High Factor VIII Antigen Levels are not Associated with Factor VIII Gene Polymorphisms

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INTRODUCTION

High factor VIII coagulant activity levels are associated with an increased risk of thrombosis[1-3]. The mechanism that lead to high plasma F VIII levels are unclear. Based on the previously reported data on familial clustering of F VIII, it would be logical to hypothesize that genetic changes in the F VIII gene may be the cause of high F VIII levels[4,5]. However, a previous study by Mansvelt et al did not reveal an alteration at the F VIII gene as the cause of high F VIII: C[6]. Further, Kamphuisen et al studied two CA repeats in the F VIII gene, and could not find an association[7].

Previous studies on different disease states indicated that certain haplotypes may have effect on the phenotype of the disease. As the previous study was performed on two CA-dinucleotide repeat polymorphisms within intron 13 and intron 22; we aimed to study two other polymorphisms in male individuals with high F VIII levels.

MATERIALS and METHODS

We studied 67 male individuals. F VIII: C levels were measured using a one-stage clotting assay (Sigma, Germany). Cut off values for our laboratory is 74.06-149.94 IU/dL. Individuals with F VIII levels above 150 IU/dL were accepted as increased levels. DNA was extracted by conventional techniques. The two intronic polymorphisms (intron 25 C-T and intron 18 Bcl I) were amplified according to the previously reported methods using the primers 5'ccagaagattaatgggatcatgtg 3' and 5'gtctcaaatctggccaacaggaag 3' for int 25 C-T alteration and 5'atgtgttcactgtacga 3' and 5'aatatcttgggatggac 3' for int 18 Bcl I polymorphism[8,9]. The former was amplified with an anelling tempature of 63°C and restricted with Bgl I (Fermentas, Lithuania). It was 50°C and Bcl I (Fermentas, Lithuania) for the Int 18 Bcl polymorphism, respectively.

RESULTS

Distribution of the polymorphic alleles are given in Table 1 with respect to F VIII levels. Statistical analysis revealed a nonsignificant association between F VIII levels and studied polymorphisms.

Table 1. Distribution of F VIII gene polymorphisms

Polymorphisms	n	F VIII levels (U/dL)	Individuals with high F VIII	n (%)	
Intron 25 C	35	164.7 ± 15.6	17	48	p > 0.05
Intron 25 T	32	146.6 ± 9.1	13	40	
Intron 18 Bcl I -	16	159.0 ± 13.8	10	62	p > 0.05
Intron 18 Bcl I +	45	149.0 ± 8.4	19	42	
Int 25 T/Int 18 Bcl I -	11	150.9 ± 17.4	6	55	p > 0.05
Int 25 T/Int 18 Bcl I +	17	136.8 ± 31.3	5	30	
Int 25 C/Int 18 Bcl I -	5	176.9 ± 22.7	4	80	p > 0.05
Int 25 C/Int 18 Bcl I +	25	157.7 ± 13.3	12	48	

DISCUSSION

Although, there appears a consensus on the genetic basis of high F VIII levels; previous studies did not reveal a possible genetic mechanism neither in F VIII nor vWF gene as high vWF levels may be the main determinant of high F VIII levels[6,7,10]. Our study confirmed the previously reported data for the association of F VIII gene and high F VIII levels. However as some of the intraexonic polymorphisms may have effect on the course and/or expression of the disease, further analysis of intraexonic polymorphisms of the F VIII gene may reveal a role for the high F VIII levels.

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