

Pharmacokinetics (PK) of recombinant and plasma-derived factor IX (FIX) products in pediatric patients with severe hemophilia B

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Introduction

Although there is widespread PK data for FIX use in adults, this data cannot be applied to pediatric patients due to several significant physiologic differences. As reported by Poon [1], there is approximately 25-30% lower in vivo recovery after administration of rFIX in younger children. Using the primary literature and FIX product inserts, we conducted a thorough review to determine whether the half-lives of available recombinant and plasma-derived FIX products are comparable in pediatric patients.

Results

Our review showed that pediatric PK studies have been conducted in BeneFIX, and MonoNine. Pediatric PK data for MonoNine was not available in the product monograph. Moreover, there is no pediatric PK data for the other plasma-derived products, thus excluding possible comparisons with the recombinant-derived product. There is also no continuity in age group definitions when reporting PK data (Table 1), thereby making it difficult to compare their half-lives. BeneFIX does demonstrate two PK trends when comparing children to adults, which include a shorter half life, and higher clearance rate in PTP patients. There is only recovery data on PUPs for BeneFIX and therefore no comparisons can be made.

Discussion/Conclusions

Pediatric PK studies are available for some FIX products. However, each FIX product defines their age groups differently when reporting PK data (Table 1), thereby making it difficult to compare their half-lives. We would suggest the use of the Bayesian method of sampling reported as continuous variables or age groups defined by Andrew et al. [4] (i.e. 1-5 years, 6-10 years, 11-16 years, adult) to report future PK studies involving both short and long acting FIX. The younger pediatric population would seem ideally suited to limited-PK time point assessment using population PK derived models as a method of tailoring treatment [5]. This will allow healthcare providers to compare the products and make evidence-based decisions regarding patient care.

Table 1: Product review

Product	Age (n)	Mean Half-life (hrs)	Mean AUC (IU*hr/dL)	Mean Clearance (mL/h/Kg)
BeneFIX ¹ (PTP)	4 to <15years (19)	20.2 ± 4	NA	NA
BeneFIX ² (PTP)	>12years (22)	36 ± 12.8	1631 ± 467	0.046 ± 0.01 (dL/Kg ⁻¹ /min ⁻¹)
BeneFIX ³ (PTP)	< 2 years (7) 2 - <6 years (16) 6 - <12 years (1) 12 - <18 years (19)	15.6 ± 1.2 16.7 ± 1.9 16.3 21.5 ± 5.0	NA NA NA NA	13.1 ± 2.1 13.1 ± 2.9 15.5 9.2 ± 2.3
BeneFIX ¹ (PUP)	0 - <1 month (3) >1 mon - <2yr (45) >2yr - <12yr (9) >15 years (37)	NA NA NA 18.8 ± 5.4	NA NA NA NA	NA NA NA NA
AlphaNine ²	>12years (25)	32.7 ± 7.4	1684 ± 42.5	0.042 ± 0.01 (dL/Kg ⁻¹ /min ⁻¹)
ImmuNine ⁴⁺⁵	18-70 years (27)	17.11 ± 6.18	NA	8.89 ± 2.91
MonoNine ⁶	Not specified (10) 1day - 20yrs (51)	22.6 NA	NA NA	NA NA
Bebulin ⁵	18-70 years (22)	15.94 ± 4.69		8.41±2.62
rFIX-FP ⁷ (PTP)	12-65 years (28) 25 IU/Kg (7) 50 IU/Kg (13) 75 IU/Kg (8)	104.71 ± 55.08 91.57 ± 20.74 98.52 ± 17.48	4192.42 ± 1627.9 7089.87 ± 1622.83 8995.24 ± 1757.80	0.73 ± 0.46 0.75 ± 0.19 0.87 ± 0.17
rFIX-Fc ⁸ (PTP)	>18 years (11) 25 IU/Kg (1) 50 IU/Kg (5) 100 IU/Kg (5)	53.5 57.6 ± 8.27 56.5 ± 14.1	766 1700 ± 548 4020 ± 986	3.56 3.44 ± 0.833 2.84 ± 0.657
N9-GP ⁹ (PTP)	21-55 years (15) 25 IU/Kg (5) 50 IU/Kg (5) 100 IU/Kg (5)	82.94 ± 18.15 96.25 ± 41.85 110.45 ± 17.48	33.04 ± 3.58 73.28 ± 23.05 158.75 ± 17.48	0.76 ± 0.08 0.74 ± 0.21 0.65 ± 0.13

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