Impact of Rivaroxaban and Dabigatran on clotting screens as performed using the Roche cobas® t 711 analyser.

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Introduction

Direct Oral Anticoagulants (DOACs) including Dabigatran (Pradaxa®) and Rivaroxaban (Xarelto®) can cause method specific prolongation of some clotting tests (1,2). The cobas® t 711 is a new analytical platform designed by Roche which is likely to be used for the analysis of samples from patients taking these drugs.

Data on the impact of the effect that these drugs have on clotting screens performed with this system are therefore needed to facilitate interpretation of such test results in the presence of DOACs (1,3).

Dabigatran

A Direct Thrombin (Factor IIa) inhibitor; blocks conversion of fibrinogen to fibrin. Active form binds active site of thrombin; Inhibits free and clot-bound thrombin; Inactive pro-drug; Metabolised by P-glycoprotein pathway; Rapidly absorbed; Half-life 12-17 hours; 85% excreted via the kidneys; Low protein binding; Easily elminated by haemodialysis. (1,3,4)

Rivaroxaban

A Factor Xa inhibitor with predictable pharmacokinetics; Fixed dose; Half-life 7-11hrs; Excreted via the renal & hepatic pathways. Not recommended in patients with a CrCl <15ml/min (1,4).

The stock solution was used to spike PPP achieving the most spiked plasma concentrations (ng/ml) for Rivaroxaban. In light of this it would be preferable to perform a specialised chromogenic Anti-Xa or clotting based DTI assay to quantify the amount of drug present in plasma samples.

Claus fibrinogen was unaffected by Dabigatran up to 1805 ng/mL. Clauss fibrinogen was unaffected by Dabigatran up to 1805 ng/mL.

Results

The clotting screen result data are shown in the table below. Both the PT and APTT were prolonged above baseline at a spiked drug concentration of >345 ng/mL for Dabigatran. At the highest concentration of 1805 ng/mL a minimum of a four fold increase of the PT result above baseline is shown respectively for cobas® t 711 and Sysmex® CS5100.

Conclusion

The comparability of the sensitivity of the effect of Rivaroxaban and Dabigatran on clotting screens is shown to be very similar to that observed when performing the studies on a comparator method, the Sysmex® CS5100 analyser. Even with the use of different branded reagents, the sensitivity is similar with regards to result prolongation.

It is apparent that coagulation tests of PT & APTT show results which are variably prolonged with Dabigatran & Rivaroxaban interference. A concentration-dependant prolongation is shown when tested using both systems.

Dabigatran is shown to cause greater prolongation effects on the results of PT & APTT than Rivaroxaban. Even at highly concentrated Rivaroxaban spiked samples, >808 ng/mL, the PT showed mild prolongation of results. This demonstrates that the PT test should not be used as a screening test for those patients receiving Rivaroxaban treatment. However the majority of the impact on results is found at the very high concentrations of Dabigatran and Rivaroxaban in spiked plasma. In light of this it would be preferable to perform a specialised chromogenic Anti-Xa or clotting based DTI assay to quantify the amount of drug present in plasma samples.

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References


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