

RISK ASSESSMENT OF FAT-SOLUBLE VITAMINS BASED ON GENETIC SCORE PREDICTIVE MODEL

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Abstract

Vitamins are vital to sustain normal physiological function, metabolism, and growth for all living organisms. Being an integral component of coenzyme, vitamins can affect the catalytic activities of many enzymes and the expression of drug transporters. Genetic variations in metabolism and/or transporter genes of drugs can influence the exposure of the human body to drugs and/or their active metabolites, thus contributing to the variations in drug responses and toxicities. The aim of this study was to prepare genetic score predictive model for risk assessment of fat-soluble vitamins and to analyse the distribution of predicted genetic score in population of 120 individuals with Slovak ancestry.

Four separate panels of genetic markers were selected for analysis. Twenty single nucleotides polymorphisms (SNPs) have been used for risk assessment of fat-soluble vitamins. Genetic score based predictive model has been used separately for every panel of SNPs. An unweighted "genetic score" based on contribution to 4 (vitamin A, D and K risk assessment) and 8 (vitamin E risk assessment) variants respectively was created. A score of '0' represented homozygote for the low-response variant; '1' represented heterozygous and '2' or '3' represented homozygous for the high-response allele. Sum of genetic score calculated for each haplotype has been enriched by probability to observe specific haplotype in European (Caucasian) population. The overall population risk has been visualized as a histogram of given genetic score based on frequencies of all possible haplotypes in the European population. The calculated rate of genetic score has been confronted to histogram of genetic score distribution of 100 individuals genotyped through Illumina chip HumanOmniExpress-24 (23andMe v3, v4, v5) and 20 genotypes of sport talented children derived from the project NU3Gen. To enrich maximal potential of used genetic chip, some of SNP markers has been imputed.

The distribution of the genetic score in individuals with Slovak origin correlates with the predicted values of the European population. However, a significant deviation from the predicted values due to a different frequency of alleles of one or more of the genes studied can be observed in the distribution of the vitamin K genetic score. In other cases (Vitamin A, D and E), it was not possible to record the difference between the predicted European Population Genetic Score and the actual distribution of the genetic score in the random individuals of Slovaks origin.

The study results indicated that the individuals with high genetic score (sport talented) showed increased genetic pressure to higher intake of fat-soluble vitamins.

Key words: Vitamines, Metabolism, HumanOmniExpress, Caucasian.