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ANALYSING CYP2D6*4 ALLELE FREQUENCY IN PATIENTS WITH SCHIZOPHRENIA

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Cytochrome P450 enzyme superfamily is involved in the metabolism of a range of endogenous and exogenous substrates. The CYP2D6 variant is involved in the metabolism of dozens of drugs such as tricyclic antidepressants, antipsychotics, beta-blockers, anti-arrhythmics, anti-diabetics, anticancer drugs and so on. CYP2D6 enzyme exhibits high polymorphism and the most frequent variant allele CYP2D6*4 is a poor metabolizer (PM). PM causes the reduction of therapeutic response, increase the risk of adverse drug reactions and increase the plasma concentration of both drug and its metabolites above the levels of toxicity. The aim of this study was to analyze CYP2D6*4 allele frequency among schizophrenic patients for further individualisation and rationalisation of therapy. For that purpose we recruited 38 schizophrenic patients and 110 healthy individuals. Allele-specific PCR was used to detect of CYP2D6*4 allele. In 55% of schizophrenic patients we found both wild type allele carriers, in 45% wild type/*4 heterozygous, while *4/*4 homozygous was not identified. A statistically significant difference in the genotype distribution ($p < 0.05$) between schizophrenic patients and healthy individuals was noted. The frequency of allele *4 (37%) is significantly higher in schizophrenics compared to controls, which indicates caution in administration of CYP2D6 substrates. A lower frequency of PMs in schizophrenic patients than in healthy individuals could be explained with CYP2D6 neuroactive substrate metabolism. However, 45% of the schizophrenic patients, who are intermediate metabolizers, carry the higher risk of adverse response to CYP2D6 substrates comparing to wild type. Since none of the analyzed patient was PM, it can be concluded that they received an adequate dose of medication.

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