Activated charcoal can be used as an effective in vitro removal agent of direct oral anticoagulants dabigatran, rivaroxaban and apixaban in plasma of patients with protein S activity testing

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ISTH VIRTUAL CONGRESS 2021 JULY 17–21 ISTH2021.ORG HOSTED FROM PHILADELPHIA SCIENCE CONQUERING DISEASE

INTRODUCTION

As other coagulation thrombophilia assays, testing of protein S (PS) activity can also be influenced and misinterpreted in patients treated with direct oral anticoagulants (DOACs).

AIM

To investigate the effect of DOACs on PS activity results and to evaluate the use of our own optimized method with activated charcoal (AC) in removing potential interference.

METHOD

The study included 45 plasma samples from patients treated with three DOACs. Concentrations of DOACs were determined in native plasma. Then, using our method earlier optimized for other thrombophilia assays, 100 mg of medical AC powder (Jadran Galenski laboratorij, Rijeka, Croatia) was added to 500 µL plasma allowing DOACs adsorption for 10 minutes. Treated samples were centrifuged 20 minutes at 1800xg and DOACs concentrations and PS activity were measured in supernatant. Rivaroxaban and apixaban were determined using commercial anti-FXa assay (Siemens Healthineers, Germany) with drug specific calibrators (Hyphen Biomed, France). Dabigatran was measured using Innovance DTI assay (Siemens Healthineers, Germany). Protein S activity was determined using coagulometric method (Protein S Ac, Siemens Healthineers, Germany). All measurements were performed on BCSXP analyzer (Siemens Healthineers, Germany). Statistical analysis was done using Wilcoxon test by MedCalc Statistical Software version 11.5.1 (MedCalc Software, Belgium). The study was funded as part of Croatian Science Foundation research project IP-2016-06-8208.

RESULTS

All three DOACs have shown significant interfering effect on PS activity results in terms of false increased values. In 37/45 of native plasma samples, results of PS activity were above upper limit of measuring range (>130%) with significantly higher values in native than in AC treated samples (P=0.0001) (Table 1 and Figure 1).

Table 1. Results of protein S (PS) activity testing before and after addition of medical activated charcoal (AC) in patients treated with DOACs.

	DOAC conc. (ng/mL) Median (95%CI); IQR	Protein S activity (%)	
		Native plasma (before AC addition)	AC treated plasma (after AC addition)
Dabigatran N=15	163 (76-323) 76-324	>130 (12/15) NA	74 (68-79) 68-79
		P = 0.0001	
Rivaroxaban N=15	150 (82-229) 82-229	>130 (13/15) NA	70 (67-76) 68-76
		P = 0.0001	
Apixaban N=15	170 (134-208) 144-219	>130 in (12/15) NA	75 (69-80) 69-80
		P=0.0001	

IQR = interquartile range; AC = activated charcoal; P< 0.05 was considered statistically significant

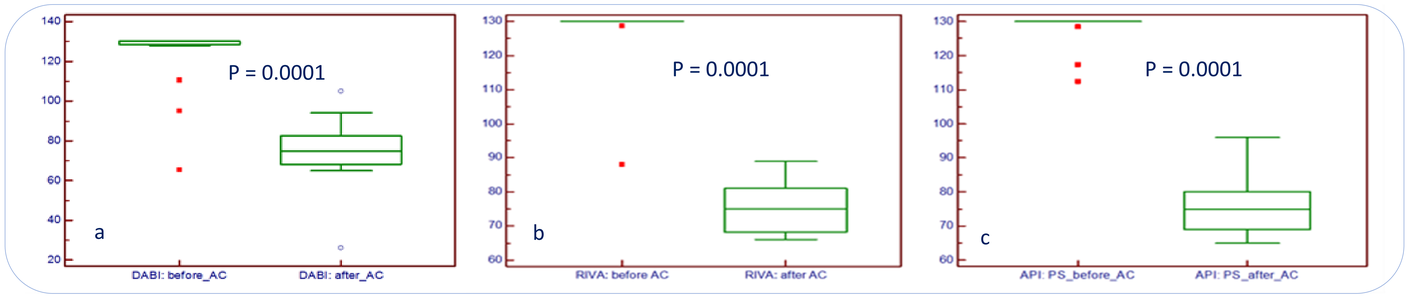

Figure 1. Differences between medians of protein S (PS) activities (%) in dabigatran (a), rivaroxaban (b) and apixaban (c) native and activated charcoal (AC) treated samples.

CONCLUSIONS

ALL DOACS HAVE STRONG INTERFERING EFFECT ON PROTEIN S ACTIVITY IN TERMS OF POSSIBLE FALSE NEGATIVE RESULT. OUR OPTIMIZED METHOD USING MEDICAL AC HAS BEEN FOUND EFFECTIVE IN OVERCOMING INTERFERENCE OF DOACS ON PS ACTIVITY TESTING.

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