PRELIMINARY COMMUNICATION

EFFECT OF METYRAPONE SUPPLEMENTATION ON IMIPRAMINE THERAPY IN PATIENTS WITH TREATMENT-RESISTANT UNIPOLAR DEPRESSION

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The paper describes the effect of metyrapone supplementation on imipramine therapy in patients (with treatment-resistant unipolar depression) who fulfilled DSM IV criteria for major depression. Nine patients were enrolled to the study on the basis of history of their illness and therapy. Following 2 weeks of washout period, the patients were treated with imipramine twice daily (100 mg/day) for 6 weeks, and then metyrapone was introduced (twice daily, 500 mg/day), and administered jointly with imipramine for further 6 weeks. Hamilton Depression Rating Scale (HDRS) and Beck Depression Inventory (BDI) were used to assess efficacy of antidepressant therapy. Imipramine changed neither HDRS nor BDI score after 6 weeks of treatment when compared with baseline (before treatment). Metyrapone supplementation significantly reduced both HDRS and BDI scores after 6-week supplementation. Moreover, pharmacokinetic data indicate that metyrapone did not influence significantly the plasma concentration of imipramine and its metabolite, desipramine in the patients during joint treatment with metyrapone and imipramine, what suggests the lack of pharmacokinetic interaction.

This preliminary study is the first demonstration of the benefit of metyrapone supplementation in imipramine therapy of treatment-resistant unipolar depression and suggests that a change in the level of neurotransmitters, hormones and immunological parameters, which are disturbed in depression, may contribute to the mechanism of the action of this drug.

Key words: imipramine, metyrapone, clinical and pharmacokinetic studies, therapy-resistant unipolar depression, human

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