LABORATORY ASSESSMENT OF DIRECT AND INDIRECT THROMBIN INHIBITORS

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Although mainly used in standardized dosage several prophylactic and therapeutic applications of anticoagulants in clinical routine need individual monitoring and tailored administration. Pediatric and intensive care patients as well as alternatively anticoagulated patients are not manageable without monitoring pharmakokinetics and -dynamics of anticoagulant drugs. New heparins and synthetic inhibitors increase the therapeutic options from year to year.

Applying global clotting assays for monitoring of anticoagulants measures the inhibitory effects of the compounds, but also any other influences on thrombin generation and fibrin polymerization already present in the patients plasma.

On the other hand chromogenic substrate assays are applied, which work in highly diluted plasma and therefore get rid of influences and disturbances from the plasma matrix of the patient.

For measuring heparins and heparin-like thrombin inhibitors the presence of antithrombin in excess or not is of crucial impact. Some assays do not provide this cofactor and are therefore dependent on the patients antithrombin (Heparin-Cofactor) activity.

Concerning implementation in clinical routine the calibration concept is important. With respect to variability and long term performance commercially available calibrants are superior to home made plasma standards obtained by spiking normal plasma samples with the pharmaceutical substances.

Another point to be discussed is how the different methods reflect efficacy and / or safety of the different compounds being measured. Acceptable correlation with single or combined clinical outcomes has been suggested for application of global clotting assays for monitoring of anticoagulants in clinical routine. This may be due to the fact that in the traditional global clotting test the patients coagulation capacity is measured together with the inhibitory drug effects. On the other hand assays in high dilution are not very sensitive to this influence of the plasma matrix. They mainly focus pharmkokinetics of these anticoagulants.