

UNDIFFERENTIATED CONNECTIVE TISSUE DYSPLASIA: STRATIFICATION OF RISK FACTORS FOR ITS DEVELOPMENT

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Phenotypic features of undifferentiated connective tissue dysplasia are largely associated with the leading clinical syndrome affecting one or another system of the body. The greatest concern in young people is caused by cardiac arrhythmias, recognized as the leading mechanism for the development of sudden cardiac death.

The aim of the study was to conduct a genetic analysis of blood in individuals with undifferentiated connective tissue dysplasia for the stratification of risk factors for the development of arrhythmia.

Materials and methods of research: We studied the associations of the polymorphic marker Lys198Asn of the EDN1 gene and the A/G polymorphism in the MMP9 gene with the risk of developing arrhythmias against the background of UCTD. The distribution of genotypes was studied in 92 patients with external phenotypic signs of connective tissue dysplasia, among whom 75 patients had various types of arrhythmias. The distribution of genotypes was also studied in 90 individuals with no signs of UCTD and a minimal (no more than 3) number of dysembryogenesis stigmas, who formed the control group.

Results of the study: The distribution frequency of alleles and genotypes of the Lys 197 Asn polymorphism in the EDN 1 gene in the patient and control groups can. The study revealed that the distribution of allele and genotype frequencies for the Lys 197 Asn polymorphism in the EDN 1 gene in a sample of people from the Uzbek population who formed the control group did not differ significantly from world literature data [1, 6] and amounted to the frequency of the Lys / Lys genotype in 70.0% of cases, the Lys/Asn genotype in 27.78% of cases, and the lowest percentage of the mutant Asn/Asn genotype - in 2.22% of cases. As a result of the expression of mutant alleles of MMP-9, massive apoptosis and accelerated cleavage of connective tissue elements from the basement membrane of cells occur, which leads to a rapid decrease in its strength characteristics and the development of clinical manifestations within the framework of undifferentiated connective tissue dysplasia. Allele was confirmed Asn in the implementation of UCTD, as well as in the development of arrhythmia against the background of this disease (Table 2). Despite the absence of a statistical difference in the frequency of the mutant allele Asn between the control group and patients with manifestations of UCTD+arrhythmia (16.1% and 24.7%, respectively; $p=0.1$), the frequency of the Asn/Asn genotype was predominant in the group of patients with arrhythmias and undifferentiated dysplasia (9.3% versus 2.2% in the control; $\chi^2 = 4.0$, $p=0.05$, $RR=4.2$, $95\% \text{ CI}=1.95-9.06$, $OR=4.5$, $95\% \text{ CI}=1.03-19.86$).

In connection with the above, we conducted a search for molecular genetic predictors of the A/G polymorphism in the MMP9 gene, which may be associated with the development of undifferentiated connective tissue dysplasia and the

development of various types of arrhythmias against its background. The contribution of the A/G polymorphism of the MMP9 gene to the development of arrhythmias against the background of dysplasia was determined (Table 5), which was expressed in a statistically higher prevalence of the mutant genotype A/A in patients with UCTD and manifestations of arrhythmia 22.7% compared to the control group 8.9% ($\chi^2 = 6.0$ $p = 0.03$, RR = 2.6, 95% CI = 1.33-4.9, OR = 3.0, 95% CI = 1.25-7.22) and the mutant allele A - 40.0% compared to 25.0% in the control group ($\chi^2 = 8.5$ $p = 0.01$, RR = 1.3, 95% CI = 0.77-2.02, OR = 2.0, 95% CI = 1.25-3.19).

Conclusions: Thus, we have established that polymorphic markers of EDN1 genes play an important role in the formation of undifferentiated connective tissue dysplasia, while an association of the mutant allele was revealed Asn and the Asn/Asn genotype with the development of this pathology. Polymorphic markers of the MMP9 gene play an important role in the formation of arrhythmias against the background of undifferentiated connective tissue dysplasia, while associations of the mutant allele A and the genotype A/A with the development of this pathology have been identified.

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