

of repeat thyroid function studies were also normal. His morning free cortisol level was slightly elevated, consistent with the diagnosis of depression. At that time his serum vasopressin level was inappropriately normal (8.6 pg/ml; normal range=1.0–13.3 pg/ml) given his hyponatremia and hypo-osmolality. A combined insulin tolerance/gonadotropin-releasing hormone/thyrotropin-releasing hormone test found no significant endocrinological abnormalities. An evaluation for occult malignancy revealed only benign colonic polyposis. Fluoxetine, the patient's only medication, was discontinued. Within 3 days his serum sodium level and osmolality returned to normal. One week later, he was rechallenged with fluoxetine, 80 mg/day, a dose that he has tolerated for 3 months to date without recurrence of hyponatremia.

The diagnosis of SIADH secondary to fluoxetine was based on the serum and urine electrolyte abnormalities, normal volume status, normal endocrinological function, and absence of malignancy and other medications. In other cases, this diagnosis was complicated by dehydration, additional medications (*Physicians' Desk Reference* and personal communication from Dista Products Co.), or the failure to assess thyroid and adrenal function (1). The SIADH resolved in 3 days, which is approximately equal to the half-life of fluoxetine but shorter than that of its primary metabolite (2). Fluoxetine has been associated with a number of endocrinological changes in animals, including increased vasopressin levels in the portal pituitary circulation in rats (2). This case confirms fluoxetine as a cause of SIADH that may be rapidly reversible and may not contraindicate subsequent use of the drug.

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Additional Cases of Suicidal Ideation Associated With Fluoxetine

SIR: I read with interest the article by Martin H. Teicher, M.D., Ph.D., and associates entitled "Emergence of Intense Suicidal Preoccupation During Fluoxetine Treatment" (1) and would like to report a similar case.

Ms. A, a 38-year-old married white woman, was admitted to an affective disorders inpatient unit for evaluation of a recent episode of depressive symptoms and suicidal ideation. She had always felt fatigued and depressed in winter but had never received psychiatric evaluation or treatment. Following two ectopic pregnancies 8 years earlier, she had developed constant knife-like pelvic pain, abdominal bloating, increased carbohydrate consumption, joint pain, and mastalgia. Oral progesterone, 400–1000 mg/day, partially

alleviated these symptoms. Eight months before admission, the patient underwent total abdominal hysterectomy and bilateral salpingo-oophorectomy. The pelvic pain and associated symptoms subsided postoperatively but then recurred.

Believing that her pain was partially psychogenic, Ms. A's gynecologist referred her to a psychiatrist, who prescribed imipramine, 10 mg/day. Because of headaches and blurred vision, imipramine was discontinued and fluoxetine, 20 mg/day, was started. Ms. A experienced initial improvement of the pelvic pain, but approximately 4 weeks after starting fluoxetine, she developed intense suicidal preoccupation and severe depression. She also experienced hypersomnia, poor concentration, anorexia, and a feeling of being "stoned." In addition, she experienced nightmares, blurred vision, lightheadedness, and a visual hallucination in which she saw her deceased mother. Whenever she saw a razor, she became intensely preoccupied with killing herself. She attempted suicide by carbon monoxide asphyxiation and was admitted to a local hospital. Fluoxetine was discontinued, and over the next 2–3 days, Ms. A's depression, suicidal ideation, and accompanying symptoms markedly decreased. On admission to our hospital 4 days after discontinuation of fluoxetine, she was completely free of these symptoms.

There are many similarities between Ms. A and the patients described by Dr. Teicher and co-workers. Ms. A developed depression and suicidal ideation approximately 30 days after beginning fluoxetine, had had no previous suicidal ideation or attempts, developed hypersomnia during fluoxetine treatment, and experienced rapid remission of depression and suicidal preoccupation after discontinuation of fluoxetine. In contrast to the previously reported cases, Ms. A experienced initial improvement with fluoxetine before she developed depression and suicidal preoccupation. Whether development of such symptoms while taking fluoxetine is coincidental or drug-related is still not known. It is important that clinicians report similar cases.

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1. Teicher MH, Glod C, Cole JO: Emergence of intense suicidal preoccupation during fluoxetine treatment. *Am J Psychiatry* 1990; 147:207–210

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SIR: A recent article in the *Journal* described six depressed patients with atypical features of hypersomnolence and hyperphagia who experienced severe suicidal preoccupation during fluoxetine treatment. We wish to report a similar patient who twice developed intense suicidal ideation in association with fluoxetine.

Mr. A, a 26-year-old man, had had no chronic medical problems and good premorbid functioning, including 3 years of college, an honorable military discharge, and steady work. He had been given a diagnosis of atypical depression, including hypersomnia, carbohydrate craving, psychomotor retardation, and depressed mood. He denied ever having had suicidal ideation. The depression was also accompanied by panic attacks, and the patient was placed on a regimen of fluoxetine, 20 mg each morning, and clonazepam, 0.5 mg t.i.d. Mr. A reported symptom resolution in 4 weeks. After 6 weeks of therapy, however, he began

abusing alcohol and feeling suicidal, both for the first time. After 8 weeks the patient discontinued fluoxetine. He had no family history of alcohol dependence, depression, suicide, or other psychiatric disorder.

Mr. A came to our facility with alcohol dependence, benzodiazepine misuse, and depressed mood. He was not taking fluoxetine and denied having suicidal ideation during the preceding month. Liver function test values were mildly elevated; CBC, thyroid, and renal function were normal. A urine drug screen was positive for benzodiazepines. Ten days after discontinuing chlordiazepoxide withdrawal, the patient had daily panic attacks consisting of 10- to 15-minute episodes of a pulse rate over 130 bpm, blood pressure up to 180/112 mm Hg, hyperventilation, diaphoresis, and a fearful state. His depressive symptoms included daily crying spells, psychomotor retardation, anhedonia, 10–12 hours of sleep per night, extreme hunger, and depressed mood. Fluoxetine, 20 mg each morning, and clonazepam, 0.5 mg, were restarted, and there was symptom resolution within 3 weeks. The patient was discharged with disulfuram added to his regimen.

After 30 days of taking fluoxetine, Mr. A was readmitted to the hospital with severe suicidal ideation. In the week before admission he had held a loaded shotgun in his mouth and later planned to crash his car into a bridge. Depressive symptoms had worsened over the previous 2 weeks, with psychomotor retardation so severe that a urinal was kept at the bedside, work was missed, and appointments were canceled. He arose for meals because of carbohydrate craving. He complained of poor concentration, decreased libido, and anhedonia. Fluoxetine, clonazepam, and disulfuram were used as prescribed, and Mr. A denied abusing other medications. There were no signs of alcohol withdrawal, and liver function test values had normalized.

Mr. A was placed on suicide precautions, and the dose of fluoxetine was increased to 40 mg each morning. On the following day he was found attempting to hang himself with his pajama top. Fluoxetine was discontinued and he continued to have fleeting suicidal ideation for 5 days, during which ECT was begun, with excellent response after 10 treatments. The patient then wished to be treated with imipramine, and with that medication he appears to be doing well.

Similar to the six patients described by Teicher et al., our patient had symptoms of atypical depression. He also briefly responded to fluoxetine but then relapsed, with development of suicidal ideation for the first time. After stopping fluoxetine he was admitted for alcohol dependence, underwent withdrawal with chlordiazepoxide, and again started to take fluoxetine because of persistent depressive symptoms. The patient returned to the hospital intensely suicidal. Although this was possibly coincidental, the case is consistent with the proposal that in "atypically depressed" patients, fluoxetine may increase the risk of attempted suicide.

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Discussion of Fluoxetine and Suicidal Tendencies

SIR: The conclusion of Martin H. Teicher, M.D., Ph.D., and associates (1) that intense suicidal preoccupation emerges with "an estimated incidence of 1.3%–7.5%" is simply not supported by their case presentations.

Over the past 2 years, I have treated 100 patients with fluoxetine. About half of this group were Cambodian immigrants who frequently had dual diagnoses of posttraumatic stress disorder and major depression. These patients had done poorly with imipramine because of side effects or with alprazolam because of addiction fears. Their response to fluoxetine was dramatically positive. My Cambodian patients reported that it helped them focus their thinking, did not feel sedating or addictive, and helped them come to terms with their extended holocaust experience. Not one of these Cambodian patients, who had been exposed to years of extreme violence against themselves and their loved ones, displayed a reaction like that mentioned in Dr. Teicher and associates' article.

My American outpatients, a heterogeneous group, were equally enthusiastic about fluoxetine's lack of side effects, along with the improved modulation of emotions. Many of my Cambodian and American patients had intrusive, obsessive, violent thoughts before taking fluoxetine that were greatly alleviated by subsequent fluoxetine treatment, rather than vice versa.

Dr. Teicher and colleagues routinely used doses of 80 mg/day. Two patients had their fluoxetine continued or the dosage increased after a rash appeared—a clear contraindication to continued use of fluoxetine. In one case, a steroid was added to ameliorate the rash while the probable offending agent was still being given. I have found doses of 20 mg every day or every other day to be effective, while higher doses have led only to increased side effects. The hypersomnia, akathisia, and fatigue noted in the authors' patients would have led me to decrease the dose, not increase it. Finally, adding a stimulant, as was done in two cases, compounds an iatrogenic problem.

The patients in the study by Dr. Teicher and associates were unique. Clearly, no generalization can be made to other psychiatric populations. These hospitalized, severely ill patients had taken many previous medications. All but one had had previous suicidal thinking, gestures, or attempts. In four of six cases, the patient was taking at least one other psychoactive medication concurrently with the fluoxetine. No statement can reasonably be made about fluoxetine when a patient is simultaneously taking seven other psychoactive medications. Finally, were any of these patients hospitalized concurrently, and might a "contagion" of suicidal ideation have developed among either the patients or the mental health observers?

Patients commit suicide every year with overdoses of traditional antidepressants. It is nearly impossible to commit suicide with a fluoxetine overdose. None of the six patients in this study did commit suicide. A study of any change in the rate of suicide by antidepressant drug overdose since the introduction of fluoxetine might be illuminating.

Fluoxetine is a revolutionary antidepressant with many effective uses. Its relative lack of side effects is impressive. Psychiatric patients could be denied an efficacious, unique medication if the conclusions of Dr. Teicher et al.'s article were accepted uncritically.

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1. Teicher MH, Glod C, Cole JO: Emergence of intense suicidal preoccupation during fluoxetine treatment. *Am J Psychiatry* 1990; 147:207–210

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