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

Nejat AKAR, Türker DUMAN, Hafize GÖKÇE

Pediatric Molecular Pathology and Genetics Department of Ankara University, Ankara, TURKEY

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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:[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’aatatatcttgggatggac 3’ for int 18 Bcl I polymorphism[8,9]. The former was amplified with an annealing temperature of 63°C and restricted with Bgl I (Fermentas, Lithuania). It was 50°C and Bcl I (Fermentas, Lithuania) for the Int 18 Bcl I 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.

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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 intralexonic polymorphisms may have effect on the course and/or expression of the disease, further analysis of intralexonic polymorphisms of the F VIII gene may reveal a role for the high F VIII levels.

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REFERENCES


Address for Correspondence:

Nejat AKAR, MD
Konukent-2 Mudanya Sokak
C-1 Blok B Giriş Daire No: 2
06530, Çayyolu, Ankara, TURKEY
e-mail: nejatakar@hotmail.com

Table 1. Distribution of F VIII gene polymorphisms

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