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

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Abstract Hepatic glucuronization of insoluble bilirubin is catalyzed by isoenzyme 1A1 of UDP-glucuronosyltransferase (UGT1A1), which is essential for efficient biliary excretion of bilirubin. The main cause of Gilbert syndrome (GS) in all populations studied to date is a TA duplication [(TA)7 allele] in the repetitive TATA-box sequence of the gene promoter, which normally consists of six TA repeats. 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 (Buyukasik et al. 2008 Am J Med Sci. 335,115-119). The aim of this work is to investigate the putative role of increased red cell mass and the (TA)7 allele in bilirubin serum levels, in the Portuguese population. This study was performed in 109 volunteer healthy young adults (20.3±1.9 years) without liver and/or hematological disorders, chronic infection, recent inflammation, malignancy, hemorrhage 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 ($p<0.05$) were found between bilirubin serum levels and haematocrit and mean cell volume. Our work showed that higher bilirubin serum levels are correlated with an increase red blood mass. However, no association was found between higher red blood mass and abnormal number of TA repeats in the promoter of UGT1A1 gene. This data suggests that in our population the presence of abnormal number of TA repeats in the UGT1A1 gene is associated with increased bilirubin levels but not with higher red blood mass, as previously described for GS patients.