Effects of the CYP3A4 genetic polymorphisms on the efficacy and safety of diazepam in patients with alcohol withdrawal syndrome

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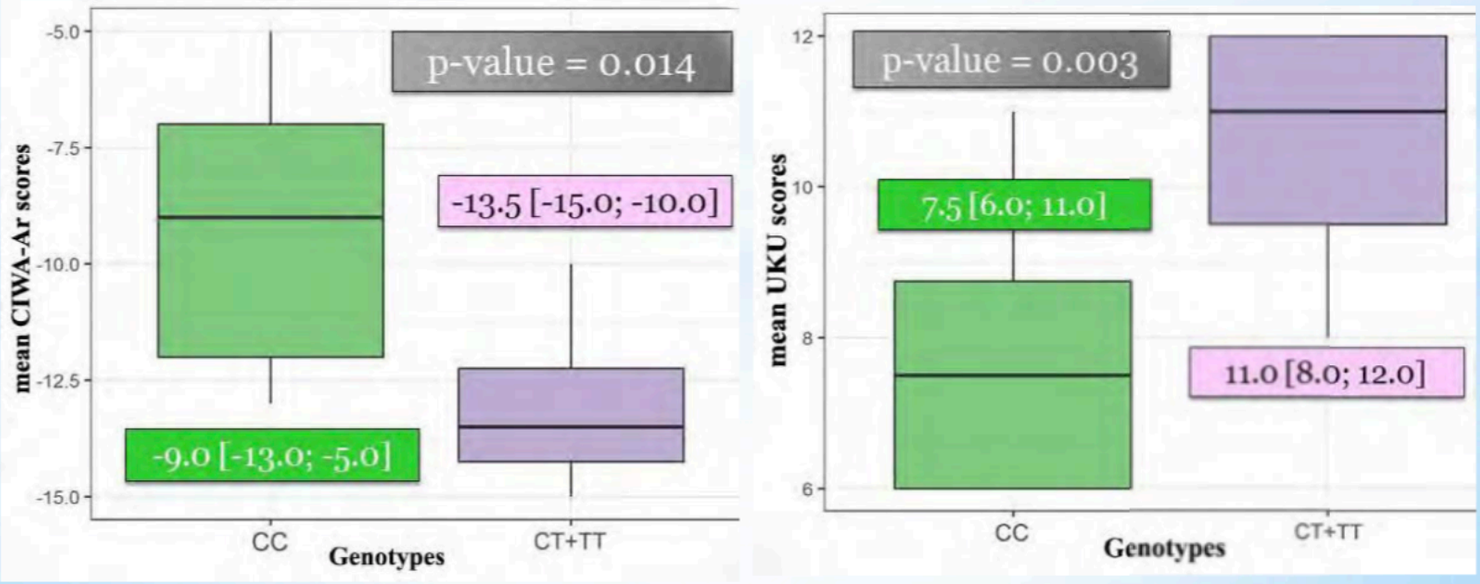
Background. Diazepam therapy is often ineffective and some patients suffer from dose-dependent adverse drug reactions, reducing the efficacy of the therapy of alcohol withdrawal syndrome. The presence of some polymorphic markers of CYP3A4 decreases the amount of isoenzyme to be expressed or reduces its activity resulting in the changes in biotransformation and elimination rates of the medication.

Objective. To investigate the effects of CYP3A4 genetic polymorphisms on the efficacy and safety of diazepam in patients with study involved 50 male patients (average age: 35.52 ± 9.84 years) with alcohol withdrawal syndrome. A series of psychometric scales were used in the research. Genotyping of C>T intron 6 of CYP3A4*22 (rs35599367) was performed using the real-time polymerase chain reaction.

Results. According to results of U-test Mann-Whitney, statistically significant differences between the efficacy and safety of diazepam were obtained on the 1st and 6th days of therapy in patients with CC and CT+TT genotypes (Differences in mean CIWA-Ar scores: -9 [-13.0; -5.0] for CC genotype carriers vs -13.5 [-15.0; -10.0] (P<0.001) for CT and TT genotype carriers; differences in mean Udvald for Kliniske Undersogelser Side Effect Rating Scale scores: 7.5 [6.0; 11.0] (P<0.001) for CC genotype carriers vs 11 [8.0; 12.0] for CT and TT genotype carriers.

Discussion. This study demonstrated the higher efficacy and lower safety of diazepam in patients with alcohol withdrawal syndrome carrying the CT and TT genotypes of CYP3A4*22 intron 6 C>T polymorphism (rs35599367).



Conflict of interest. The authors declare that there is no conflict of interest.