CONTRIBUTION OF RED CELL MASS AND UGT1A1 ALLELES IN SERUM BILIRUBIN LEVELS OF THE PORTUGUESE POPULATION

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Hepatic glucuronization of insoluble bilirubin is catalyzed by isoenzyme 1A1 of UDP-glucuronosyltransferase (UGT1A1), which is essential for efficient biliary excretion of bilirubin. Genetic polymorphisms that include a TA duplication [(TA)7 allele] in the repetitive TATA-box sequence of the UGT1A1 promoter, which normally consists of six TA repeats, is the main cause of Gilbert syndrome (GS). However, this genetic polymorphism is not sufficient for the clinical phenotype of GS. By this reason, some studies have been performed to provide information about additional factors that could contribute to the pathogenesis of this disease. Recently, it was described that increased red cell mass probably plays a role in the pathogenesis of GS. In order to compare which factors contribute for the hiperbilirubinemia that characterize patients with GS, we first determine the effect of some of these factors in the normal Portuguese population.

This work is focus in the establishement the putative role of increased red cell mass and the (TA)7 allele in bilirubin serum levels, in the healthy Portuguese population. This study was performed in 109 volunteer healthy young adults (20.3 ± 1.9 years) without liver and/or haematological disorders, chronic infection, recent inflammation, malignancy, haemorrhage and medication. Blood samples were collected and processed in order to determine bilirubin serum levels, complete blood cells count, and DNA extraction. The TATA-box region was analyzed by PCR amplification followed by subsequent analysis by automated capillary electrophoresis.

Among our population, 6 were homozygous for the (TA)7 allele, 55 were heterozygous and 48 were homozygous for the normal allele. One of the subjects was a compound heterozygous for the (TA)5 and (TA)7 alleles. Comparing the blood cells counts and the bilirubin serum levels according to the UGT1A1 genotype, we found statistically differences only in bilirubin levels [(TA)6/(TA)6: 0.49 ± 0.20 mg/dL; (TA)6/(TA)7: 0.70 ± 0.32 mg/dL; (TA)7/(TA)7: 1.10 ± 0.74 mg/dL, p<0.05]. A positive statistically significant correlation (p<0.05) was found between bilirubin serum levels and haematocrit and mean cell volume.

In our population, this work showed that higher bilirubin serum levels are correlated with an increase of red blood mass and also with the presence of abnormal number of TA repeats in the UGT1A1 gene. Moreover, increased values of haematocrit and cell volume average may also contribute for this phenotype. Based on these results, further studies involving a larger group of GS patients, homozygous for the (TA)7 allele, will be performed to clarify how red blood mass can contribute to the hiperbilirubinemia.