LETTER TO THE EDITOR

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.

Haptoglobin is genetically determined by two autosomal codominant alleles, Hp1 and Hp2. Recently, the Hp0 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 Hp0 allele) and associated serum haptoglobin concentrations in Koreans.

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Abbreviations: Hp, haptoglobin; PCR, polymerase chain reaction

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%; Hp1Hp2, 37.7%; Hp2Hp1, 49.3%; Hp2Hp2, 2.2%; Hp1Hp0, 3.5%; Hp2Hp0, 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.
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. Therefore, polymerase chain reaction (PCR) analysis using primers C and D was also performed for the complete genotyping. In a PCR with primers C and D, a 349 bp product was generated from genomic DNA of individuals homozygous or heterozygous for the Hp2 allele, whereas no product was formed in the presence of the Hp1 allele (lanes 3 and 4, DNA from the individual with the Hp1Hp3 genotype).

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, Hp0Hp2, 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.

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