Effect of ganaxolone in patients with posttraumatic stress disorder

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Dear Editor;

Rasmusson et al. (2017a) reported a negative data concerning the effect of ganaxolone (a synthetic 3β -methylated derivative of allopregnanolone) in patients with posttraumatic stress disorder (PTSD). Ganaxolone is a GABAergic neuroactive steroid, and there were no significant differences of Clinician-Administered PTSD Symptom (CAPS) scores, global well-being, negative mood, or sleep between ganaxolone and placebo groups by intent-to-treat repeated measure analysis. The authors speculated that under-dosing would have contributed to no significance for the effect of ganaxolone in patients with PTSD. I have some concerns about their study.

First, the same authors recommended clinical studies to investigate the effect of neuroactive steroid therapy in patients with PTSD by considering effective dosing regimens and by identifying neuroactive steroid system abnormalities (Rasmusson et al. 2017b). Although the authors conducted an appropriate power analysis for a randomized controlled trial, statistical procedure in sensitivity analysis might be reconsidered for keeping enough statistical power. In addition, the authors discussed of keeping plasma level of ganaxolone ≥ 20 ng/ml. Appropriate dosing of ganaxolone should also be considered by keeping safety, and continuous survey is needed.

Second, the authors selected 80% of males in their trial. The same study group reported a negative relationship between serum (plasma) allopregnanolone and affective symptoms such as depression and anxiety in women by considering body mass index (Dichtel et al. 2017). I

suppose that sex difference for the effect of ganaxolone in patients with PTSD should be clarified by the stratified analysis by sex.

Finally, Hoskins et al. (2015) conducted a systematic review with meta-analysis to determine the efficacy of pharmacotherapy for reducing symptoms of PTSD. Although selective serotonin reuptake inhibitors, such as fluoxetine, paroxetine, and venlafaxine, showed a significant positive impact on PTSD symptoms with acceptability, the level of efficacy was not satisfactory. In order to improve evidence regarding efficacy for PTSD, clinical study on neuroactive steroid for PTSD should be continued.

Compliance with ethical standards

Conflict of interest The author declares that there is no conflict of interest.

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