

The Effect of DOAC-Stop® on Several Oral and Parenteral Anticoagulants

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Background: DOAC-Stop® is a recently manufactured product which can neutralise the direct oral anticoagulants (DOAC) in plasma samples *in vitro*. However, there are still some grey areas regarding its use.

Aims: To investigate the effect of DOAC-Stop® on several oral and parenteral anticoagulants using standard and research-based coagulation assays.

Methods: We analysed pools of normal platelet poor plasma (PPP), warfarinised PPP (INR 2.1, 3.2, 4.2), normal PPP spiked with direct factor Xa inhibitors (apixaban 182, 265 ng/mL; edoxaban 151, 220 ng/mL; rivaroxaban 241, 339 ng/mL), direct thrombin inhibitor (dabigatran 203, 318 ng/mL), indirect factor Xa inhibitors (enoxaparin 0.93, 1.68 U/mL; fondaparinux 1.62, 2.16 µg/mL). Samples treated with DOAC-Stop® were compared with untreated samples. The following assays were performed: anti-Xa, diluted thrombin time, APTT, PT/INR, lupus anticoagulant (LA), factor assays (I, II, VII, VIII, IX, X, XI, XII), calibrated automated thrombography (CAT) with TF 5pM, thromboelastography (TEG).

Results: After DOAC-Stop® treatment, the DOACs showed undetectable anticoagulant concentrations and complete normalisation of APTT and PT/INR. The false positive LA results obtained with rivaroxaban were normalised.

Direct factor Xa inhibitors were completely normalised on the CAT, while for dabigatran only lag time and time-to-peak were normalised (Table 1). On the TEG, the MA of all DOACs was normalised, whereas a variable degree of normalisation of the other parameters was observed (Table 2).

Normal and warfarinised PPP on the CAT showed shortening of lag time and time-to-peak and prolongation of ETP and peak; on the TEG they showed an increase of R time. There showed also a trend towards a reduction of factors VIII, IX, X, XI, XII levels.

Conclusions: Our preliminary findings indicated that while basic coagulation assays were normalised by DOAC-Stop®, there might be potential for reduction of plasma levels of several coagulation factors, suggesting a certain level of DOAC-Stop® binding which could affect other assays.

	Lag time (ref. 3.54-4.34 min)		ETP (ref. 1852.7-2225.4 nM*min)		Peak (ref. 243.45-349.02 nM)		Time to peak (ref. 6.86-8.53 min)	
<i>Sample</i>	<i>Before</i>	<i>After</i>	<i>Before</i>	<i>After</i>	<i>Before</i>	<i>After</i>	<i>Before</i>	<i>After</i>
Normal PPP	4.17 (0.23)	3.84 (0.23)	1911.0 (52.3)	2013.0 (12.7)	270.33 (5.48)	301.69 (4.96)	8.00 (0)	7.33 (0)
Warfarinised PPP INR 4.2	11.67 (0)	10.84 (0.23)	275.0 (12.7)	296.5 (19.1)	46.67 (1.62)	51.17 (3.17)	15.00 (0)	14.00 (0)
Apixaban 265 ng/mL	8.92 (0.47)	3.91 (0)	643.0 (0)	1855.5 (23.3)	27.57 (2.54)	262.72 (3.20)	14.43 (1.65)	7.58 (0)
Edoxaban 220 ng/mL	11.59 (0)	3.74 (0.24)	643.0 (5.7)	1945.5 (132.2)	31.25 (0.64)	282.46 (11.67)	24.78 (0.24)	7.42 (0.23)
Rivaroxaban 339 ng/mL	12.09 (0.23)	3.91 (0)	467.5 (20.5)	1956.0 (123.0)	15.66 (0.33)	259.95 (11.79)	28.28 (0.47)	7.91 (0)
Dabigatran 318 ng/mL	18.50 (0.71)	3.84 (0.23)	748.0 (2.8)	1652.5 (23.3)	148.06 (3.37)	224.60 (2.05)	20.83 (0.71)	7.84 (0.23)
Enoxaparin 1.68 U/mL	Flat CAT traces							
Fondaparinux 1.62 µg/mL	14.00 (0)	11.50 (0.24)	242.5 (0.71)	274.5 (3.54)	12.90 (0.20)	16.56 (0.11)	24.84 (0.23)	20.33 (0)

[Table 1. CAT results before and after DOAC Stop® treatment]

	R time (ref. 9.23-15.01 min)		K time (ref. 1.56-4.12 min)		Angle (ref. 40.27-63.44 deg)		MA (ref. 28.83-36.57 mm)	
<i>Sample</i>	<i>Before</i>	<i>After</i>	<i>Before</i>	<i>After</i>	<i>Before</i>	<i>After</i>	<i>Before</i>	<i>After</i>

Normal PPP	10.05 (0.64)	12.55 (0.49)	3.05 (0.21)	3.15 (1.06)	51.45 (2.05)	47.30 (9.48)	30.80 (0.42)	32.15 (2.19)
Warfarinised PPP INR 4.2	18.15 (0.21)	23.80 (1.41)	6.60 (0.57)	5.90 (0.28)	26.80 (3.25)	35.50 (2.69)	32.35 (0.49)	33.65 (0.35)
Apixaban 265 ng/mL	17.70 (0.14)	16.55 (1.91)	8.55 (0.21)	4.50 (1.84)	28.25 (2.47)	37.90 (14.42)	23.45 (0.64)	29.05 (1.77)
Edoxaban 220 ng/mL	25.35 (3.18)	16.50 (0.42)	8.90 (0.14)	3.65 (0.49)	25.05 (3.89)	40.15 (5.59)	25.95 (1.63)	30.55 (2.05)
Rivaroxaban 339 ng/mL	29.80 (2.40)	16.30 (0.14)	13.25 (0.49)	3.70 (0.42)	17.40 (0.71)	43.75 (0.21)	23.30 (1.84)	31.0 (1.27)
Dabigatran 318 ng/mL	47.75 (1.34)	17.80 (1.27)	10.20 (7.35)	4.15 (0.92)	25.60 (15.27)	41.05 (6.01)	33.55 (2.62)	35.35 (0.49)
Enoxaparin 1.68 U/mL	Flat TEG traces							
Fondaparinux 1.62 µg/mL	Flat TEG traces							

[Table 2. TEG results before and after DOAC Stop® treatment]

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