Letters to the Editor

Topiramate Produced Weight Loss Following Olanzapine-Induced Weight Gain in Schizophrenia

Sir: Anticonvulsants are increasingly used as an augmentation strategy in schizophrenia.[1] Topiramate, with the unique side effect of reducing appetite and weight,[2] was found effective as a mild-to-moderate mood stabilizer.[3] Topiramate was found to produce weight loss after clozapine induced weight gain in a schizophrenic patient.[4] We report here the effect of topiramate in a patient with schizophrenia and olanzapine-induced weight gain.

Case report. Mr. A, a 34-year-old man, has diagnoses of paranoid schizophrenia (DSM-IV) and Crohn's disease. Olanzapine was added to his medication regimen in April 1997 during his 10th and last hospitalization for a suicide attempt. At that time, his body mass index (BMI) was 21.9 (weight [68.5 kg]/height [1.77 m^2] = 21.9). He had no history of significant weight gain prior to his use of olanzapine.

In October 2000, Mr. A was referred to our clinic for residual symptoms of schizophrenia and weight gain of 41 kg (BMI = 35.0 at time of referral) since olanzapine initiation 3.5 years ago. His total Positive and Negative Syndrome Scale (PANSS)[5] score was 47 (positive score = 9, negative score = 13, general score = 25). Results of routine blood tests were within normal limits, including HbA_{1C} at 5%. At the time of referral, his medications were haloperidol, 20 mg/day; olanzapine, 20 mg/day; clonazepam, 3 mg/day; lamotrigine, 50 mg/day; trazodone, 75 mg/day; procyclidine, 30 mg/day; loperamide, 8 mg/day; and mesalamine, 1000 mg/day. Our initial goal was to replace lamotrigine with topiramate. Long-term goals included the discontinuation of haloperidol, trazodone, and clonazepam. Topiramate was introduced at referral and was gradually increased from the starting dosage of 25 mg/day to 125 mg/day over 5 weeks. Lamotrigine was simultaneously discontinued over 2 weeks.

After 8 weeks of treatment with 125 mg/day of topiramate, Mr. A's total PANSS score was reduced to 38 (positive score = 13, negative score = 7, general score = 18). On starting topiramate, Mr. A reported that his intense hunger cravings subsided. The use of topiramate resulted in a loss of 15 kg over the first 6 months and an additional 13.5 kg at the end of 15 months. Topiramate permitted Mr. A to improve eating habits and start a new exercise program. His BMI is now 26.0.

When Mr. A presented with residual symptoms and weight gain, we chose to replace lamotrigine with topiramate. His psychopathology improved as indicated by a reduction in score on the PANSS. Furthermore, he lost 28.5 kg in the 15 months following topiramate initiation. The mechanism of action of topiramate involves blockade of voltage-dependent sodium channels, potentiation of GABAergic transmission, and inhibition of excitatory pathways through an action at adenosine monophosphate A (AMP-A) receptor sites.[6] The antiglutamatergic profile of topiramate can be identified as having "activating" effects such as weight loss.[7] Use of adjunctive topiramate in schizophrenia should be further investigated in patients who experience antipsychotic-induced obesity, since it appears to have a selective effect on hunger cravings.

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Emmanuelle Levy, M.D.
Howard C. Margolese, M.D., C.M., F.R.C.P.(C.)
Guy Chouinard, M.D., M.Sc.(Pharmacol.), F.R.C.P.(C.)
McGill University Health Centre
Montreal, Quebec, Canada

High Frequency of Residual Depressive Symptoms in Bipolar II Disorder: The Need for a Better Treatment

Sir: Kupfer et al.[1] reported very important findings on the clinical features of a large sample of bipolar case registry patients. The authors reported that the median age at onset was 17.5 years, that family history (not using research-level family history methodology) of bipolar disorder was present in 54.0% of patients, and that 64% of the patients were unemployed (indicating severe impairment). The authors stressed that the high level of impairment could result from inadequate treatment of depression (maybe for fear of inducing mania).

My studies on bipolar II disorder in a large outpatient private practice setting (more representative of bipolar patients than tertiary care settings[2–4]) are in line with the findings of the au-

thors and support the authors' view that untreated/inadequately treated depression may be both common and persistent among bipolar patients. In a recent study,[5] I found that prevalence of persistent (more than 2 years) residual depressive symptoms from the index major depressive episode (MDE) was high (44.9%) among 138 consecutive bipolar II outpatients and that residual depressive symptoms were related to the number of MDE recurrences.

These findings stress the importance of preventing recurrences, but also suggest that treatment of depression should be much better in bipolar II patients. The fear of inducing hypomania could be much reduced by the findings of a previous study in the same setting[6] showing that only 17.3% of bipolar II depressed outpatients switched to hypomania when treated with different antidepressants. In my new sample of bipolar II outpatients (N = 241), studied with the same methodology in the same setting, the median age at onset of the first MDE is 20 years, persistent residual depressive symptoms are present in 44.3% of patients, history of bipolar I disorder is present in first-degree relatives of 9.5% of probands, and history of bipolar II disorder is present in first-degree relatives of 50.7% of probands (assessing family history by the Weissman et al. Family History Screen[7]). The high bipolar family loading reported by Kupfer et al. is replicated by the findings in my sample and supports the authors' view that so many impaired family members may be of little help for bipolar patients.

Studies on bipolar II patients in settings different from the usual university settings, such as private practice, may give new and relevant information on clinical features and treatment of this common (but often misdiagnosed) disorder, which may be present in up to 1 in 2 depressed outpatients.[8–10]

Dr. Benazzi reports no financial affiliation or other relationship relevant to the subject matter of this letter.

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Franco Benazzi, M.D.
National Health Service
Forlì, Italy

Dr. Kupfer Replies

Sir: My colleagues and I appreciate the comments of Dr. Franco Benazzi and his emphasis on several points we addressed in reporting the results of our bipolar registry sample.[1] First, we are also impressed with the high family history of recurrent mood disorder (both bipolar and unipolar). Dr. Benazzi's family history data are consistent with our data suggesting that over 50% of bipolar patients have at least 1 family member with bipolar disorder and that over 50% have at least 1 family member with unipolar depressive disorder. Second, the data on early onset of bipolar I and bipolar II disorders reinforce our contention that we need to identify individuals with such disorders in adolescence and develop targeted, age-appropriate therapeutic efforts. Third, the ongoing, pervasive low-to-moderate level of depressive symptomatology appears to be present in both bipolar I and bipolar II patients. This level of symptomatology is coupled with ongoing functional impairment and the vital need to devise therapeutic regimens that will do more than prevent mania. As we stated in our report, inadequate attention is devoted to addressing depressive symptomatology and concurrent functional impairment in the targeted efforts to treat and prevent mania. In this vein, Dr. Benazzi raises the issue of the fear of inducing mania that prevents clinicians from more aggressively treating the depressive symptoms in bipolar I and II disorder.

Dr. Kupfer is a consultant for Novartis and a speakers/advisory board member for Pfizer, Lilly, and Forest.

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David J. Kupfer, M.D.
University of Pittsburgh Medical Center
Pittsburgh, Pennsylvania

Quetiapine Augmentation of Sertraline in Obsessive-Compulsive Disorder

Sir: Patients affected by obsessive-compulsive disorder (OCD) often do not respond to specific pharmacologic treatments such as clomipramine and selective serotonin reuptake inhibitors (SSRIs) (approximately 40%–60% of cases).[1] In up to 65% of this large subgroup of treatment-resistant patients, the addition of traditional neuroleptics appears to be useful,[2,3] especially if comorbid chronic tics or schizotypal personality disorder is present.[4] However, the long-term administration of traditional antipsychotics often leads to undesirable side effects such as tardive dyskinesia.

Atypical neuroleptics have a safer side effect profile, and they have been investigated recently in the management of this disorder. Risperidone has shown efficacy as adjunctive treatment in fluvoxamine-refractory OCD in a double-blind, placebo-controlled study[5] in which comorbidity for tics or schizotypal personality disorder was not a predictor of response. Olanzapine augmentation of SSRI medications in the treatment of refractory OCD was effective in about two thirds of cases.[6,7]

Quetiapine has received little investigation in OCD: only 1 report of the use of quetiapine for treatment of OCD, in which quetiapine exacerbated obsessive-compulsive symptoms in a

patient with bipolar II disorder, trichotillomania, and delusional disorder, was found via a MEDLINE search from 1966 to 2001 using the search terms *quetiapine* and *OCD*.[8] The following case report describes the effect of quetiapine augmentation in the management of treatment-resistant OCD.

Case report. Mr. A, a 25-year-old white man, had a 9-year history of OCD (DSM-IV criteria) consisting of contamination obsessions and washing, counting, and checking compulsions, without comorbid tics. He had no history of psychotic features or significant mood disorders.

Prior to presenting to our center, he had received several trials of medication, each lasting 10 to 12 weeks: clomipramine, 250 mg/day; fluvoxamine, 300 mg/day; sertraline, 200 mg/day; sertraline, 100 mg/day, plus lithium, 900 mg/day; and sertraline, 100 mg/day, plus risperidone, 1 mg/day. After this last trial, his Yale-Brown Obsessive Compulsive Scale (YBOCS)[9] score was 25 and his Clinical Global Impressions scale (CGI)[10] score was 5. Mr. A considered this partial response to be unsatisfactory (he was working in the warehouse of a large shopping center and found that his obsessions of checking and counting were still stressful).

At the time he presented to our center, he had discontinued risperidone and was still taking sertraline. He was assessed by a senior specialist using the YBOCS (score = 30) and the CGI (score = 6). A trial of quetiapine augmentation to sertraline therapy was initiated after Mr. A had given informed consent. Quetiapine was started at a dose of 50 mg b.i.d. (sertraline was maintained at 100 mg/day), and clinical response was evaluated 6 weeks later. After 6 weeks, he reported a satisfactory response: his YBOCS score decreased to 12, and CGI score decreased to 2. He reported a considerable decrease in obsessions and compulsions, with substantial advantages at work. Six months later, treatment was maintained unchanged. There has been no reduction in efficacy, and quetiapine is well tolerated (no adverse events have been observed).

Even atypical neuroleptics have an antagonistic action on 5-HT_2 and D_2 receptors, which are probably both involved in the pathogenesis of OCD[11]; when clozapine,[12] risperidone,[13] olanzapine,[14] and quetiapine[8] were administered singularly or in combination in patients with primary psychotic disorder such as schizophrenia or delusional disorder, they lacked efficacy or worsened obsessive symptoms.

On the other hand, there is evidence suggesting that risperidone[5] augmentation may be effective in the treatment of a subgroup of OCD patients. Augmentation with olanzapine also seemed to show efficacy in treatment-resistant OCD in 2 recent open-label, uncontrolled studies.[6,7] To our knowledge, there are no prior studies or reports suggesting that quetiapine is effective in OCD.

The observed reduction in obsessions and compulsions could not have been due to the continued sertraline antidepressant therapy, because this patient was treated with quetiapine after having received sertraline alone and in combination with other drugs for at least 35 weeks at an adequate dose. Although plasma levels of the 2 drugs were not measured, we do not believe that the improvement was due to an increase of blood sertraline levels mediated by quetiapine, because quetiapine is a weak inhibitor of the activities of cytochrome P450 isoenzymes,[15] with a clinically irrelevant effect in vivo.

In conclusion, our data suggest that quetiapine addition to ongoing sertraline treatment could be an option for patients suffering from treatment-resistant OCD. Further investigations with larger samples and a placebo-controlled design are needed to investigate the efficacy of this association strategy and identify response predictors.

Dr. Francobandiera reports no financial affiliation or other relationship relevant to the subject matter of this letter.

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Giorgio Francobandiera, M.D.
SPDC di Morbegno, ASL della Provincia di Sondrio
Morbegno, Italy

EMDR for Women Who Experience Traumatic Events

Sir: In their article for a recent supplement to the *Journal*, Foa and Street[1] summarize psychotherapeutic interventions for posttraumatic stress disorder (PTSD). They indicate that 2 procedures, exposure therapy and stress inoculation training (SIT), are effective in reduction of PTSD symptoms. They describe other psychotherapy procedures, but they do not mention an important therapeutic method for PTSD: eye movement desensitization and reprocessing (EMDR).[2,3]

In *Effective Treatments for PTSD: Practice Guidelines From the International Society for Traumatic Stress Studies* [ISTSS],[4]

2 psychotherapy treatments for PTSD are listed as having been shown to be effective: exposure therapy (p. 78) and EMDR (p. 151). SIT (p. 78) is reported to have had 2 well-controlled studies published on the treatment of PTSD. Both SIT studies were with female sexual assault victims.

Scheck et al.[5] found EMDR to be effective with a group of 60 women having experienced assault. Given that EMDR has been established as effective in the ISTSS guidelines,[4] it may be important for the reader to know that this form of therapy may be applied when confronting the issues addressed in this article.

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Gary Peterson, M.D.
Southeast Institute for Group and Family Therapy
Chapel Hill, North Carolina

Dr. Foa Replies

Sir: In his letter to the editor, Dr. Peterson noted our omission of eye movement desensitization and reprocessing (EMDR) as an important therapeutic method for posttraumatic stress disorder.

Several studies evaluated the efficacy of EMDR, but all suffer from methodological problems (see Chemtob et al.).[1] Accordingly, in our view the efficacy of EMDR with traumatized women has not yet been established.

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Edna B. Foa, Ph.D.
University of Pennsylvania
Philadelphia, Pennsylvania

High Degree of Tolerability for Monotherapy With High Doses of Quetiapine: A Case Report

Sir: Quetiapine is a relatively new third-generation antipsychotic with a labeled dose range of 400 to 800 mg/day. Quetiapine has demonstrated efficacy in the management of patients with a history of partial response to conventional antipsychotics.[1] We report the case of a schizophrenic woman who achieved full clinical remission without significant side effects with a high dose of quetiapine (1600 mg/day). To our knowledge, evidence from daily clinical practice or controlled clinical trials has never been published on high doses of this new antipsychotic.

Case report. Ms. A, a 34-year-old woman, was diagnosed with schizophrenia (DSM-IV criteria) at the age of 18 years and has suffered several acute episodes of the illness, for which she has been treated with a variety of antipsychotic drugs. At the age of 25 years, she attempted suicide and was admitted to the intensive care unit at a regional hospital for 5 days. In August 2000, she suffered an exacerbation of her illness with paranoid delusions, affective and psychomotor symptoms, aggressiveness, irritability, and physical exhaustion. In October 2000, her medication was changed from olanzapine (40 mg/day) to quetiapine (800 mg/day) (crossover was titrated over a period of 1 week) due to excessive weight gain. She received 800 mg/day of quetiapine for 1 month; because her clinical picture did not show sufficient improvement, it was decided to gradually increase quetiapine until either an adequate therapeutic response (per the clinical evaluation made by the psychiatrist) was achieved or side effects emerged. She began taking 1200 mg/day during the second month and has been taking 1600 mg/day of quetiapine (400-400-800) from the third month (December 2000) until the present. Ms. A has remained in full clinical remission from the episode since then. Despite good compliance, only a partial response to neuroleptic treatment had been previously achieved. Furthermore, the emergence of side effects (extrapyramidal symptoms and hyperprolactinemia in the case of conventional antipsychotics and weight gain in the case of olanzapine) advised against dosage maintenance or increments in an attempt to reach clinical remission.

Quetiapine at this high dose continues to be well tolerated by Ms. A. There has been no evidence of extrapyramidal symptoms or clinical signs of hyperprolactinemia. Her sex life has improved considerably (as reported by Ms. A herself, as well as her husband), and her body weight has returned to normal. The only adverse effect reported by Ms. A was moderate constipation, which responded to dietary measures alone. At treatment initiation, she also reported dizziness, which disappeared after a few days. Clinical examination results, red blood cell (RBC) count, Holter electrocardiogram, and prolactinemia levels (8.4 ng/mL) have all been within normal ranges.

Plasma quetiapine levels were determined on 2 occasions, at 5 and again at 8 months after reaching the maximum dose. Because the dose at which remission was achieved was well above that described as being efficacious in the literature and in clinical trials, and because Ms. A reported full treatment compliance, the decision was made to determine plasma drug levels, since we suspected that she might, in fact, be a rapid metabolizer, thus explaining her need for such high doses. In following the usual procedures, plasma levels were measured at 3 different times during the day: 9:00 a.m., 10:30 a.m., and 2:30 p.m. Drug levels ranged from 128.6 to 496.6 ng/mL, which were within the expected range following extrapolation of plasma levels from pivotal studies. A genotype analysis was performed for cytochrome P450 isoenzyme (CYP) 2D6-B and CYP3A4-V. Ms. A was of the "extensive metabolizer" genotype for both. The following polymorphisms were also obtained for the serotonin-2A gene: T102C: C/C (C/C is the most frequent genotype in schizophrenic patients)[2] and A-1438G: G/G; the serotonin transporter gene: 5HTTLPR: L/s (the s allele has been linked to an increased risk of suicide attempts)[3] and VNTR (5-HTT): 12rep/10rep; and the tryptophan hydroxylase gene: A218C: C/C (C/C is the most frequent genotype in patients who have attempted suicide).[4]

We conducted a MEDLINE search (January 1996–June 2001) with the keywords *quetiapine*, *tolerability*, and *high dose* and found no reports on this subject.

The clinically effective dose range of quetiapine reported in the literature is between 250 and 750 mg/day.[5–7] Nevertheless, Ms. A required a considerably higher daily dose of quetiapine to achieve optimal clinical effectiveness. Initially, we considered that her need for high doses of quetiapine might be related to her metabolizer genotype as identified by the CYP2D6-B and CYP3A4-V polymorphisms, as observed with other compounds[8,9] and as suggested by quetiapine pharmacokinetics.[10,11] However, the patient genotype obtained has led us to reject this hypothesis. Her need for high doses is more likely a combination of several factors such as the interindividual variability in the pharmacodynamic response, interindividual variability in the pharmacokinetics of quetiapine, and the type of dosing regimen employed.

Another outstanding feature of the case we present is the high degree of tolerability that the patient showed to this high dose of quetiapine, with no clinical or laboratory evidence of extrapyramidal effects, RBC abnormalities, hyperprolactinemia, or adverse cardiac events. Furthermore, Ms. A reports satisfaction with her current body weight and with her sex life.

The clinical results and the absence of adverse effects that were bothersome to Ms. A, particularly the weight gain that she had experienced with a previous atypical antipsychotic, have contributed to her satisfaction and acceptance of the treatment over the middle to long term (8 months).

We have since seen other cases that have required high doses of quetiapine with similar efficacy and tolerability results. These cases highlight some interesting points, having both clinical and practical implications. First, there may be a subgroup of patients who require high doses of quetiapine, and future research aimed at identifying endophenotypic characteristics of such a group would be of great value in clinical practice. Second, the present case suggests that, when required, high doses of quetiapine can be prescribed to produce satisfactory clinical responses without increasing the risk of treatment side effects.

The authors report no financial affiliation or other relationship relevant to the subject matter of this letter.

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Julio Bobes, M.D., Ph.D.
Maria P. Garcia-Portilla, M.D., Ph.D.
Pilar A. Saiz, M.D., Ph.D.
Maria-Teresa Bascaran, M.D.
Manuel Bousoño, M.D., Ph.D.
University of Oviedo
Oviedo, Spain
Celso Arango, M.D., Ph.D.
Hospital Gregorio Marañon
Madrid, Spain

Hypokalemia With Venlafaxine

Sir: The antidepressant venlafaxine has the desirable quality of being selective for both serotonin and norepinephrine reuptake inhibition.[1] Venlafaxine-induced hyponatremia has been reported, and the syndrome of inappropriate antidiuretic hormone secretion (SIADH) has been proposed as the possible mechanism.[2] Serotonin has been observed to increase concentrations of vasopressin in rats,[3] and an increased level of vasopressin is the underlying cause of SIADH. The effect of venlafaxine on serum potassium and magnesium levels has not been mentioned in any previous report. Gitelman syndrome, an inherited hypokalemic renal tubulopathy observed in older children and adults, is characterized by intermittent episodes of muscle weakness, carpopedal spasm, tetany, hypokalemia, and hypomagnesemia.[4] We present the case of a depressed man with Gitelman syndrome who experienced a dramatic reduction of serum concentration of potassium and magnesium after intake of venlafaxine.

Case report. Mr. A, a 45-year-old Taiwanese man, was diagnosed with Gitelman syndrome about 15 years previously, when he suffered from sudden onset of tetany and consciousness disturbance brought on by hypokalemia and hypomagnesemia and was admitted to a medical ward. After complete laboratory investigations and consultations with metabolic specialists, the diagnosis of Gitelman syndrome was established. Since then, he has received potassium supplementation to keep his serum potassium level in the range of 2.5 to 3.1 mmol/L. No further episodes of tetany were noted during the subsequent 15 years. During this period, Mr. A did receive treatment with fluoxetine for 1 month due to a depressive episode. About 5 years after the episode, in October 2000, a second depressive episode was diagnosed, which did not respond to fluoxetine. Venlafaxine was prescribed to replace the fluoxetine, with the dosage gradually titrated to 112.5 mg/day. Mr. A's depressive mood improved 2 weeks after the initiation of venlafaxine treatment. However, episodic carpopedal spasm developed 3 weeks after the initia-

Table 1. Serum Electrolyte and Endocrine Levels by Length of Time After Exposure to Venlafaxine

	Day					
Serum Level	0[a]	0[b]	1[c]	2	3	4
Sodium (mmol/L)	124	122	121	125	130	129
Potassium (mmol/L)	2.1	2.9	2.3	3.0	2.8	2.7
Magnesium (mmol/L)	0.60	0.76	0.51	0.54	0.87	0.72
Renin (ng/mL/h)	…	…	3.84	…	…	2.04
Aldosterone (ng/dL)	…	…	57.0	…	…	13.3

[a]Metabolic profile was checked on day 0, when the patient was sent to the hospital.
[b]Metabolic profile was rechecked 8 hours after the first check, when the carpopedal spasm and tetany subsided gradually after supplementation of intravenous fluid and electrolyte.
[c]Metabolic profile was rechecked 6 hours after a single dose of venlafaxine (37.5 mg) was given on day 1, and the carpopedal spasm and episodic tetany recurred.

tion of venlafaxine treatment, with the frequency of the spasms increasing over time. About 4 weeks after the start of venlafaxine treatment, sudden-onset tetany developed, with laboratory data from the local hospital revealing hyponatremia (serum sodium level: 124 mmol/L), hypokalemia (serum potassium level: 2.1 mmol/L), and hypomagnesemia (serum magnesium level: 0.60 mmol/L). Mr. A was then transferred to a medical center for further management.

Intravenous electrolyte supplementation with sodium chloride, potassium chloride, and magnesium sulfate quickly corrected his carpopedal spasm, tetany, and metabolic profile (serum potassium: 2.9 mmol/L, serum magnesium: 0.76 mmol/L). Four months after the diagnosis of the second depressive episode, Mr. A was sent to our hospital. After thorough discussion with the patient, 37.5 mg of venlafaxine was again prescribed (day 1), and the patient's clinical condition was carefully observed. On day 1, carpopedal spasm and episodic tetany recurred. Laboratory data (Table 1) revealed hyponatremia (serum sodium: 121 mmol/L), hypokalemia (serum potassium: 2.3 mmol/L), and hypomagnesemia (serum magnesium: 0.51 mmol/L) with serum osmolality of 273 mOsm/kg H_2O, urine osmolality of 370 mOsm/kg H_2O, and urine sodium level of 49 mmol/L. Serum renin level was 3.84 ng/mL/h (normal range: 1–5 ng/mL/h), and serum aldosterone level was 57.0 ng/dL (normal range: 5–30 ng/dL). Therefore, venlafaxine was discontinued. The patient experienced no consciousness change, nausea, or vomiting. Electroencephalography showed no focal epileptic activity. Carpopedal spasm and tetany subsided gradually over the next 3 days, with intravenous electrolyte supplementation discontinued after correction of the serum electrolyte imbalance. By day 4, the patient's serum renin level had decreased to 2.04 ng/mL/h, with aldosterone level recovering to 13.3 ng/dL. Mr. A was discharged on day 5, and no further carpopedal spasm or tetany was observed.

This patient suffered from significant electrolyte imbalance and clinical symptoms after venlafaxine was prescribed. Venlafaxine-induced SIADH could be responsible for hyponatremia,[2] but no previous report has mentioned the influence of venlafaxine on potassium level. Because of the evidence of severe hypokalemia and elevation of aldosterone level in this patient, the pathophysiology of Gitelman syndrome should be considered in order to understand the complex interactions of electrolytes in body fluid. With the advance of molecular biology in the research of Gitelman syndrome, mutations have been identified at the gene-encoding thiazide-sensitive sodium chloride cotransporter.[5] This cotransporter is located in the distal nephron and is responsible for the reabsorption of sodium chloride. A dysfunction of this cotransporter, as in Gitelman syndrome, leads to sodium chloride wasting, activating the renin-angiotensin-aldosterone axis, which causes hypokalemia. Although the mechanism of hypomagnesemia is not well defined, hypokalemia has been suggested to be the basis of increased magnesium excretion.[6]

This patient with Gitelman syndrome received venlafaxine to treat depressed mood, and a temporal relationship was identified for initiation of venlafaxine therapy and onset of hypokalemia and hypomagnesemia. When venlafaxine was discontinued, the electrolyte imbalance resolved in the next 3 days. The mechanism by which venlafaxine might cause hypokalemia and hypomagnesemia in Gitelman syndrome, however, remains to be established. It seems reasonable to suggest that venlafaxine caused hyponatremia as a consequence of SIADH, with the renin-angiotensin-aldosterone system stimulated for renal sodium retention. Due to the dysfunction of sodium retention in the pathology of Gitelman syndrome, the renin-angiotensin-aldosterone system is overactivated to maintain an adequate amount of sodium in the body. Therefore, the resulting elevation of aldosterone level increased the severity of hypokalemia, and, in turn, hypokalemia led to hypomagnesemia. We present this case of hyponatremia, hypokalemia, and hypomagnesemia, which was almost certainly caused by venlafaxine therapy, to emphasize the importance of close monitoring of serum electrolyte concentration when venlafaxine is prescribed to patients with renal tubulopathy.

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Chi-Yung Shang, M.D.
Wei-Tsuen Soong, M.D.
Hsin-Nan Lin, M.D.
National Taiwan University Hospital
Taipei, Taiwan