P-954 - DOES C3435T GENETIC POLYMORPHISM OF MDR1 GENE INFLUENCE THERAPEUTIC EFFECTIVENESS OF PAROXETINE? (PRELIMINARY RESULTS)

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Clinical efficacy of antidepressants is unsatisfactory, full remission occurs in one-third of the patients after monotherapy with antidepressant. Personalized medicine is promising aspect of modern medicine.
P-glycoprotein (P-gp) encoded by the multidrug resistance 1 (MDR1) gene, acts as a cellular efflux pump. It is expressed in blood-brain barrier. In depressed patients prescribed with paroxetine, which is substrate of P-gp, the higher activation of P-gp would result in a lower level of paroxetine in brain and, thus, in resistance to clinical response.
C3435T polymorphism has been found to be associated with altered expression of P-gp, the results are contradictory.
We identified the C3435T polymorphism of MDR1 gene in 33 patients with major depression, panic disorder and mixed anxiety and depression disorder, who were treated with paroxetine in monotherapy. PCR-restriction fragment length polymorphism was used for genotyping. Therapeutic response was evaluated at baseline and after 6 weeks of therapy using the Hamilton Rating Scale for Depression and Anxiety (HAM-D, HAMA).
Comparison of allele frequencies between responders and non-responders showed no significant difference (CC vs CT: p=0.673; CC vs TT: p=1.000; C vs T: p=0.805; Fisher exact test or χ^2-test). We also evaluated a quantitative changes in HAM-D and HAMA score in relation to particular genotypes. No significant difference was found (p=0.622; Kruskall-Wallis test).
According to our preliminary results, MDR1 polymorphism C3435T is not associated with therapeutic response to paroxetine in Slovak population. Further studies are needed to elucidate the implication of other polymorphisms of MDR1 gene.

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