LETTER TO THE EDITOR

Haptoglobin genotypic distribution (including Hp^0 allele) and associated serum haptoglobin concentrations in Koreans

K U Park, J Song, J Q Kim

Background: Haptoglobin polymorphism is associated with the prevalence of infections, autoimmune diseases, cardiovascular diseases, and other disorders. Congenital haptoglobin deficiency is associated with anaphylactic transfusion reactions in anhaptoglobinaemic patients with antihaptoglobin antibody.

Aims: To investigate haptoglobin genotypic distribution (including the Hp^0 allele) and associated serum haptoglobin concentrations in Koreans.

Methods: Five hundred and nine healthy Korean adults were randomly selected. Two methods were used: haptoglobin genotyping based on a polymerase chain reaction (PCR) system that exploited the structural difference of the Hp^1 and Hp^2 alleles, and another PCR method that detected haptoglobin gene deletion by amplification of the junctional region of the Hp^0 allele. Serum haptoglobin concentrations were measured by nephelometry.

Results: The haptoglobin genotypes of 509 subjects were as follows: Hp^1Hp^1, 7.1%; Hp^2Hp^1, 37.7%; Hp^2Hp^2, 49.3%; Hp^0Hp^1, 2.2%; Hp^0Hp^2, 3.5%; Hp^0Hp^0, 0.2%. The gene frequency of Hp^0 in Koreans was calculated to be 0.031. Significant differences were seen among the concentrations of each haptoglobin genotype (Kruskal-Wallis test). Hp^0Hp^2, but not Hp^0Hp^1, was associated with hypohaptoglobinaemia.

Conclusions: PCR methods for differentiating between haptoglobin genotypes, including the Hp^0 allele, may be useful in a broad spectrum of basic studies and clinical examinations.

Haptoglobin is genetically determined by two autosomal codominant alleles, Hp^1 and Hp^2. Recently, the Hp^0 allele, which is an allelic deletion in the haptoglobin gene cluster, has been identified. Because haptoglobin polymorphism has an effect on a broad range of diseases, a rapid and practical method for the distinction between haptoglobin variants is needed for large scale routine laboratory use. In our present study, we have adopted a haptoglobin genotyping method based on the polymerase chain reaction (PCR) and a simple method to detect haptoglobin deletion by PCR. Using these methods, we investigated haptoglobin genotypic distribution (including the Hp^0 allele) and associated serum haptoglobin concentrations in Koreans.

Because haptoglobin polymorphism has an effect on a broad range of diseases, a rapid and practical method for the distinction between haptoglobin variants is needed for large scale routine laboratory use

Abbreviations: Hp, haptoglobin; PCR, polymerase chain reaction
DISCUSSION

Using PCR analysis with primers A and B, the heterozygous genotype Hp²Hp¹ could not easily be detected because, in the presence of the 1757 bp band, it was not possible to determine conclusively whether the 3481 bp band was also present. With the Hp²Hp¹ genotype, the 1757 bp band was considerably more intense than the 3481 bp band (fig 2; lane 1 and 2). Such a problem can occur in cases in which the PCR is run under suboptimal conditions, with extensively degraded DNA, or with limited quantities of DNA. Therefore, PCR using primers C and D was also performed for the complete genotyping of the common haptoglobin polymorphism.

Haptoglobin genotype frequencies and their associated serum haptoglobin concentrations were similar to the haptoglobin phenotyping results in Koreans using sodium dodecyl sulfate–polyacrylamide gel electrophoresis. However, electrophoresis phenotyping could not discriminate between hypohaptoglobinemia and true anhaptoglobinemia. In our study, Hp²Hp², but not Hp⁰Hp¹, was shown to be associated with hypohaptoglobinemia. These results signify a gene–dosage effect, similar to that reported by Koda et al.¹

In conclusion, PCR methods for differentiating between haptoglobin genotypes, including the Hp⁰ allele, may be useful in a broad spectrum of basic studies and clinical examinations.

Table 1 Serum haptoglobin concentrations according to haptoglobin genotype (including the Hp⁰ allele) in Koreans

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Number</th>
<th>Mean (SD) (g/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hp¹Hp¹</td>
<td>26</td>
<td>1.216 (0.418)</td>
</tr>
<tr>
<td>Hp²Hp¹</td>
<td>168</td>
<td>1.189 (0.521)</td>
</tr>
<tr>
<td>Hp²Hp²</td>
<td>211</td>
<td>0.829 (0.509)</td>
</tr>
<tr>
<td>Hp²Hp⁰</td>
<td>8</td>
<td>0.426 (0.200)</td>
</tr>
<tr>
<td>Hp³Hp¹</td>
<td>16</td>
<td>0.178 (0.119)</td>
</tr>
<tr>
<td>Hp³Hp⁰</td>
<td>430</td>
<td>0.001</td>
</tr>
</tbody>
</table>

The p value was obtained using the Kruskal–Wallis test among the six haptoglobin genotypes.

REFERENCES


Accepted for publication 6 May 2004

Authors’ affiliations

K U Park, J Song, J O Kim, Department of Laboratory Medicine, Seoul National University College of Medicine, Seoul, 463–707 Korea

Correspondence to: Dr K U Park, Department of Laboratory Medicine, Seoul National University Bundang Hospital, 300 Gumi-dong, Bundang-gu, Seongnam-si, Gyeonggi-do, 463–707, Korea; m91w95@dreamwiz.com
Haptoglobin genotypic distribution (including Hp\(^0\) allele) and associated serum haptoglobin concentrations in Koreans
K U Park, J Song and J Q Kim

*J Clin Pathol* 2004 57: 1094-1095
doi: 10.1136/jcp.2004.017582