ASSESSMENT OF BIOLOGICAL RESPONSE TO DESMOPRESSIN USING VON WILLEBRAND FACTOR MULTIMERS ANALYSIS

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This study was approved by the Tallinn Ethics Committee on Medical Research.

Methods

Efficacy of DDAVP was investigated in 7 patients with bleeding tendency and family history of bleeding. Plasma VWF:Ag, VWF:Ac, FVIII:C and VWF multimers analysis was performed before, 1 hour after (peak), 2 hour and 4 hour after (clearance) the administration of DDAVP. Plasma VWF multimeric distribution was analyzed by agarose gel electrophoresis and immunofixation followed by densitometric analysis using new Hydragel 5 von Willebrand Multimers kit on the Hydrosys system (Sebia, France).

Patients were classified according to response to DDAVP as complete responders (both VWF:Ag and FVIII:C were 50 % or higher after desmopressin), partial responders (VWF:Ac or FVIII:C were lower than 50 % but increased at least 3-fold) and nonresponders (neither of the forementioned criterion) [2].

Results

6 patients, who did respond to desmopressin, had reduced VWF:Ag, normal VWF:Ac levels, VWF:Ac/VWF:Ag >0.7, normal ristocetin-induced platelet aggregation (RIPA) and normal multimeric structure of VWF. The baseline medians were as follows: VWF:Ag – 56.5 (IQR 47.3–66.5), VWF:Ac – 63.0 (IQR 61.0–70.5), FVIII:C – 98.5 (IQR 70.8–106.5). The medians of the peak point, 1h after DDAVP administration, were: VWF:Ag – 133.5 (IQR 87.3–187.3), VWF:Ac – 178.5 (IQR 133.8–234.0), FVIII:C – 302.0 (IQR 257.5–372.8). High-molecular-weight multimers (HMWM) slightly increased after DDAVP administration and this proportion did not change significantly during 4h. One patient was classified as type 2A VWD patient, demonstrating partial response to DDAVP: VWF:Ag 25% vs 67%, VWF:Ac 12% vs 36%, FVIII:C 41% vs 119%, VWF:Ac/VWF:Ag 0.48 vs 0.54, reduced RIPA (evaluated at baseline) and a decreased fraction of HMWM.

Conclusion

New Sebia Hydragel 5 von Willebrand multimers test compared to difficult in-house methods is rapid (within-day results) and sensitive. It provides useful information not only for differentiating types/subtypes of VWD, but also for monitoring the response to therapeutic interventions such as DDAVP. In this study, all cases yielded the release of HMWM after DDAVP administration.

Background

Desmopressin (DDAVP) is a synthetic analog of vasopressin that increases plasma levels of von Willebrand factor (VWF) and factor VIII:C (FVIII:C) from storage sites and is used in the treatment of von Willebrand disease (VWD) and mild hemophilia A. It is known that response to DDAVP might be variable. A test dose of DDAVP is recommended, as second-level treatment of von Willebrand disease (VWD) (FVIII:C) from storage sites and is used in the clinical efficacy during bleeding [1]. The aim of this study was to assess the response of VWF multimers distribution in responders to DDAVP treatment.

References

2. Castaman G, Lethagen S, Federici AB et al. Response to desmopressin is influenced by the genotype and phenotype in type 1 von Willebrand disease (VWD): results from the European Study MCMOD-1VWD. Blood 2008; 111:3531–9

Figure 1. VWF multimers distribution in responders to DDAVP treatment.

Figure 3. An example of a „low VWF level“ plasma with normal pattern of VWF multimers: gel and densitogram. PNP - pooled normal plasma.

Figure 2. An example of a non-VWD plasma with normal pattern of VWF multimers: gel and densitogram. PNP - pooled normal plasma.

Figure 4. An example of a type 2A VWD plasma with a relative loss of HMWM multimers: gel and densitogram. PNP - pooled normal plasma.