Characterizing Global Hemostasis throughout the Factor VIII Prophylaxis Dosing Interval: A Pilot Study

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OBJECTIVES

Hemophilia A patients receiving FVIII prophylaxis have a wide inter-individual variation in clinical bleeding phenotype that is not well characterized by FVIII:C. A potential alternative may be to guide FVIII dosing by global hemostasis markers (TEG and Hemodyne). To quantify inter-individual dose-response variation we conducted a clinical study that characterized global hemostasis throughout a 48 hour FVIII prophylaxis interval.

METHODS

Ten non-bleeding severe FVIII deficient patients received prophylactic FVIII (mean dose 32.1 IU/kg) and blood was collected at baseline and 0.5, 1, 2, 4, 8, 12, 24 and 48 hours post-dose to assess FVIII:C, platelet function markers (platelet contractile force [PCF], clot elastic modulus [CEM], force onset time [FOT]) and TEG (reaction time [R], kinetics time [K], maximum amplitude [MA]).

RESULTS

Parameter (Mean)	Hours Following rFVIII Dose								
	0	0.5	1	2	4	8	12	24	48
FVIII:C (IU/dL)	0.6	88.2	78.4	71.1	61.2	42.1	29.7	16.2	3.4
PCF (kdyne)	0.3	6.7	7.4	5.7	5.9	3.5	3.9	3.1	0.6
CEM (kdyne/cm^2)	0.0	22.1	24.5	19.5	20.8	10.7	16.5	12.6	1.6
FOT (min)	18.1	6.7	6.1	7.5	7.5	9.8	10.5	12.2	18.0
R (min)	22.5	7.2	6.4	7.3	7.5	9.8	8.5	12.2	19.6
K (min)	7.1	2.2	2.1	2.2	2.4	2.6	2.4	3.3	5.2
MA (mm)	53.5	62.2	63.0	61.0	60.0	59.2	61.2	58.9	54.2

CONCLUSIONS

- Mean FVIII:C remained above 1 IU/dL throughout the 48 hour dosing period
- Platelet function and TEG markers responded correspondingly to FVIII:C levels
- 24 hours post FVIII dosing, most of the hemostatic markers were outside the normal target range
- 48 hours FVIII dosing, despite a FVIII:C level of 3.4 IU/dL, the hemostatic markers were grossly abnormal and similar to baseline values
- FVIII:C may not be a sensitive measure of platelet function and viscoelastic changes
- Further study is needed to establish the link between laboratory makers and the clinical effects of FVIII

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