

RESEARCH OUTPUTS / RÉSULTATS DE RECHERCHE

A Rapid, Practical and Ergonomic Device to Prepare Plasma Sample Free of Platelets and Direct Oral Anticoagulant for Routine Hemostasis Tests

Gheldof, Damien; Delvigne, Anne-Sophie; Bouvy, Céline; Douxfils, Jonathan; Dogne, Jean-Michel

Published in:

Research and Practice in Thrombosis and Haemostasis

DOI:

<https://doi.org/10.1002/rth2.12229>

Publication date:

2019

Document Version

Publisher's PDF, also known as Version of record

[Link to publication](#)

Citation for pulished version (HARVARD):

Gheldof, D, Delvigne, A-S, Bouvy, C, Douxfils, J & Dogne, J-M 2019, A Rapid, Practical and Ergonomic Device to Prepare Plasma Sample Free of Platelets and Direct Oral Anticoagulant for Routine Hemostasis Tests. in *Research and Practice in Thrombosis and Haemostasis*. 1 edn, vol. 3, Research and Practice in Thrombosis and Haemostasis, Wiley, pp. 139 - 140, ISTH 2019 : The XXVII Congress of the International Society on Thrombosis and Haemostasis, Melbourne, Australia, 6/07/19. <https://doi.org/10.1002/rth2.12229>

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal ?

Take down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

calibrator ranged from 3.6 - 17.3% (2016-2018). The corresponding CVs for FIX were 2.9 - 26.2% (2013-2015) and from 5.5 - 17.8% (2016-2018).

Conclusions: Laboratory performance of FVIII and FIX testing has improved over the past six years. Assessments based against calibrator rather than reagent showed reduction in the numbers of outliers in each peer group and provided improved comparability of results with reduced CVs. The decreasing trend in outliers also supports the retention of the assessment criteria being based on calibrator.

PB0140 | Are Global Coagulation Assays Better Measures of the Intensity of Anticoagulation in Patients with Antiphospholipid Syndrome?

W.H. Wong¹; M.C. Kong²; E.J.S. See²; S.H. Yeang²; S.K. Koh³; Y.T. Shim²; C.W. Tan¹; H.J. Ng¹

¹Singapore General Hospital, Haematology, Singapore, Singapore, ²Singapore General Hospital, Pharmacy, Singapore, Singapore, ³Singapore General Hospital, Singapore, Singapore

Background: Antiphospholipid antibodies may interfere with the prothrombin time and higher international normalized ratio (INR) targets have been proposed for warfarinized antiphospholipid syndrome (APS) patients for perceived higher thrombogenicity.

Aims: To investigate if prothrombin time-based clot wave analysis (PT-CWA) and platelet-poor plasma calibrated automated thrombogram (CAT) thrombin generation, provide better measures of the intensity of anticoagulation in APS patients by comparing them to non-APS warfarinized patients.

Methods: Plasma samples from warfarinized APS patients were analysed for INR and PT-CWA using the Sysmex CS2100i analyzer, with remaining plasma used for thrombin generation analysis with

the calibrated automated thrombogram (CAT) system. Similar parameters from warfarinized atrial fibrillation (AF) and deep vein thrombosis (DVT) patients were compared. Correlation to INR was performed using Pearson's correlation. Parameter means were compared using multivariate analysis with correction for the age and INR values at 5% significance.

Results: 15 APS plasma samples were compared to 28 and 59 samples from AF and DVT patients. Increasing INR did not correspondingly increased PT-CWA parameters in the APS and DVT group and minimally in the AF group. Despite similar INR range samples in the APS and AF groups, the ETP for the APS group (379.19 ± 79.90) was lower than the AF (455.14 ± 57.25) group after age and INR corrections. The PT-CWA did not significantly differ amongst the various groups, was not affected by the INR with no significant differences between the groups for samples within the therapeutic range.

Conclusions: PT-CWA parameters do not provide a different measure of anticoagulation intensity in APS patients who display lower thrombin generation potential compare to similar warfarinized AF and DVT patients. The role of such global assays remain unsubstantiated in the management of APS.

PB0141 | A Rapid, Practical and Ergonomic Device to Prepare Plasma Sample Free of Platelets and Direct Oral Anticoagulant for Routine Hemostasis Tests

D. Gheldof¹; A.-S. Delvigne¹; C. Bouvy²; J. Douxfils^{1,2}; J.-M. Dogné¹

¹University of Namur, Namur, Belgium, ²Qualiblood s.a., Namur, Belgium

TABLE 1 TG and PT-CWA correlations to INR

Group	INR range	Correlations to INR			
		ETP	PTMin1	PTMin2	PTMax2
AF (n=28)	1.94 - 6.29	-0.261	-0.376	0.326	0.042
APS (n=15)	1.81 - 7.38	0.128	0.061	0.053	-0.010
DVT (n=59)	1.55 - 5.38	-0.350	0.043	0.018	-0.087

TABLE 2 Means of various parameters obtained from all samples in the groups and within therapeutic range, after adjustment for age and INR

INR range	Group	Adjusted means ± SE			
		ETP	PTMin2	PTMin2	PTMax2
All	AF	455.14 ± 57.25	3.03 ± 0.22	0.786 ± 0.06	0.575 ± 0.04
	APS	379.19 ± 79.90	3.31 ± 0.31	0.842 ± 0.08	0.578 ± 0.05
	DVT	440.24 ± 38.22	3.04 ± 0.15	0.790 ± 0.04	0.577 ± 0.03
Therapeutic range (2.0 - 3.5)	AF	517.16 ± 100.15	2.86 ± 0.37	0.757 ± 0.10	0.599 ± 0.07
	APS	262.79 ± 116.86	3.15 ± 0.44	0.795 ± 0.11	0.524 ± 0.08
	DVT	517.15 ± 58.73	2.90 ± 0.22	0.766 ± 0.06	0.597 ± 0.04

Background: Direct oral anticoagulants (DOACs) are known to interfere with almost all clotting tests to varying degrees. This may lead to false positive or false negative test results and to unnecessary investigations.

Aims: To assess the effectiveness of the one step plasma preparation by filtration with the original DOAC & Platelets Filter (DP-Filter) device from the University of Namur on i) the removal of platelets from plasma in substitution of the second centrifugation and ii) the removal of all types of DOAC including dabigatran, apixaban, rivaroxaban and edoxaban from test plasma (with minimal effect on hemostasis variable).

Methods: i) Platelet-poor plasma was prepared in two different ways: i) by a double centrifugation at 2500g during 15 min or by a single centrifugation at 2500g during 15 min followed by one filtration by centrifugation at 200g during 2 min with the DP-Filter. Platelets count was assessed using a Sysmex XN-9000 analyzer. ii) Normal pooled plasma were mixed with either dabigatran, apixaban, rivaroxaban and edoxaban at 0-100-300-1000 ng/ml. Plasma DOAC concentrations were assessed before and after filtration with DP-Filter using calibrated STA-Liquid anti-Xa or STA-ECAII for anti-Xa and anti-IIa drugs, respectively. Prothrombin time (PT) and activated partial thromboplastin time (aPTT) were also assessed before and after filtration to assess the impact of DP-Filter on hemostasis parameters. **Results:** DP-Filter efficiently removed platelets and DOACs to concentrations until 1000 ng/mL to levels below the limits of detection of the instrument/tests. DP-Filter was able to restore normal prothrombin time and activated partial thromboplastin time at all DOACs concentrations. **Conclusions:** DP-Filter can be used to efficiently substitute the second centrifugation step for platelet poor plasma preparation and efficiently remove dabigatran, apixaban rivaroxaban and edoxaban from plasma to concentrations up to 1000 ng/ml. Global hemostasis parameters were restored and are not influenced by the device.

PB0142 | Pronounced Alterations of Thrombin Generation Profiles are Found in Whole Blood Compared to Plasma of Liver Disease Patients

J. Wan^{1,2}; W. Hendrix¹; T.-W. Ow³; R. Arya⁴; L. Rabinowich³; O. Barbouti³; J. Konings^{1,2}; B. de Laat^{1,2}; T. Lisman⁵; L. Roberts⁴; W. Bernal³; M. Roest^{1,2}

¹Synapse Research Institute, Maastricht, the Netherlands, ²Maastricht University, Cardiovascular Research Institute, Maastricht, the Netherlands, ³King's College Hospital NHS Foundation Trust, Institute of Liver Studies, London, United Kingdom, ⁴King's College Hospital NHS Foundation Trust, King's Thrombosis Centre, Department of Haematological Medicine, London, United Kingdom, ⁵University Medical Center Groningen, Department of Surgery, Groningen, the Netherlands

Background: Severe distortions of both pro- and anticoagulant drivers in liver disease patients result in a 'frailly rebalanced' haemostatic system. Novel global coagulation tests like thrombin generation (TG) assess the integration of the pro- and anticoagulant system.

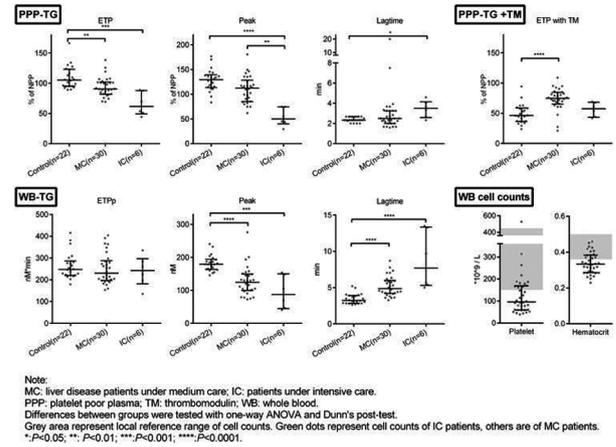


FIGURE 1 Thrombin generation parameters and cell counts of liver disease patients

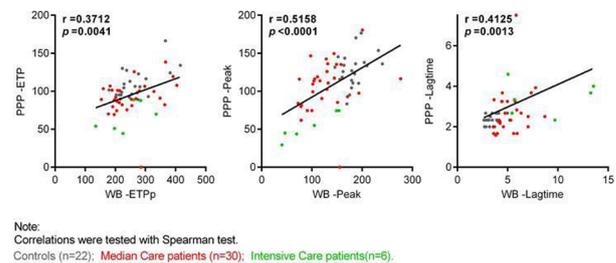


FIGURE 2 Correlations between thrombin generation parameters in whole blood and in plasma

Function of the blood cells may cause additional influence on the global coagulation.

Aims: To study the whole blood (WB) and plasma TG profiles of liver disease patients.

Methods: Liver disease patients under medium care (MC; n=30), intensive care (IC, n=6) and controls were recruited at King's College Hospital, London. The study was approved by the local ethic committee and all participants gave consent for the study. TG in Citrated WB samples was measured with a miniaturized device at 2.5 pM tissue factor (TF). TG in Platelet poor plasma (PPP) was measured at 5 pM TF, with or without 10 nM thrombomodulin (TM).

Results: MC and IC patients had significantly prolonged APTT and INR, lower FII, FX and antithrombin, but higher FVIII compared to controls. Most patients had lower platelet count and hematocrit than local reference range (Figure 1). In PPP-TG, only IC patients showed significantly lower peak and longer lagtime than controls, while with WB-TG this was found in both MC and IC patients. Plasma endogenous thrombin potential (ETP) of patients was comparable or higher than controls when TM was present. ETP until peak (ETPp) in WB-TG was similar between patients and controls (Figure 1). TG parameters in WB and PPP showed significant correlation (Figure 2). Significant