

EFFECTS OF CYP2D6 GENETIC POLYMORPHISMS ON THE EFFICACY AND SAFETY OF FLUVOXAMINE IN PATIENTS WITH DEPRESSIVE DISORDER AND COMORBID ALCOHOL USE DISORDER

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Background: Alcohol addiction is often comorbid with the affective disorders, in particular - with the depressive disorder, worsening the prognosis of both diseases and their outcome. Selective serotonin reuptake inhibitors (SSRIs) are a widely used type of antidepressant medication and fluvoxamine is a typical representative of this group. Fluvoxamine therapy is often ineffective and some patients suffer from dose-dependent undesirable side effects: vertigo, headache, indigestion, xerostomia, increased anxiety, etc., reducing the efficacy of the therapy of depressive disorder comorbid with alcohol use disorder. CYP2D6 and CYP2C19 are involved in the biotransformation of fluvoxamine. Meanwhile the genes encoding these enzymes have a high level of polymorphism, which may affect the protein synthesis. The presence of some polymorphic markers increases the amount of isoenzyme to be expressed or enhances its activity resulting in the accelerated biotransformation and the reduced efficacy of medication. In contrast, some polymorphisms reduce the isoenzyme activity resulting in the decreased biotransformation and elimination rates of medication. It increases the risk of dose-dependent undesirable side effects.

Objective: The primary objective of our study was to investigate the effects of CYP2D6 genetic polymorphisms on the efficacy and safety of fluvoxamine in patients with depressive disorder and comorbid alcohol use disorder, in order to develop the algorithms of optimization of fluvoxamine therapy for reducing the risk of dose-dependent undesirable side effects and pharmacoresistance.

Methods: The study involved 45 male patients (average age: 36.44±9.96 years) with depressive disorder and comorbid alcohol use disorder. A series of psychometric scales were used in the research. Genotyping of CYP2D6 (1846G>A) was performed using real-time polymerase chain reaction.

Results: According to results of U-test Mann-Whitney, statistically significant differences between the efficacy and safety of fluvoxamine were obtained on 9th and 16th days of therapy in patients with GG and GA genotypes (The Hamilton Rating Scale for Depression: 10.0 [10.0; 23.0] vs 25.0 [24.0; 16.0] (P<0.001) on 9th day and 4.0 [2.0; 5.0] vs 6.0 [6.0; 7.0] on 16th day; Udvald for Kliniske Undersogelser Side Effect Rating Scale: 6.0 [4.0; 6.0] vs 9.0 [9.0; 10.0] (P<0.001) on 9th day and 5.0 [1.0; 9.0] vs 19.0 [18.0; 22.0] on 16th day.

Conclusion: This study demonstrated the lower efficacy and safety of fluvoxamine in patients with depressive disorder and comorbid alcohol use disorders with GA genotype in CYP2D6 1846G>A polymorphic marker.

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ALCOHOLISM, GROUP THERAPY TREATMENT EFFICIENCY, CASE REPORT

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In this case, we can see the case report of a 35-year-old patient who has been admitted to psychiatric treatment over a year ago, due to behavioral issues, and the development of alcohol dependence. She is also part of a social care treatment, alongside a measure for protection of the personal rights and safety of her child, with intensive expert care and supervision for the caretaking of the child, and adequate help with resolving everyday issues. Among other illnesses present, there is a long-term hyperthyreosis (hyperthyroidism) present that is currently under therapy.

The patient finished an education for children with development issues. She is currently employed, unmarried, and a mother to a young child.

In the clinical picture the dominant traits are anxiety, emotional oversensitivity, and mild cognitive reduction. Due to the exaggerated reactive anxiety towards partner, existential and work issues, we can see a generalized dysfunctionality with which she copes with alcohol abuse. The patient hasn't been treated psychiatrically in the past. In our clinic, she was involved in a monthly treatment in the day hospital for alcoholism and other addictions. She regularly attended the "KLA", or Alcoholism Treatment Club, and has been regular in taking her prescribed pharmacotherapy.