Laboratory assays for the measurement of Factor VIII and IX

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The most common reason for measuring the factor VIII/IX (FVIII/IX) level in plasma is to assess the risk of bleeding due to hereditary or acquired FVIII/IX deficiency and to classify the severity of deficiencies. These indications are expanded further to monitoring of patients after infusion of FVIII/IX concentrates and turned to be a prerequisite for a patient-tailored treatment strategy. Additionally, the correct identification of patients with sub-haemophilia and carriers of haemophilia is important as these patients need to be protected against bleeding complications. Labeling and quality control FVIII/IX treatment concentrates are further applications of FVIII/IX determination. According to ISTH-SCC recommendation hemophilia is classified in: severe (<1IU/dl), moderate (1–5IU/dl) and mild (>5IU/dl) based on FVIII/IX activity measurements. Therefore, FVIII/IX assays must be able to differentiate FVIII/IX levels above and below 1IU/dl.

Two main kinds of assay principals are available for assessment of FVIII/IX in plasma and provide an accurate evaluation of an individual's in vivo hemostatic state and response to treatment. The traditional plasma-based coagulation assays as one-stage and two-stage clotting assays or chromogenic assays, which results in thrombin generation and clot formation. Although these assays remain the standard methods in most laboratories, high inter-and intra laboratory discrepancies have been observed based on number of pretest variables, wide heterogeneity of available procedures, qualities and properties of reagents used. The global haemostasis assays such as the thrombin generation test, thromboelastography, and aPTT waveform, all measuring the kinetics of clot formation could be better suited to predict clinical phenotype as they can more effectively assess the rate and total thrombin generated, individual haemostatic capacity, and clot structure and stability. Still all these analyses are labor intensive, require specific equipment, qualifications and rigorous process of pre-analytical and analytical standardization which limit their implementation within the routine practice of most clinical laboratories.

An understanding of the tests used to diagnose haemophilia will bring to more appropriate determination the severity of disease, improve interpretation and individualization of patient responses to treatment therapy and allow an optimal treatment dosing.