Riluzole Augmentation for Treatment-Resistant Depression

TO THE EDITOR: Glutamate is implicated in the pathophysiology and treatment of mood disorders (1). The following case reports pertain to the use of riluzole, a putative antiglutamatergic agent indicated for the treatment of amyotrophic lateral sclerosis, as add-on therapy for treatment-resistant major depressive disorder.

Ms. A was a 42-year-old woman with a history of major depressive disorder. Despite pharmacotherapy strategies, including fluoxetine, fluoxetine augmented with lithium, and her current regimen of bupropion (100 mg b.i.d.) and venlafaxine (up to 300 mg/day), she remained depressed, with scores of 21 on the 25-item Hamilton Depression Rating Scale and 17 on the Beck Depression Inventory. After we obtained written informed consent, riluzole, 50 mg b.i.d., was added to her current medication regimen. Within 1 week, her Hamilton depression scale and Beck Depression Inventory scores decreased by 16 and 10 points, respectively. Repeated measures of her depression severity reflected scores in the remitted range, with a score of 1 on the Hamilton depression scale and 0 on the Beck Depression Inventory at the end of 6 weeks and a Hamilton depression scale score of 4 and a Beck Depression Inventory score of 4 at the end of 12 weeks of continued treatment.

Ms. B was a 55-year-old woman with a 33-year history of major depressive disorder. Her pharmacotherapy history included adequate courses of various tricyclic and selective serotonin reuptake inhibitor monotherapies, nefazodone, and the combination of sertraline and bupropion. Immediately after an index course of seven bifrontal ECT treatments, her Beck Depression Inventory score was 15; however, within 2 weeks, her score rose to 32 despite continued weekly ECT treatments. For the previous 6 months, while her mood was maintained with fluoxetine (80 mg/day), methylphenidate (58 mg/day), and ongoing cognitive behavior therapy, her Beck Depression Inventory scores fluctuated between 17 and 31. After we obtained written informed consent, treatment with riluzole, 50 mg b.i.d., was started. Ms. B's Hamilton depression scale and Beck Depression Inventory scores before riluzole were 34 and 27, respectively. Within 1 week, her Hamilton depression scale score dropped to 22, and her Beck Depression Inventory score decreased to 11. At week 6, her Hamilton depression scale and Beck Depression Inventory scores were both 7; at week 12, her scores were 9 and 5, respectively.

Baseline laboratory evaluations, including liver function tests and a CBC with differential, were collected before study initiation. Additional tests were performed at 2–3-week intervals for 12 weeks and then monthly to monitor riluzole's known risk of serum aminotransferase elevations and neutropenia. Neither patient experienced significant aminotransferase elevations (more than five times the normal upper limits) or neutropenia or endorsed any other side effect.

Although case studies necessitate cautious interpretation, these results are consistent with a recent finding suggesting riluzole's effectiveness in treating depression (2) and further substantiate accruing evidence indicating that several classes of glutamatergic agents possess antidepressant properties (3).

References

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Carbamazepine and Rebound Mania

TO THE EDITOR: Carbamazepine is a dibenzazepine derivative used in the treatment of temporal lobe epilepsy and neuropathic pain. It is also widely prescribed for bipolar disorder (1). In bipolar patients treated with carbamazepine, rebound mania appears to be relatively uncommon; a case series of six bipolar patients found that none had developed manic symptoms when assessed 3 months after sudden discontinuation (2). This is in contrast to sudden lithium withdrawal in bipolar disorder, in which rebound affective episodes are well recognized (3, 4).

Mr. A was a 59-year-old Caucasian man with no personal or family history of mood disorder who was treated for neuropathic pain with carbamazepine at a dose of 1 g/day. His concurrent medications included 10 mg/day of ramipril, 20 mg/day of simvastatin, and 75 mg/day of aspirin. His pain responded well to carbamazepine, but after 18 months, he abruptly stopped this medication without consulting his physician. Four days later, his mood became elevated and irritable, with overactivity and a decreased need for sleep. He did not seek medical attention at this stage, but 3 weeks later, he restarted carbamazepine and returned to euthymia within 10 days.

Eighteen months after this, he again stopped carbamazepine abruptly on the advice of his dermatologist because there were concerns that it may have been exacerbating his psoriasis. Within 3 weeks, his mood again became elevated. He then had several clear features of mania, including overactivity, reduced sleep, social disinhibition, pressured speech, flight of ideas, and several grandiose delusions. His insight was significantly impaired, and he required admission to the hospital under mental health legislation. Carbamazepine was reinstated but this time with no response. Ultimately, he required intensive inpatient treatment over a 5-month period, finally recovering by taking a combination of sodium valproate, 1 g/day, plus olanzapine, 20 mg/day. Olanzapine was discontinued 2 months later, and for the next 4 months, he remained well while taking a maintenance dose of sodium valproate, 1 g/day.

In this case report, the close temporal relationship between stopping carbamazepine and the emergence of manic symp-