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Utilization of factor concentrate and frequency of bleeds among patients with Haemophilia A and Haemophilia B in Northwest of Iran

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1 Background

Traditional teaching has been that the clinical manifestations of Haemophilia A (HA) and Haemophilia B (HB) are identical and cannot be differentiated without measurement of the specific FVIII and IX clotting factor activities . In haemophilia the clinical diagnosis has been largely determined by the differences in bleeding type associated with the level of coagulation factor VIII or IX activity. Recent studies confirmed the validity of the original haemophilia classification by Biggs and MacFarlane from 1958 , as well as, the standard classification by the Scientific and Standardization Committee of the International Society on Thrombosis and Homeostasis in 2001. However , it has been suggested that HA and HB may be different in terms of severity of the bleeding tendency. More recently a preliminary report found that patients with HA bled more often and used more factor concentrates than those with HB with comparable plasma factor levels.

The aim of this study was comparison of bleed frequency and factor concentrate use between HA and HB patients.

2 Methods

We examined the frequency of bleeds and the utilization of factor concentrate among the patients with any severity FVIII and FIX deficiency.
A retrospective electronic medical record review of all patients treated in a single Haemophilia Treatment Center was conducted. Adult patients (age≥11years), with no history of high titer inhibitors and treated exclusively on demand since diagnosis were considered to be eligible. Information was gathered from home infusion logs records by patients, and treatment records from our Haemophilia Treatment Center.

We gathered information from records of our Haemophilia Treatment Center over one year , from October 2010 to September 2011. All of our patients used on-demand treatment with plasma derived factor concentrates. Data were available on 176 Haemophilia A and 35 Haemophilia B severe(FVIII ,IX<1 IU dL^{-1}) and moderate(FVIII,IX 1-5 IU dL^{-1}) and mild (FVIII,IX ≥5 IU dL^{-1})deficient patients, HA patients were between ages 11-74 years (32.29±11.32) , and HB patients between 12-70(28.77±10.69).

3 Results

Among 176 HA patients, FVIII levels were between 0.14-15.50 IU/dL(Mean=4.18±3.92 SD).Factor IX levels were between 0.17-8.36 IU/dL (Mean=2.24 ±2.23 SD) in 27 HB patients. Factor VIII Inhibitor levels were between 0-1.60 BU (Mean=0.40±0.52 SD) , and FIX Inhibitor levels were between 0-0.65 BU (Mean 0.10±0.23 SD) in 27 HB patients. Overall, 2.84% of HA and 7.40% of HB patients had a low titer inhibitor rates.

Our 176 HA patients experience overall admission rates of 550 bleeds during 12 months , compared with 27 bleeds experienced by 35 HB patients .There was a statistically significant difference between HA and HB patients, as 3.125 bleed/patient/year for HA and , 0.77 bleed/patient/year for HB (P=0.031).The amount of factor concentrates used by our HA patient was 3731500IU of FVIII (21201.704 IU/patient/year), and 611000 IU of Factor IX , by patients with hemophilia B(17457.142 IU/patient/year).The difference in the usage of factor concentrate was not statistically significant (P=0.57).

4 Data

Type	Number	Age (year)	Bleed		Factor concentrates used	
			Per Year	P value	IU/Year	P value
Severe HA	62	31.50±8.79	320	0.04	3026000	**0.11**
Severe HB	16	25.18±8.00	13		481500	
Moderate HA	57	31.21±10.97	182	0.028	516500	**0.09**
Moderate HB	13	28.69±7.75	9		67000	
Mild HA	57	34.03±13.74	48	0.76	189000	**0.00**
Mild HB	**6**	**41.20±10.69**	**5**		**62500**	

5 Conclusion

Because of the high cost and limited availability of factor concentrates in our HTC, all of the patients in this study received on-demand treatment with factor concentrates, so it seems that determining of the number of bleeds is more realistic in our study.
Moreover, although the presence on inhibitors might introduce bias as they were in HA and HB, the presence of this complication generally discourages clinicians from performing elective orthopedic surgery. Thus, bias should play against our hypothesis that the type of coagulation defect affects the need for joint arthroplasty , and also for utilization of factor VIII and IX concentrates. The low inhibitor rate with low titer in our patients may be reduced the bias introducing in study.
Our findings may have potential clinical implications, because they add another piece of evidence to previous observations that HB patients less bleed than HA patients.
Furthermore, it is not known if the lack of Factor VIII, compared with Factor IX results in more bleeds, if the bleeds respond less well to treatment, or if the bleeds are more severe or more destructive. Can we decide that this would direct clinicians to plan less primary prophylaxis in HB?
Well-designed randomized controlled trials and prospective observational controlled studies are needed to establish the best results.

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