. de Laat^{1,2}, M. Roest^{1,2}, R. Kremers^{1,2}

¹Synapse Research Institute, CARIM, Maastricht University, Maastricht, The Netherlands, ²CARIM, Maastricht University, Department of Biochemistry, Maastricht, The Netherlands, ³Namur Research Institute for Life Sciences, University of Namur, Department of Pharmacy, Namur, Belgium, ⁴Université Catholique de Louvain, CHU UCL Namur, Hematology Laboratory, Namur Thrombosis and Hemostasis Center, Yvoir, Belgium

Background: Direct oral anticoagulants (DOACs) are commonly provided without monitoring. However, reliable assays to measure DOAC levels and activity in emergency situations are needed. We developed a test based on the inhibition of α_2 macroglobulin-thrombin (α_2 M-IIa)

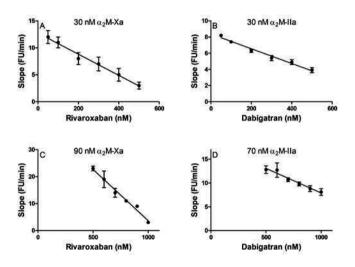


FIGURE 1 Dose-response of several DOAC concentrations at chosen α 2M-Xa and α 2M-IIa concentrations

by dabigatran (DAB) and of α_2 M-factor Xa (α_2 M-Xa) by rivaroxaban (RIV), making it possible to evaluate both DOAC classes in combination with thrombin generation (TG).

Aims: To quantify DOAC levels and activity in plasma.

Methods: Consenting patients using RIV (n=50) and DAB (n=28) were included. TG was performed in platelet poor plasma (5 pM tissue factor), with idarucizumab in calibrator wells for DAB samples. The new DOAC assays measured the effect of diluted plasma samples on Z-Gly-Gly-Arg-AMC conversion by α_2 M-Xa or α_2 M-IIa. The slopes of these curves were compared to a reference curve with known DOAC concentrations. DOAC levels were also estimated by 'classical' assays. Spearman correlation coefficients were determined.

Results: A concentration of 30 nM α_2 M-Xa or α_2 M-IIa was optimal to measure 50-500 nM RIV/DAB and 90 nM α_2 M-Xa or 70 nM α_2 M-IIa, respectively were optimal for 500-1000 nM RIV/DAB (Fig.1).

The intra- and inter-assay CV were below 2.5 % and 5% (n=2). Both the RIV and DAB assay correlated with TG parameters. The RIV assay correlated with ,classical' assays and had a very good correlation with Biophen DiXal. The DAB assay did not correlate with hemoclot thrombin inhibitor (probably since DAB concentrations were too low), but showed variable correlation with the other assays (Table1).

Conclusions: The new DOAC assays show good correlations with other assays that were confirmed to accurately assess DOAC levels (particularly the RIV assay with the Biophen DiXal, which had the best correlation with mass spectrometry). Our assay can simultaneously evaluate DOAC concentrations as well as the DOACs effect on thrombin generation, providing an overview of the anticoagulation status of a patient in relation to circulating DOAC levels.

TABLE 1 Correlation (Spearman) of rivaroxaban or dabigatran concentration (as determined by the new assay) with TG and other calibrated assays

Correlation Correlation	
Assay coefficient p-value Assay coefficient	p-value
RivaroxabanCalibrated prothrom-0.4680.002DabigatranActivated partial thrombo-0.581bin time (ng/ml)plastin time (s)	0.002
Dilute Russel viper0.7600.000Dilute Russel viper venom0.649venom time (s)time (s)	0.001
Biophen DiXal (ng/ml) 0.915 0.000 Hemoclot thrombin inhibitor 0.391 (ng/ml)	0.097
TG endogenous -0.525 0.000 Ecarin chromogenic assay 0.591 thrombin (ng/ml) potential(nM.min)	0.001
TG Peak (nM)-0.5500.000TG endogenous thrombin-0.323potential(nM.min)	0.100
TG lag time (min) 0.671 0.000 TG Peak (nM) -0.354	0.201
TG time-to-peak (min) 0.702 0.000 TG lag time (min) 0.423	0.028
TG time-to-peak (min) 0.339	0.084