Haptoglobin genotypic distribution (including Hp⁰ 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 Hp⁰ 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 Hp¹ and Hp² alleles, and another PCR method that detected haptoglobin gene deletion by amplification of the junctional region of the Hp⁰ allele. Serum haptoglobin concentrations were measured by nephelometry.

Results: The haptoglobin genotypes of 509 subjects were as follows: Hp¹Hp¹, 7.1%; Hp²Hp¹, 37.7%; Hp²Hp², 49.3%; Hp⁰Hp¹, 2.2%; Hp⁰Hp², 3.5%; Hp⁰Hp⁰, 0.2%. The gene frequency of Hp⁰ in Koreans was calculated to be 0.031. Significant differences were seen among the concentrations of each haptoglobin genotype (Kruskal-Wallis test). Hp⁰Hp², but not Hp⁰Hp¹, was associated with hypohaptoglobinaemia.

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

Materials and Methods

Healthy Korean adults (509 subjects) were randomly selected. Primers A and B were used for amplification of the Hp¹ and Hp² specific sequences, respectively, and primers C and D were used to amplify the Hp² specific sequence. Primers Del-U and Del-L were used to amplify the Hp⁰ allele, and exon 1 of the haptoglobin gene was coamplified in the same tube, as an amplification control. The primers and the amplification protocols have been described previously. PCR products underwent electrophoresis in a 1.8% agarose gel. The serum haptoglobin concentration was measured by nephelometry.

Results

Figures 1–3 show representative electrophoresis patterns. The haptoglobin genotypes of 509 subjects were as follows: Hp¹Hp¹, 7.1%; Hp²Hp¹, 37.7%; Hp²Hp², 49.3%; Hp⁰Hp¹, 2.2%; Hp⁰Hp², 3.5%; Hp⁰Hp⁰, 0.2%. The gene frequency of Hp⁰ in Koreans was calculated to be 0.031, according to the Hardy-Weinberg law. Table 1 shows the serum haptoglobin concentrations. Significant differences were seen among the concentrations of each haptoglobin genotype. In addition, Hp⁰Hp², but not Hp⁰Hp¹, was shown to be associated with hypohaptoglobinaemia.

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

Using PCR analysis with primers A and B, the heterozygous genotype Hp1Hp2 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 Hp1Hp1 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, HplHp2, 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.

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.

Authors’ affiliations
K U Park, J Song, J Q 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

Accepted for publication 6 May 2004

REFERENCES

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>HplHp1</td>
<td>26</td>
<td>1.216 (0.418)</td>
</tr>
<tr>
<td>HplHp1</td>
<td>168</td>
<td>1.189 (0.521)</td>
</tr>
<tr>
<td>HplHp1</td>
<td>211</td>
<td>0.829 (0.509)</td>
</tr>
<tr>
<td>HplHp1</td>
<td>8</td>
<td>0.426 (0.200)</td>
</tr>
<tr>
<td>HplHp1</td>
<td>16</td>
<td>0.178 (0.119)</td>
</tr>
<tr>
<td>HplHp1</td>
<td>1</td>
<td>0.001</td>
</tr>
<tr>
<td>HplHp1</td>
<td>430</td>
<td></td>
</tr>
</tbody>
</table>

The p value was obtained using the Kruskal-Wallis test among the six haptoglobin genotypes.
Haptoglobin genotypic distribution (including Hp0 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

Updated information and services can be found at:
http://jcp.bmj.com/content/57/10/1094

These include:

**References**
This article cites 3 articles, 2 of which you can access for free at:
http://jcp.bmj.com/content/57/10/1094#BIBL

**Email alerting service**
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

**Notes**

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/