Pharmacokinetic (PK)-guided daily dosing: a significant reduction in weekly factor VIII consumption

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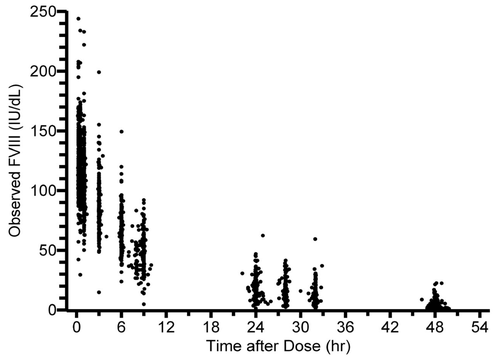
Background

- Prophylaxis with factor VIII (FVIII) concentrate is common practice in most severe and some moderate hemophilia A patients.
- Interindividual variation exists in FVIII clearance *(Bjorkman et al. 2012).*



- PK-guided dosing may lead to individualization of prophylaxis.

Objective

To investigate potential effects on FVIII consumption of PK-guided dosing at various infusion intervals.

Patients & Methods

- Eleven hemophilia A patients (FVIII:C ≤ 0.03 IU/mL); Table 1
- Individual PK profile: FVIII bolus 50 IU/kg, measurement of FVIII:C at t=4, t=24, t=48 hours
- Prophylactic FVIII dosing regimens at 24, 48 and 72 hours, aiming for FVIII trough levels >0.01 IU/mL
- Individual PK parameters were calculated using Bayesian analysis in NONMEM® software
- NONMEM® analysis was performed using a population PK model described by Bjorkman in 2012.

Results

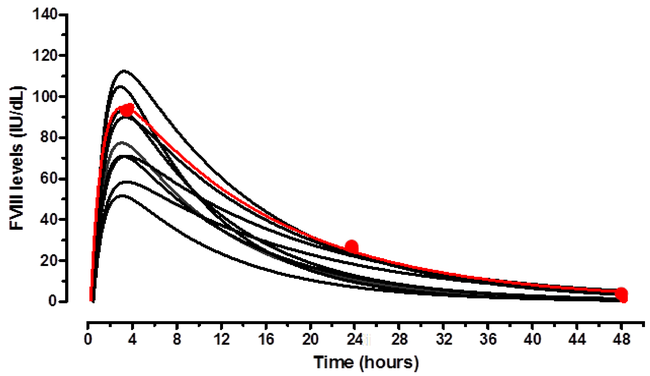


Figure 1. Pharmacokinetic (PK) profile of factor VIII (FVIII) concentrate in (moderate) severe hemophilia A patients. A bolus of 50 IU/kg FVIII concentrate is administrated followed by FVIII:C measurements at t=4, t=24 and t=48 hours (red points). Using a population PK model, FVIII plasma levels (red line) are calculated using individual PK parameter estimates derived from Bayesian analysis.

Table 1. Patient characteristics.

ID	Age (years)	Body weight (kg)	Baseline FVIII:C (IU/mL)	FVIII product	Clearance (mL/h)	Vss (mL)
1	33	85.3	<0.01	Advate	325	3598
2	33	93	<0.01	Advate	198	3341
3	70	103	<0.01	Advate	304	4828
4	13	76	<0.01	Helixate	130	2252
5	17	63	<0.01	Advate	177	2894
6	8.7	28	<0.01	Advate	124	1411
7	7	36	0.03	Kogenate	118	1702
8	11	65	<0.01	Advate	127	2235
9	40	74	<0.01	Refacto	322	4354
10	60	88.5	<0.01	Advate	294	4153
11	13.1	56.8	<0.01	Helixate	169	2176

Conclusion

More frequent prophylactic dosing may strongly reduce FVIII concentrate consumption and therefore costs. However, when considering more frequent dosing, quality of life measures should always be taken into account.

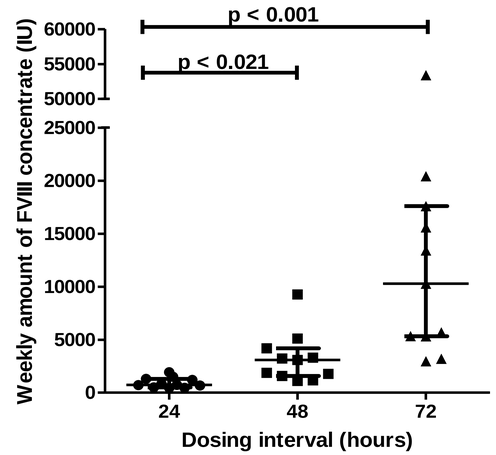


Figure 2. Simulations show that frequent dosing reduces weekly FVIII concentrate consumption. Statistical analysis was performed using Kruskal-Wallis (H(2) = 24.88, p < 0.001).

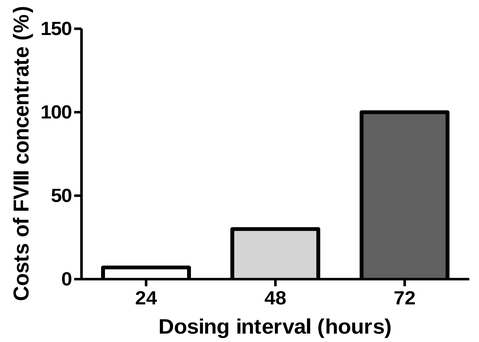


Figure 3. Simulations show that more frequent dosing reduces costs of prophylaxis (%).

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