Oxcarbazepine for Mood Disorders

TO THE EDITOR: The Food and Drug Administration approved oxcarbazepine on Jan. 14, 2000, for the treatment of epilepsy. It has been reported to be effective in the treatment of mood disorders (1, 2). This report is about four Caucasian patients with bipolar II disorder with comorbid substance abuse who experienced significant improvement with oxcarbazepine.

Mr. A was a 52-year-old married man who was referred by a therapist in his employment assistance program for hostile behavior, which affected his relationships with family members and co-workers. He had been treated unsuccessfully with divalproate and psychotherapy. He began oxcarbazepine monotherapy, up to 1200 mg/day. He experienced better work productivity, an absence of physical violence toward his wife and co-workers, and fewer depressive days. He reported no side effects.

Ms. B was a 27-year-old single woman who was in treatment for childhood sexual abuse, self-mutilation, several suicide attempts, and episodic violent behavior. Since her adolescence, she had been in numerous inpatient and outpatient treatments, which had not produced significant improvement in her symptoms or function. Oxcarbazepine was initially added to her regimen of lorazepam, buproprion, fluvoxamine, trazodone, quetiapine, levothyroxine, and modafinil. Over the next year, she reduced her medications to oxcarbazepine, 600 mg b.i.d., levothyroxine, and trazodone. She had no hospitalizations and no temper outbursts or depressive episodes, was working full-time, and was not receiving Medicaid.

Mr. C was a 40-year-old married man who was referred to the clinic for treatment of agitation and conflict with his wife. He was taking buspirone, buproprion, and lithium. Oxcarbazepine, up to 1200 mg/day, was added to his dose of lithium, 900 mg/day. His irritability decreased, his depression lifted, his relationship with his wife improved, and he obtained full-time employment. In the past year, he has been well maintained with oxcarbazepine, 1200 mg b.i.d., and modafinil, 400 mg/day, before his shift work.

Mr. D was a 33-year-old man who was referred for treatment of domestic violence. He began oxcarbazepine monotherapy, up to 1200 mg/day. Since then, he has controlled his angry outbursts, felt happier, improved his home life, reduced his alcohol and cannabis consumption to occasional use, and given up his part-time job as a bar bouncer. His friends have also noted the improvement.

These patients were initially given 150 mg/day of oxcarbazepine; the dose was increased every 3–4 days by 150 mg until it reached 600 mg at bedtime. Morning dosing was then added, as needed, up to the maximum dose reported per patient. None of these patients had developed hyponatremia when tested within 1 month of initiation of treatment.

These patients showed improvement in mood stabilization. Oxcarbazepine was well tolerated and was the initiating factor in decreasing their symptoms of anger and irritability, as well as their depressive symptoms. We have also reported separately on the benefits of oxcarbazepine in a series of 87 patients with various subtypes of mood disorders (3). Prospective, double-blind, placebo-controlled trials of oxcarbazepine are indicated.

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Sibutramine and Panic Attacks

TO THE EDITOR: Sibutramine, a nonamphetamine appetite suppressant, is a selective norepinephrine, serotonin, and—to a lesser extent—dopamine reuptake inhibitor (1). There have been previous reports of psychosis (2), depression, mood changes, palpitations, and chest tightness associated with sibutramine, and hypomania has been linked to the combination of sibutramine and citalopram (3). However, to our knowledge, there have been no reported exacerbations of panic attacks. We report on a patient who had a history of panic attacks and experienced a recurrence of panic symptoms shortly after starting sibutramine.

Ms. A, a 62-year-old woman, had been diagnosed as having panic attacks during her mid-20s and had been initially treated with anxiolytics. She had been panic-free without treatment since her mid-30s, except for two attacks, both of which had occurred after minor surgical procedures.

Ms. A started taking sibutramine, 10 mg/day, for weight loss. After 1½ weeks of taking sibutramine, she had two panic attacks in rapid succession. She discontinued the medication for several days and had no further attacks. She then restarted sibutramine and had another panic attack within approximately 3 days. She again discontinued sibutramine and has been asymptomatic for 5 months. Ms. A declined a third exposure to sibutramine. She was not unduly apprehensive about taking medication, and there were no obvious psychological stressors present at the time.

While it is not possible to definitively prove a causal relationship between sibutramine and panic attacks, the temporal relationship of the onset and disappearance of the panic attacks to the initiation and discontinuation of sibutramine is suggestive. With the Naranjo Adverse Drug Reactions Probability Scale (4), a high-probability relationship between sibutramine and the panic attacks was demonstrated in our patient. Although the mechanism for this reaction is unknown, physicians prescribing sibutramine should be aware of this potentially important side effect.

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Catatonia and Transcranial Magnetic Stimulation

TO THE EDITOR: A painless and noninvasive stimulation of the brain has become possible by using transcranial magnetic stimulation (TMS). Most studies, but not all (1), have proven efficacy for TMS in treating depression. Fast repetitive TMS of the dorsolateral prefrontal cortex (2) and slow repetitive TMS of the opposite area (3) have been shown to improve depressive symptoms. Some studies have shown improvement of paranoid symptoms in schizophrenia patients (4). However, we know of only one study that has dealt with catatonia by using repetitive TMS (5). We report the case of a catatonic patient whose symptoms were relieved with TMS treatment.

Ms. A, an 18-year-old woman, was brought to the hospital in a catatonic state, according to DSM-IV criteria. She had no personal or family history of psychiatric disease. She was socially involved and was attending school regularly. Seven months before, she had experienced social withdrawal, a decline in school performance, panic attacks, and marked behavioral disturbances. Four days before hospitalization, she had developed acute catatonic syndrome.

When we examined Ms. A, her catatonic symptoms were found to involve mutism, waxy flexibility, negativism, rigidity, and catalepsy. Her symptoms were rated with the Bush Francis Catatonia Rating Scale (6) at baseline and every 3 days thereafter. After the failure of a short trial (3 days) of lorazepam, she was treated with fast repetitive TMS of the left dorsolateral prefrontal cortex for 2 weeks (10 sessions, 1600 stimuli/day, 10 Hz, 80% of the motor threshold).

Almost all of her catatonic symptoms had disappeared by the end of the TMS treatment, allowing a diagnosis of schizophrenia, according to the clinical picture (auditory hallucinations and delusions). The severity of the catatonic symptoms on the catatonia rating scale had dropped from 19 at baseline to 3 by days 12 and 15. Antipsychotic medication (amisulpride, 600 mg b.i.d.) was then initiated. Ms. A was discharged 4 weeks later.

The primary clinical picture seen in our patient is believed to be rare. To our knowledge, there has been only a single clinical instance of repetitive TMS working for catatonic patients (5). Our report corroborates previous findings of the efficacy of this technique in the treatment of catatonia, although the condition might have resolved spontaneously. TMS might offer a therapeutic alternative for the treatment of catatonia. However, further controlled studies are required to confirm the beneficial effect of TMS.

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Ethnicity, Depression, and Suicide

TO THE EDITOR: This letter is in response to an article written by Maria A. Oquendo, M.D., et al. (1). The authors expanded on previous work by looking at the relationship between affective disorders and suicide (2). In using statistical procedures to standardize data from the Epidemiologic Catchment Area (ECA) study and the Hispanic Health and Nutrition Epidemiological Survey and suicide rates from the Centers for Disease Control's National Health Statistics on Mortality, the authors exerted an admirable effort to tease out 1-year prevalence rates for major depression and suicide rates relative to depression for specific Hispanic ethnic groups. They found data that complicated the substantiated claim that major depression is positively associated with suicide. The results clearly revealed that Puerto Rican Americans have the highest rate of major depression while they have the lowest suicide rate relative to depression. These findings support research into why certain ethnic groups have protective factors against suicide, which is an important question in mental health policy and practice.

However, I would like to offer some critical remarks on the methods used in this study. The "ecological fallacy," or the error of assuming an association between two characteristics of a community will generalize at the individual level (3), undermines these findings. The authors assumed that because depression and suicide are associated in the larger community, and in the literature, that they are also associated at the individual level. The question arises, were there no suicide indicators in the ECA study and/or the Hispanic Health and Nutrition Epidemiological Survey?

The conceptual problems are magnified in the authors' use of a proxy measure—i.e., depression for suicide. From my understanding of the research question, the dependent variable of interest is suicide. It is a significant leap to use depression

as a proxy measure for suicide. The finding that Puerto Rican men and women had significantly higher rates of major depression and the lowest rate of suicide relative to major depression challenges the choice of the proxy measure.

These limitations notwithstanding, the article offers new insight into an increasingly vital area of inquiry in mental health research. It is imperative that we begin to look at cultural experiences and the potential differences they impose on prevalence of illness, service use, and suicidality. However, it is equally important that we use careful methods.

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Drs. Oquendo and Mann Reply

TO THE EDITOR: We would like to clarify the methods of our study in response to Ms. Munson's comments. We were interested in understanding the relationship between the lifetime prevalence of major depression in five ethnic groups and the rates of suicide in those same groups. Our assumptions were not about the association of these two phenomena at the individual level; rather, we attempted to see if the same associations that were reported at the group level for majority populations also existed in five ethnic populations. The ECA study and the Hispanic Health and Nutrition Epidemiological Survey assessed the frequency of suicide attempts but not of completed suicide. Suicide attempts and completions are related—but not the same—behavior; we were interested in the relationship of major depression to suicide completion.

In addition, we obtained our suicide figures from a report based on a separate database. We did not use depression as a proxy for suicide. We analyzed the relationship between these two variables, each from a separate database, at the population level.

Ms. Munson comments that our data suggested that depression cannot be used as a proxy for suicide. Part of the basic hypothesis of this article—namely, that ethnic groups may have different relationships between depression rates and suicide rates—reflects our belief that factors other than mood disorders contribute to suicide. Some of these factors may be protective, and others may add risk; these factors may vary between ethnic groups.

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