Letter to the Editor

Uses of Newer Anticonvulsants: An Update

Sir: Since the publication of a recent review of the psychiatric uses of newer anticonvulsants in the *Companion,*[1] 2 new anticonvulsants have come to market. The first is levetiracetam, which is U.S. Food and Drug Administration–approved as an adjunctive agent in treating partial-onset seizures in adults with epilepsy.[2] Its precise mechanism of action is not known, but does not appear to be due to any interaction with known mechanisms involved in inhibitory or excitatory neurotransmission.[3] Levetiracetam possesses a unique pharmacologic profile, a high margin of safety, and potential antiepileptogenic properties by potent inhibition of kindling.[4] The principal route of elimination is renal, with about 66% of a dose excreted unchanged.[5] To date, there are no published data on levetiracetam and bipolar disorder. However, 2 pilot studies on the treatment of bipolar disorder with levetiracetam are ongoing.[6,7] There is 1 case report on the use of levetiracetam as monotherapy in acute mania in a patient who had failed more conventional mood stabilizers.[8]

The second new agent is zonisamide, approved as an add-on agent for partial seizures in adults.[9] It appears to have several mechanisms of action, including blockade of voltage-sensitive sodium channels and T-type calcium currents, modulation of dopaminergic and GABAergic systems, and free-radical scavengers.[10] The drug, which has been used in Japan for over 11 years as an anticonvulsant, is metabolized through the liver, is a mild liver enzyme inducer, and is titrated slowly.[11] Because zonisamide has been used in Japan since 1989,[10] most of the published data describing psychiatric uses are in Japanese without translation.[12–14] To date, there is 1 open-label add-on study in English examining zonisamide as an adjunct in 24 patients with mania (15 diagnosed with bipolar mania; 6, with schizoaffective manic state; and 3, with schizophrenic excitement).[15] Eighty percent of the bipolar patients, 66% of the schizoaffective patients, and 50% of the schizophrenic patients showed a moderate to remarkable improvement by the end of the fourth or fifth week.[15] Kanba and Yagi[16] earlier studied zonisamide in 6 patients with acute mania; 2 patients responded very well to zonisamide monotherapy, 1 patient with rapid cycling experienced a decrease in the severity of the episode, 1 schizoaffective patient stabilized, 1 schizoaffective patient progressed from hypomania to moderate depression, and 1 patient with mania did not respond to treatment. More data obtained in a controlled fashion will be required to determine if these new agents will prove to be of value in treating psychiatric disorders.

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