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Pregnenolone and dehydroepiandrosterone as an adjunctive treatment in schizophrenia and schizoaffective disorder: an 8-week, double-blind, randomized, controlled, 2-center, parallel-group trial.

Ritsner MS[1], Gibel A, Shleifer T, Boguslavsky I, Zayed A, Maayan R, Weizman A, Lerner V.

Author information

Abstract

OBJECTIVE: Pregnenolone (PREG) and dehydroepiandrosterone (DHEA) are reported to have a modulatory effect on neuronal excitability, synaptic plasticity, and response to stress; they are associated with mood regulation and cognitive performance. We investigated the influence of PREG and DHEA on psychotic symptoms and cognitive functioning as an add-on to ongoing antipsychotic treatment of patients with chronic schizophrenia or schizoaffective disorder.

METHOD: This 8-week, double-blind, randomized, placebo-controlled, 2-center study compared 30 mg/d of PREG (PREG-30), 200 mg/d of PREG (PREG-200), 400 mg/d of DHEA, and placebo as an adjunctive treatment of 58 chronic schizophrenia or schizoaffective disorder patients (DSM-IV). The data were collected from February 2005 until June 2007. The outcome measures were symptomatic and neurocognitive changes, functioning, and tolerability as assessed primarily by the Clinical Global Impressions-Severity of Illness scale and the Positive and Negative Syndrome Scale. Analyses are presented for 44 patients who completed 8 weeks of treatment and for 14 noncompleters.

RESULTS: Compared with subjects who received placebo, those administered PREG-30 had significant reductions in positive symptom scores and extrapyramidal side effects (EPS) and improvement in attention and working memory performance, whereas subjects treated with PREG-200 did not differ on outcome variable scores for the study period. The general psychopathology severity and general functioning of patients receiving placebo and PREG-30 improved more than that of those subjects treated with DHEA, while EPS improved more in subjects treated with DHEA than in patients receiving placebo. Negative symptoms and akathisia were not significantly benefited by any treatment. The administration of PREG and DHEA was well tolerated.

CONCLUSIONS: Low-dose PREG augmentation demonstrated significant amelioration of positive symptoms and EPS and improvement in attention and working memory performance of schizophrenia and schizoaffective disorder patients. Further double-blind controlled studies are needed to investigate the clinical benefit of pregnenolone augmentation.

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