CONGRESUL CONSACRAT ANIVERSĂRII A 75-A DE LA FONDAREA USMF „NICOLAE TESTEMIȚANU"
20 23 octombrie 2020

GENETIC VARIATION OF THE SCN10A GENE IN YOUNG POPULATION OF REPUBLIC OF MOLDOVA

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Introduction

The electrocardiogram (ECG) is a valuable clinical tool for assessing the function of the cardiac conduction system. The electrocardiographic PR interval represents conduction through the atria and atrioventricular (AV) node to the Purkinje fibers. Delayed conduction in the above parts of the cardiac conduction system, results in prolongation of this ECG parameter. Prolongation of the PR interval leads to increased risk of atrial fibrillation, heart block, and mortality. The duration of the PR interval has an important heritable component, with heritability estimates ranging up to 50% in populations of European and Asian ancestry . Genome-Wide Association studies (GWAS) have identified a common loci associated with PR interval duration. The strongest association was observed between nonsynonymous single nucleotide polymorphism, rs6795970 (G > A), in the *SCN10A* gene and the PR interval . The SCN10A gene is mapped to chromosome 3p22.2 and encodes the alpha subunit, type X, of a voltage-gated sodium channel. The SCN10A gene is expressed in the dorsal root ganglion (DRG), nociceptive nerve fibers, retina, in the myocardium and preferentially in the Purkinje fibers of the cardiac conduction system. The allele A of the *SCN10A* gene polymorphism (rs6795970) was associated with increased risk of first-degree heart block, bundle-branch block, bifascicular heart block, idiopathic sick sinus syndrome [1-5].

Keywords
SNP, PR interval, genotype, GWAS

Purpose

. Determine distribution of the genetic variants of rs6795970, associated with PR interval in young population of Republic of Moldova.

Material and methods

1390 students from *Nicolae Testemitsanu* State University of Medicine and Pharmacy, aged between 19-25 years, enrolled in our cross-sectional study. Written informed consent was obtained from all the participants. Personal identifiers associated with medical information and blood samples were encrypted with a special codification and then analyzed. The study was approved by the *Nicolae Testemitsanu* SUMPh Research Ethics Committee.

Genomic DNA was isolated from buffy coat using silica-based membrane technology in the form of a spin column Gene JET Genomic DNA Purification Kit (Thermo Scientific, USA) according to the manufacturer's protocol. Genotype analysis of all 1390 participants to detect rs6795970 (G > A) in the *SCN10A* gene was performed with commercially available TaqMan assay kit (Assay ID: C__29261054_10) on a QuantStudio 6 Flex instrument (Thermo Fisher Scientific). The differences of genotype frequencies of the rs6795970 have been analyzed by the chi-square Test ($\chi 2$), also used to test deviations of genotype distribution from the Hardy-Weinberg equilibrium.

Results

Out of 1390 samples, the genotyping successful call rate was 99.7%. The validity of the genotyping results is in concordance with the allele frequency distribution predicted by Hardy-Weinberg equilibrium for rs6795970 ($\chi 2 = 0.161$, $p = 0.688$). The distribution of genotypes and allele frequencies of the rs6795970 in the sample tested is shown in table 1.

Table1

The genotypes and alleles distribution of the rs6795970 *SCN10A* polymorphism

	Young population of Republic of Moldova		European
	(n=1390)	%	%
Genotype frequency			
G/G	515	37%	35%
G/A	668	48%	48%
A/A	207	15%	17%
Allele frequency			
G allele	848	0.61	0.59
A allele	542	0.39	0.41

In our study, the minor allele frequency (MAF) was 0.39 for rs679570, consistent with 1000 Genomes data in the European population – 0.41. Furthermore, we performed the comparative analysis of the obtained frequencies with those established in other studies on populations (Figure1).

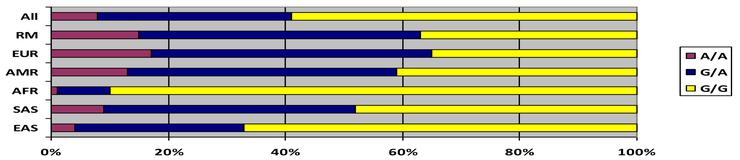

Fig. 1. Genotype frequency of the *SCN10A* polymorphism rs6795970

Notes:
ALL – All (phase 3 individuals, 1000 Genomes Project); RM - Population in Republic of Moldova; EUR – European; AMR- American; AFR – African; SAS – South Asian; EAS – East Asian (1000 Genomes Project).

Conclusions

In this study, we determined that distribution of the genetic variants of rs6795970, associated with PR interval in young population of Republic of Moldova was consistent with 1000 Genomes data in the European population.

Thus, our data demonstrate that at least 15% of all participants (the AA genotype), may have an increased risk of conduction abnormalities.

References

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