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Cytochrome CYP2D6, CYP2C19, CYP1A2 and p-glycoprotein MDR (C3435T) genetic polymorphisms frequency in patients with pharmacoresistance to antidepressants and antipsychotics: Real clinical practice

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Treatment resistance to antipsychotics and antidepressants (TR to AP/AD) is one of the most important issues in psychopharmacotherapy. TR to AP/AD is identified in 20-60% of patients [1]. In many cases, it is the result of genetic polymorphisms cytochromes involved in drug metabolism (CYP2D6, CYP2C19, CYP1A2) and/or drug transport (p-glycoprotein (MDR)) [2]. Pharmacogenetic testing of these genetic polymorphisms allows personalized treatment selection patients and can help to overcome treatment resistance in each individual case. The research goal was to investigate the prevalence of cytochrome CYP2D6, CYP2C19, CYP1A2 and p-glycoprotein MDR (C3435T) polymorphisms in patients with PR to AP/AD and compare the results with the data available in the literature on a healthy population of the European part of Russia.

Materials and methods: Pharmacogenetic testing was performed in 19 patients with identified PR to AP/AD diagnosed with: 1) schizophrenia, 2) major depressive disorder, 3) schizoaffective disorder. The PR criteria included at least 2 courses of therapy; treatment duration of at least 6 weeks in appropriate doses; inadequate treatment effect/no effect or the development of adverse reactions that prevented further therapy. Pharmacogenetic testing was performed in the MedLab medical laboratory. Cytochrome CYP2D6 gene polymorphisms (*1, *3, *4, *5), CYP1A2 (*A, *F, *C), CYP2C19 (*1, *2, *3, *17), and MDR1 p-glycoprotein gene (C3435T) were identified in each patient. The results obtained were compared with the published results of a healthy population of the European part of Russia [3, 4, 5] using the χ 2 criterion in the VassarStats program.

Results: The study involved 64 men and 55 women with PR to AP/AD aged 18 to 70 years, a mean age was 33 years, median was 32 years. Compared to the healthy population of the European part of Russia, patients with PR to AP/AD have been found to have:

1. A decrease in prevalence of extensive metabolizer genotypes of CYP2D6 (*1/*1) ($p = 0.006$) by 1.2 times and CYP2C19 ($p < 0.001$) by 2,4 times, and of ultra-rapid metabolizer genotype of CYP1A2 (*1F/*1F) ($p<0.001$) by 8 times;

2. A decrease in prevalence of CYP2D6 wild-type allele (*1) by 1.4 times ($p <0.001$) and the CYP1A2 mutant allele (*F) by 1.9 times ($p <0.0001$);

3. An increase in prevalence of extensive metabolizer genotype of cytochrome CYP1A2 (*1A/*1A) by 2.4 times ($p <0.001$) and the wild-type allele (*A) by 1.6 times ($p <0.0001$).

Conclusions: The identified differences in cytochrome enzyme genotypes allows to suggest that drugs-substrates of CYP1A2 might be preferable in patients with PR to AP/AD to adjust therapy and overcome the TR.

Biography

Zhiganova T.A. and Arslanova P.R. are esteemed researchers from the Department of Pharmacology and Pharmacy at North-Western State Medical University named after I.I. Mechnikov in Saint Petersburg, Russia. They are recognized for their contributions to pharmacology, with a focus on advancing pharmaceutical practices and research within the Russian medical community. Based at the university's main campus on Piskarevsky Avenue, they actively engage in research, education, and the development of innovative pharmacological solutions to address contemporary health challenges. Their work reflects a commitment to improving healthcare and pharmaceutical knowledge in Russia and beyond.