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Distribution of Haptoglobin Phenotypes among Sudanese Leukemic patients

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Abstract:

This study aimed to investigate the correlation between haptoglobin (Hp) phenotypes and leukaemia among Sudanese.

Hp phenotypes were determined in 106 Sudanese patients with the four most common types of leukemia: acute myeloid leukemia (AML), chronic myeloid leukemia (CML), acute lymphoblastic leukemia (ALL) and chronic lymphocytic leukemia (CLL), and were compared to 106 normal controls.

We could not confirm the previously suggested increased incidence of the Hp1 gene and the Hp1-1 phenotype among leukemic patients. A higher frequency of haptoglobin 2-1 was observed among both patients and the control group.

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Key words: Haptoglobin phenotypes, Leukemia, Sudanese patients.

Introduction

Haptoglobin (Hp) is a α_2–sialoglycoprotein with hemoglobin (Hb) binding capacity [(1)]. The best–known biological function of Hp is capture of Hb to prevent both iron loss and kidney damage during hemolysis [(2)].

Hp is also a positive acute–phase protein and is characterized by a molecular heterogeneity with three major phenotypes: Hp 1-1 Hp 2-2 and the heterozygous Hp 2-1, which are the expression of two alleles (*HP1* and *HP2*) on chromosome 16q22.1 . Several researches have evaluated the correlation between HP types in different diseases and cancers, such as leukemia, rheumatoid arthritis, cardiovascular diseases, malaria, diabetes, inflammation, and nephritic syndrome [(3,4,5, 6)]. The significance of this polymorphism in leukemia has also been investigated, with controversial results, suggesting an association of the *HP1* gene and the Hp1-1 phenotype with acute myeloid leukaemia (AML), chronic myeloid leukaemia (CML), chronic lymphoid leukaemia (CLL) and acute lymphoid leukaemia (ALL) [(7,8, 9)].

In order to contribute to this matter, we investigated the correlation between Hp phenotypes and leukaemia among Sudanese patients.

Materials and methods

Serum samples were obtained from 106 adult leukemia patients, 39 with AML, 22 with CML, 29 with ALL, and 15 with CLL. Diagnosis and classification were based on the morphologic characteristics of the peripheral blood and bone marrow cells, associated with leukocyte cytochemistry. The control group (CG) was composed of 106 healthy blood donors

from the same geographical region. Data of this study was analyzed using statistical package for social sciences (SPSS). Chi^2- test was used to examine the correlation between the distribution of Hp phenotypes and different types of leukaemia.

Results

Figure (1) showed the patterns of haptoglobin phenotypes on polyacrylamide gel. In Hp1-1 phenotype, only one thick band was seen somewhere closer and cathodic to the free hemoglobin band. In Hp2-2 phenotype, apart from the free hemoglobin band, there were multiple cathodic bands which were fine and closer to one another; as shown, the fastest moving band among the multiple bands appeared fainter than its preceding band.

In Hp2-1 phenotype, there was a band close to the free hemoglobin band, which corresponded to the Hp band in Hp1-1 type and multiple fine bands that were more cathodic as in Hp2-2, but with greater distance between them. The last band in this series was not fainter than the preceding band as observed in the Hp2-2 phenotype.

Frequencies of haptoglobin phenotypes

Of the 106 leukaemic patients, 40(37.6%) had AML, 22(21.7%) had CML, 29(27.3%) had ALL, and 15(14.1%) had CLL.

The distributions of Hp phenotypes in leukaemic patients were 23.5% for Hp 1-1, 47.2% for Hp 2-1, 26.3% for Hp 2-2 and 2.7% for Hp0.

In AML patients, the phenotype 2-1 was the most frequent (45%), followed by the phenotype Hp1-1 (27.5%), Hp2-2 (25%), and Hp0 (2.5%).

Also in acute lymphoid leukemia the phenotype Hp2-1 also was the most frequent (59%), followed by the phenotype Hp2-2(24%), Hp1-1 (14%), and Hp0 (3%)

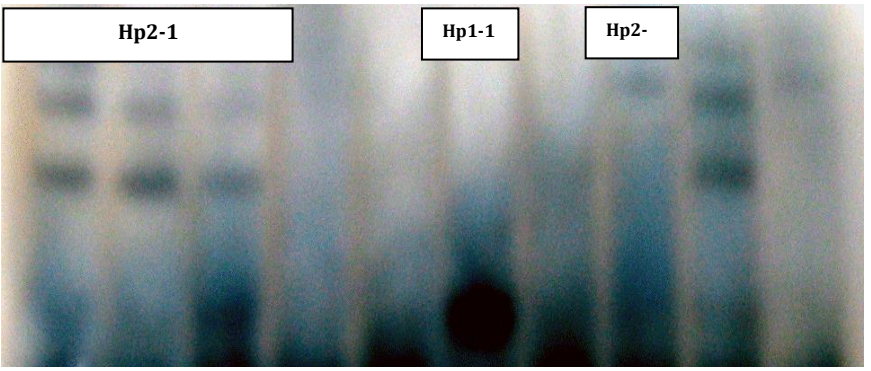
The phenotypic distribution in CML was Hp1-1(36%), Hp 2-1(50%), and Hp 2-2(14%); the phenotype Hp0 was absent.

In chronic lymphoid leukemia the frequency of the phenotype Hp1-1 was (13%), Hp 2-1 (27%),Hp2-2(53%) and Hp0 (7%).

Haptoglobin phenotypes frequencies in healthy controls

In healthy controls Hp1-1 frequency was 31.4%, Hp2-1 (49%), and Hp 2-2 20(19.6%); the phenotype Hp0 was absent.

Figure (1): patterns of haptoglobin phenotypes on polyacrylamid gel



Discussion

Haptoglobin, beside the hemoglobin binding function, is an acute-phase reactant protein; its antioxidant and immunomodulatory properties have been extensively investigated [11,12, 13,14].

Recently has been demonstrated that different Hp phenotypes showed distinct antioxidant activities and that Hp 2-2 phenotype is a less effective protector than Hp1-1[1, 14]. The latter corresponds to a small and dimeric protein, while 2-1 is a linear polymer with intermediate dimension and 2-2 is a large

cyclic polymer. These characteristics are important determinants of the biological activities of each Hp subtype [14]. In diabetes, for instance, HP has been focused as one major genetic factor involved in the susceptibility to coronary artery diseases [15]. In cancer, this correlation is not so clear. Awadallah and Atoum, investigated patients with breast cancer, found that the family history plays a relevant role in determining the degree of association between the disease and Hp polymorphism [16].

Hp polymorphism appears to be related to immune response and to autoimmune and inflammatory disorders. On other hand the inhibitory effects of Hp 2-2 and Hp 2-1 on prostaglandin synthesis are less pronounced than that of Hp 1-1 [17]. Angiogenesis function for Hp plays an important role in a variety of physiological and pathological conditions, including tumor growth, wound healing, and chronic inflammatory diseases. The Hp2-2 phenotype is overrepresented in autoimmune diseases and Hp2-2 subjects are characterized by a higher immune reactivity. The concentration of Hp in serum decreases after intravascular hemolysis, whether whether in infectious (e.g., malaria) there a results suggest that the haptoglobin phenotype (1-1) is associated with susceptibility to falciparum malaria and the development of severe complications; alternatively, the other phenotypes may confer resistance [23].

In this study the haptoglobin phenotypes were determined and Hp2-1 was the most frequent in healthy controls and all leukaemia subtypes. This finding agrees with Frohlander who confirmed that, there was no an association between Hp 1-1 and leukemia patients [17]. Also this study agrees with study in Sudan to determine Hp phenotypes in cancer patients and reported that, the most common phenotype of haptoglobin among healthy control Sudanese was Hp2-1 [9].
This study disagrees with Peacock who was confirmed an association between Hp1-1 and leukemia [7].

The previously reported high incidence of the Hp1 gene and the Hp1-1 phenotype among patients with AML, CML, and ALL [7, 16, 17] could not be confirmed in this study, since no significant differences were found in the comparisons. On the contrary, here the patients with CLL showed the highest incidence of the Hp2 gene.

The HP0 phenotype may be primarily due either to deletions that remove the Hp genes or to point mutations that inactivate them [22, 23]. These data must be carefully evaluated. However, patients with leukemia often have associated conditions that can reduce the plasmatic Hp levels, such as hemolysis or hepatic disease [8].

Conclusion

The haptoglobin phenotype "Hp2-1" is the most frequent among leukaemic Sudanese patients and healthy controls.

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