Hemophilia Therapy III

PP-TH-566

Visualising the coagulation process and hemophilia in 3D, a unique and valuable educational tool for patients and health care professionals

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Visualising the coagulation process and hemophilia in 3D, a unique and valuable educational tool for patients and health care professionals: Cedric Hermans, MD, PhD and Catherine Lambert, MD; Department of Haematology, Haemostasis and Thrombosis Unit, Cliniques universitaires Saint-Luc, Brussels, Belgium. Being able to visualize the coagulation process helps both physicians and health care professionals to explain the pathophysiology of haemophilia and patients to understand their disease and its treatment. Right from the discovery of the role of the different clotting factors, man has always tried to schematize and visualize the complex coagulation process. We added an extra dimension by using the most recent imaging technology. Together with a specialized production house we developed a set of 3D video animations, explaining the coagulation process in a normal situation and in a hemophiliac patient without and after factor replacement. Following this stepwise approach, in about 14 min spectators get a better understanding of the coagulation process, the role of both factor VIII and Factor IX, the mechanisms of haemophilia and its consequences as well as the need of replacement therapy with clotting factor concentrate. This movie provides a unique and valuable educational tool for instructing patients and relatives, and leveraging their compliance. This 3D animation should also contribute to improve the awareness and understanding of haemophilia among health professionals.

Disclosure of interest: none declared.

PP-TH-567

Effects of rFVIIA analogue (NN1731) on platelet function, clot structure and clot kinetics in whole blood from patients with hemophilia A

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Introduction: NN1731 is a recombinant factor VIIa (rFVIIa) analogue with greater enzymatic activity than rFVIIa on the activated platelets. We compared NN1731's hemostatic potential to rFVIIa in an *ex-vivo* study in hemophilia patients ($N = 10$) with different degrees of hemophilia (two with severe FVIII deficiency with FVIII inhibitor, six with moderate FVIII deficiency, and two with mild FVIII deficiency) and in healthy volunteers ($N = 10$) using the Hemodyne HAS and the Thromboelastogram (TEG) to monitor clot formation.

Methods: Whole blood samples were spiked with rFVIIa and NN1731 at concentrations 0.64 and 1.28 μg/mL corresponding to a clinical dose of 45 and 90 μg/kg. Platelet contractile force (PCF), clot structure (CEM, MA) and clot kinetics (FOT, R, and K) were determined using the HAS and TEG.

Results: NN1731 shortened FOT and R more markedly than rFVIIa in both normal and FVIII deficient blood (Table). In hemophiliacs, NN1731 0.64 μg/mL shortened the R and FOT values, and increased the CEM and PCF more than rFVIIa 1.28 μg/mL. It also normalized the clotting parameters equivalent to the baseline values of healthy volunteers.

Conclusion: NN1731 increases the rate of platelet activation, and improves clot structure and function in hemophilic blood at lower concentrations than rFVIIa.

Table for PP-TH-567

	PCF (kdynes)	CEM (kdynes/cm^2)	FOT (min)	R (min)	K (min)	MA (mm)
Healthy vols.: ($n = 10$)	7.1 (0.9)	24.3 (4.7)	7.2 (1.0)	7.5 (0.5)	2.7 (0.5)	57.2 (5.1)
Patients: ($n = 10$)						
Baseline	1.0 (0.7)	1.7 (2.7)	> 20*	24.1 (9.0)*	13.0 (14.5)	42.1 (22.7)
0.64 μg/mL rFVIIa	3.7 (2.1)	12.0 (6.9)	12.2 (3.7)	12.9 (4.2)	3.6 (1.2)	57.3 (4.7)
1.28 μg/mL rFVIIa	4.7 (2.0)	17.9 (7.2)	10.1 (2.9)	10.5 (3.2)	3.2 (1.4)	57.8 (4.6)
0.64 μg/mL NN1731	7.6 (2.2)	31.4 (6.8)	5.1 (1.2)	5.3 (0.6)	2.9 (1.1)	57.0 (7.6)
1.28 μg/mL NN1731	9.0 (2.3)	37.0 (4.0)	3.5 (0.4)	3.6 (0.5)	2.1 (0.6)	59.0 (5.4)

Results presented as: Mean (±SD)

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PP-TH-568

No evidence for neonatigens formation in differents batchs of a double-virus inactivated factor VIII concentrate manufactured in Argentina

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Background: To improve the safety of plasma derived factor VIII (FVIII) concentrates, in UNC-Hemoderivados was introduced a double virus-inactivation procedure such as solvent/detergent and dry-heat (100°C for 30 min) treatments. Theoretically, modifications to FVIII molecule during manufacture procedure could result in neonatigen formation with the potential to enhance the rate of inhibitory antibodies induction. Some studies showed that the type of FVIII preparation and viral inactivation steps used could have a determining critical effect on the development of antibodies anti-FVIII in hemophilia A patients.

Aims: Using an enzyme-immunoassay (EIA) developed in our laboratory, we tested different lots of concentrate of FVIII looking for the potential neoantigen formation in order to assess if the procedures employed for viral inactivation caused antigenic changes in the products.

Material and Methods: Different batch ($n = 6$) of concentrate of FVIII were prepared from cryoprecipitate using ion-exchange and affinity chromatography and double virus inactivation steps. The EIA was performed using rabbit antisera prepared by immunization with dry-heat (HT) and not dry-heat (non-HT) treatments of concentrates of FVIII. The study was aimed to reveal possible differences in the immunological properties performed from a mixture of antisera HT and non-HT with increasing amounts of product (incubation-absorption in liquid phase) and assayed in microplate wells coated with HT and non-HT FVIII.

Results: The results showed that both antibodies (HT and not-HT) neutralized the same amount of factor VIII with and without heating and also they were able to show that this behavior was repeated when factor VIII, with and without heat treatment, was used in the