Genetically determined drug resistance to commonly used AES in children in the Kazakh population.

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Introduction:

Drug resistance in epilepsy is still a serious problem in pharmacotherapy. Pharmacogenetic data is one of the most important elements that can help doctors determine the response to medications and provide more effective drug therapy, especially in cases of drug resistance. Sodium channel blocking antiepileptic drugs (SCB-AED) are common effective medications available for epilepsy.

Sodium channels are a target for a number of antiepileptic drugs, and the genes encoding these channels may play a crucial role in the development of drug-resistant epilepsy.

Objectives:

The aim of the study was to determine polymorphisms in genes associated with pharmacokinetic and pharmacodynamic features of AEP for drug resistance in children with epilepsy.

Methods:

from 2021 to 2023, data from 700 children under the age of 5 were analyzed. 300 did not have epileptic paroxysms and 400 had EEG-confirmed epilepsy. anamnesis of diseases, clinical, electroencephalographic, and radiological data were collected for each child, as well as genetic analysis using the GWAS method to determine polymorphisms in genes associated with pharmacokinetic and pharmacodynamic features of commonly used AES in children with epilepsy and to determine possible resistance to therapy.

Results:

The GWAS method identified 10 polymorphisms in the genes ABCB1, SCN1A, UGT1A1 associated with resistance to AEP, of which 5 were responsible for the resistance of sodium channel blockers: rs2032582 (ABCB1), rs2298771 (SCN1A), rs3812718 (SCN1A), rs28365063 (UGT2B7), rs7668258 (UGT2B7). It was revealed that the heterozygous genotype prevailed in children of the Kazakh population and resistance to therapy could depend on the type of polymorphism.

Patients with polymorphism in the ABCB1 rs2032582 gene, there is no correlation between the phenotype and resistance to carbamazepine and therefore standard dosages of sodium blockers can be used..

Patients with polymorphism in the SCN1A rs2298771 gene, the TT allele also lacks a correlation between the phenotype and resistance to carbamazepine, and changes in the dosage regimen of sodium blockers will not be required.

Patients with polymorphism in the SCN1A rs3812718 gene, higher doses of carbamazepine may be required (the degree of evidence is average).

Patients with polymorphism in the UGT2B7 gene rs28365063 may have increased clearance of carbamazepine.

Patients with polymorphism in the rs7668258 UGT2B gene require high doses of lamotrigine.

Conclusion:

The results showed that gene polymorphisms may play a role in the treatment of epilepsy.

Thus, we found that higher doses of sodium channel blockers may be required in the Kazakh population with polymorphism in the SCN1A rs3812718 gene and UGT2B rs7668258 gene, whereas polymorphism in the ABCB1 rs2032582 and SCN1A rs2298771 genes does not affect AEP resistance in the Kazakh population, and in other populations may be of great importance for the development of resistance In particular, in European and South Asian ethnic groups, which should be taken into account when selecting dosages, interaction schemes of various drugs used to treat different ethnic groups.

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