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Interference of routine coagulation tests with the new oral anticoagulant dabigatran – a multicenter study

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Background

- Dabigatran etexilate, approved for prophylaxis of thromboembolism in patients undergoing total knee or total hip replacement, has shown promising results for treatment of VTE and the prevention of stroke in patients with atrial fibrillation.
- To investigate the extent of interaction of this direct thrombin inhibitor with coagulation assays the task-force-group on new-oral-anticoagulants of the Austrian Society of Lab Med & Clin Chem started a multicenter pilot-trail with the first CE-labeled dabigatran-spiked (0.0 – 0.48 µg/ml) plasma samples (Hyphen BioMed kindly gifted by CoaChrom Diagnostica) in coagulation laboratories of six Austrian hospitals.

Methods

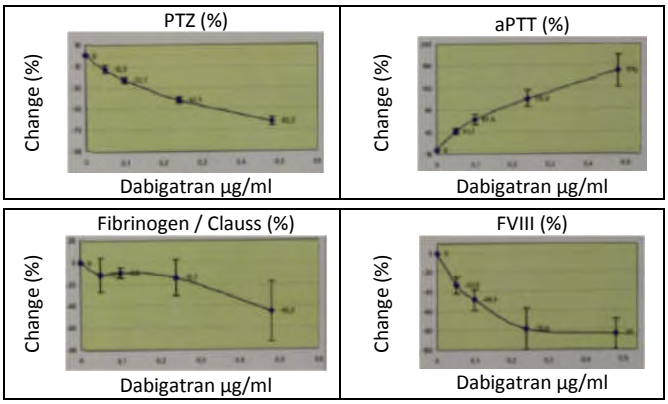
- Assays were performed under routine conditions using reagents and analyzers representative for Austrian laboratories.
- Results of coagulation tests were calculated as percentual differences from the dabigatran free plasma calibrator.

Results

- Dabigatran led to a dose-dependent prolongation of the clotting times in coagulometric tests and thus influenced the majority of the parameters measured.
- Strongest influences were seen for aPTT and aPTT-based assays, thrombin time and protein S activity followed by interferences with PTZ, PTZ-based and fibrinogen (Clauss) measurements.
- Also thrombin-dependent, non-clotting tests such as the colorimetric F XIII activity assay and to a minor extent also the amidolytic (via IIa) ATIII activity assay were influenced.
- Immunologic and thrombin-independent assays (plasminogen, protein C, ATIII via FXa) were not affected by dabigatran.

Conclusion

- This is the first multicenter-study with CE-labeled plasmas demonstrating that laboratories have to expect strong interferences of routine coagulations tests with increasing concentrations of dabigatran up to 0.48 µg/ml.
- Apparently, this might become important especially in the elderly and in patients with renal impairment at least when blood is sampled at peak levels.



Strong Influence		Moderate Influence		Weak/no influence	
	% change		% change		% change
Protein S Activity	∞			**ATIII (via Xa)**	11(16)
APC-Ratio	∞	**FX activity**	-35(12)	**Plasminogen activity**	1(3)
Thrombin Time	∞	**FVII activity**	-29(10)	**vWF-activity**	-7(4)
FXI activity	∞	**ATIII (via FIIa)**	+31(15)	**vWF:RCo-activity**	1(2)
aPTT	177(37)	**Fibrinogen Clauss**	-38(30)	**Protein C activity**	-2(2)
FVIII activity	-85(16)				
FXIII activity	-70(34)				
FIX activity	-93(4)				
FXII activity	-68(25)				
PTZ	-62(4)				
FII activity	-59(4)				
FV activity	-45(5)				

Table 1: The results of the different coagulation tests were calculated as percentual differences of dabigatran-free plasma calibrator (0 µg/ml). Mean and SD of the percentual differences measured by the participating laboratories were calculated for increasing dabigatran concentrations. Table 1 summarizes the mean (± SD) percentual changes at 0.48 µg/ml dabigatran.

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