A Case of Persistent Delirium Resolved Promptly With Suvorexant

To the Editor: Delirium is a significant clinical issue, but evidence regarding its treatment and prevention is insufficient. Atypical antipsychotics have proved effective[1,2] and are widely used to treat delirium. However, their unwanted adverse events such as falling,[3] pneumonia,[4] and even increased mortality[5,6] have limited their use.

Ramelteon, a nonbenzodiazepine, melatonin receptor agonist, has been reported[7] to prevent delirium with lower risk of adverse events. Suvorexant is another nonbenzodiazepine sleep agent and an orexin receptor antagonist,[8,9] and its effectiveness has not yet been determined with regard to delirium. Here, we report a case of persistent delirium that markedly improved with suvorexant.

Case report. A 53-year-old Japanese man with bipolar disorder (*ICD-10* criteria) and a history of cranial surgery for cerebellar hemangioblastoma was admitted to a hospital in December 2015 with an exacerbation of depressive state. He was currently taking lithium carbonate 800 mg/d along with olanzapine, aripiprazole, estazolam, and flunitrazepam. At admission, he was reportedly incoherent.

The patient's serum lithium level was 1.09 mmol/L, which is within the therapeutic level but high. Lithium intoxication was suspected, and lithium carbonate was decreased to 400 mg/d. The patient was given quetiapine and biperiden for insomnia and suspected akathisia, respectively, but his agitation worsened. All medications were discontinued except for lithium carbonate and quetiapine. His delirious state persisted even after increasing quetiapine to 250 mg/d and trying risperidone 2 mg/d, mianserin 30 mg/d, mirtazapine 15 mg/d, and, eventually, an intravenous infusion of haloperidol 5 mg. After a 1-month hospitalization, the patient was transferred to our unit for further assessment of his refractory delirium.

At arrival to our unit, he was disoriented to time and had a Mini-Mental State Examination (MMSE)[10] score of 24. He soon became agitated, standing up on his bed, with visual hallucinations and delusions of observation. Blood analysis and lumbar puncture revealed no signs of inflammation, thyroid dysfunction, or electrolyte imbalance. Computed tomography and magnetic resonance imaging of the brain indicated past tumor resection, but no other abnormality was noted. Hypoxia and recent alcohol or drug abuse were denied. Thus, there was no distinct organic etiology except his past cranial surgery. Electroencephalography (EEG) showed slow alpha activity (8 Hz) with occasional theta waves (6 Hz) but no epileptiform activity, which was compatible with a delirious state. Because of suspicion of lithium-induced delirium, all medications were discontinued. Suvorexant 20 mg at bedtime was started the first day of hospitalization in our unit.

The patient's agitation subsided the next day. His EEG on day 9 ameliorated, showing predominant faster alpha activity (9 Hz) with fewer slow waves. His disorientation continued to improve until he scored 29 on his repeat MMSE on day 32. Quetiapine 50 mg at bedtime was restarted for persistent middle insomnia, which improved his sleep quality. There were no apparent manic or hypomanic symptoms. The patient was discharged home in a euthymic mood on day 32.

Lithium can cause delirium within the therapeutic range,[11] and delirious symptoms may persist even after its discontinuation.[12] Delirious mania could be a differential diagnosis, although it is unlikely with no apparent manic symptoms.[13] In our case, multiple sedative agents did not resolve, but rather aggravated, his persistent delirium.

Suvorexant was effective in our patient, along with withdrawal of all previous medications, by restoring disrupted sleep through a different mechanism via orexin after the activation of multiple neurotransmitters. Since orexin plays a key role in maintaining arousal and wakefulness,[14,15] its antagonist effects may improve sleep differently without changing physiologic sleep architecture.[16] Therefore, suvorexant with its unique pharmacodynamic profile can be an option to treat persistent delirium when other medications are intolerant or ineffective.

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