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A randomized, double-blind, placebo-controlled trial of pregnenolone for bipolar depression (Article)

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Abstract

Depression in bipolar disorder (BPD) is challenging to treat. Therefore, additional medication options are needed. In the current report, the effect of the neurosteroid pregnenolone on depressive symptoms in BPD was examined. Adults (n=80) with BPD, depressed mood state, were randomized to pregnenolone (titrated to 500 mg/day) or placebo, as add-on therapy, for 12 weeks. Outcome measures included the 17-item Hamilton Rating Scale for Depression (HRSD), Inventory of Depressive Symptomatology - Self-Report (IDS-SR), Hamilton Rating Scale for Anxiety (HRSA), and Young Mania Rating Scale (YMRS). Serum neurosteroid levels were assessed at baseline and week 12. Data were analyzed using a mixed model ANCOVA with a between factor of treatment assignment, a within factor (repeated) of visit, and the baseline value, as well as age and gender, as covariates. In participants with at least one postbaseline visit (n=73), a significant treatment by week interaction for the HRSD ($F(5,288)=2.61$, $p=0.025$), but not IDS-SR, was observed. Depression remission rates were greater in the pregnenolone group (61%) compared with the placebo group (37%), as assessed by the IDS-SR ($\chi 2\ (1)=3.99$, $p=0.046$), but not the HRSD. Large baseline-to-exit changes in neurosteroid levels were observed in the pregnenolone group but not in the placebo group. In the pregnenolone group, baseline-to-exit change in the HRSA correlated negatively with changes in allopregnanolone ($r(22)=-0.43$, $p=0.036$) and pregNANolone ($r(22)=-0.48$, $p=0.019$) levels. Pregnenolone was well tolerated. The results suggest that pregnenolone may improve depressive symptoms in patients with BPD and can be safely administered.