Development of diagnostic algorithm for von Willebrand disease within WFH the Twinning Tallinn-Helsinki program

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Introduction and Objectives

It was not possible to make a definite diagnosis of von Willebrand disease (VWD) subtypes or severe forms of haemophilia A in Estonia until 2016. To close these diagnostic gaps, a specific goal of the World Federation of Hemophilia (WFH) centre twinning link between Tallinn (Estonia) and Helsinki (Finland) Haemophilia Treatment Centre (HTC) was to update the protocols for laboratory diagnosis of bleeding disorders in Estonia.

Materials and Methods

Adult and paediatric ISTH-BAT (International Society on Thrombosis and Haemostasis - Bleeding Assessment Tool) were translated into Estonian and

incorporated into routine practice to identify individuals with clinically relevant bleeding tendency/symptoms.

New fully automated assay protocols were implemented in STA-R Evolution analyzer (Stago, France) and their analytical performance was evaluated:

- Von Willebrand factor (VWF) activity assay (INNOVANCE® VWF Ac, Siemens, Germany) – part of the VWD screening panel;
- FVIII low-range assay for the correct classification of severe haemophilia A and of type 3 VWD (available 24/7).

A new VWF multimer electrophoresis assay (Sebia, France) was evaluated preclinically, including the main VWD types and 2B, 2A and 2N subtypes.

suboptimal

Genetic consultation

VWF:FVIII binding assay

• Genetic consultation

Regular meetings and discussions focusing clinical on cases were established between clinicians and laboratory.

Results

Coagulation tests were verified and accredited according to ISO 15189:2012. Based on available laboratory assays in Estonia, diagnostic algorithms for VWD and acquired von Willebrand syndrome created. The response desmopressin was evaluated in Tallinn Children's Hospital. The assessment of desmopressin response will also be addressed among adults.

Conclusion

Tallinn-Helsinki WFH Twinning Program has played a pivotal role in developing coagulation test methods in the North Estonia Medical Centre laboratory promoting interdisciplinary and meetings and international cooperation in the Baltic region.

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Diagnostic algorithm for VWD and AVWS Patient with bleeding tendency Personal and family history ISTH-BAT abnormal: ISTH-BAT normal: Children ≥3, men ≥4, women ≥6: (questionnaire) Children < 3, men < 4, women < 6: Bleeding disorder more likely Physical examination Low probability of bleeding disorder, no future evaluation • ISTH-BAT CBC, Bleeding time or PFA, PT, APTT, fibrinogen, No abnormalities in first analyses TT, VWF:Ag, VWF:Ac, FVIII:C, RIPA • Repeat testing in 1-3 months in high suspicion for VWD 1 or more test abnormal: VWF:Ag, VWF:Ac, FVIII:C, RIPA Other cause identified, e.g., Consider 1 or more test abnormal low platelets, isolated abnormal • combined mild deficiency of coagulation factors PT or APTT, abnormal TT, disorder of vascular hemostasis Repeat testing hyperfibrinolysis (antiplasmin deficiency, ROTEM) low fibrinogen VWF:Ac /VWF:Ag ratio • Factor XIII deficiency VWF multimers Probable Type 1 Probable: Probable **Type 2M** Probable: Probable Type 2A Probable **Type 3** -Type 2B VWD -Type 2N VWD -Hemophilia A (male) VWF:Ag- ↓ VWF:Ag- ↓ -PLT-VWD VWF:Ag- ↓ VWF:Ag-↓↓↓ / VWF:Ac- ↓ VWF:Ac- ↓↓ VWF:Ac- ↓↓ -Hemophilia A Carier (female) undetectable F-VIII - N or ↓ • F-VIII- N or ↓ VWF:Ag- ↓ F-VIII- N or ↓ VWF:Ac- ↓↓↓ / ● BT or PFA - N or ↑ ● BT or PFA - 个 VWF:Ac- ↓↓ ● BT or PFA - ↑ VWF:Ag-N or ↓ undetectable VWF:Ac- N or ↓ Platelet count - N Platelet count –N • F-VIII- N or ↓ Platelet count- N ● F-VIII - ↓ ● BT or PFA- 个个个 • RIPA: RistoHigh- often N ■ RIPA : RistoHigh- ↓ ● BT or PFA - 个 ■ RIPA: RistoHigh- ↓ ● F-VIII- ↓↓ • BT or PFA - N VWF:Ac /VWF:Ag - N VWF:Ac /VWF:Ag - ↓ Platelet count- N or ↓ VWF:Ac/VWF:Ag -N or ↓ Platelet count –N Multimer pattern – N • Multimer pattern – • RIPA: RistoHigh- often N Multimer pattern – Platelet count- N ■ RIPA: RistoHigh-↓↓ Response to DDAVP -● RIPA: RistoLow- ↑ • RIPA: RistoHigh –N • Multimer pattern – Abnormal Normal Response to DDAVP -VWF:Ac /VWF:Ag - N • Response to DDAVP -VWF:Ac/VWF:Ag- N or ↓ Undetectable good mild to moderate Multimer pattern – mild to moderate Multimer pattern – normal • Response to DDAVP -• Response to DDAVP -Abnormal no responce

DDAVP not indicated

Genetic consultation







Genetic consultation

Genetic consultation