Letters to the Editor

Financial Support for Letter Writing?

Sir: While I appreciated the honesty of Lee and Fowler[1] in revealing that their letter to the editor was supported by Eli Lilly and Company ("Funding for this letter was provided by Eli Lilly and Company"), I remain puzzled as to why and what it was that was funded by the pharmaceutical industry. Having written my share of letters to the editor (including this one), I wonder if anybody really needs funding for writing letters that do not contain any data? Does the funding reimburse the writer's employer for the fraction of time spent on writing a letter? Is it the paper and printer toner they get the money for? I can understand that the pharmaceutical industry would support small or large investigator-initiated studies that may be published as letters to the editor or larger articles. Maybe even a case series if any expensive laboratory studies were required. But a letter perpetuating the endless "seesaw" debate on diabetes mellitus and specific "atypical" antipsychotics? Truly puzzling!

Maybe the authors could educate us by elucidating this issue.

Dr. Lee was shown this letter and declined to comment.
Dr. Balon has received grant/research support from and served on the speakers/advisory board for Eli Lilly.

REFERENCE

1. Lee DW, Fowler RB. Olanzapine/risperidone and diabetes risk [letter]. J Clin Psychiatry 2003;64:847–848

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Response to Commentary: "Using Questionnaires to Screen for Psychiatric Disorders"

This letter is in response to Zimmerman et al., pages 605–610.

Sir: Zimmerman and colleagues[1] have raised several issues regarding the use of the Mood Disorder Questionnaire (MDQ) as a screening instrument for bipolar disorder in the community.[2] They express concern that the reported sensitivity of 28% and the specificity of 97% in the community sample may undermine its usefulness as a screening instrument in the community.

Put into context, these rates are consistent with existing self-report screening instruments for lifetime depression and other psychiatric disorders in the community. For example, in the Epidemiologic Catchment Area study, Eaton and colleagues[3] report a sensitivity of 29% and a specificity of 96% when using a self-report to screen for a lifetime history of depression. Tuunainen and colleagues[4] report a sensitivity of 34% and a specificity of 90% for lifetime major depression and dysthymia using the Center for Epidemiologic Studies-Depression scale (CES-D). Roberts et al.[5] report a sensitivity of 49% and a specificity of 74% for a past history of dysthymia. Murray and colleagues[6] used the Michigan Alcohol Screening Test (MAST) to screen for a lifetime diagnosis of alcohol dependence and alcohol abuse and report a sensitivity of 38% and a specificity of 97%. Using the short form of the Alcohol Dependence Data scale (SADD), the sensitivity was 11% and specificity 99% for the same conditions.

The situation changes substantially when screening for current illness rather than lifetime illness. For example, Beekman and colleagues[7] used the CES-D in a sample of older adults in the Netherlands and reported a weighted sensitivity of 100% and specificity of 88%. Garrison et al. reported a sensitivity of 85% and specificity of 49% for males using the CES-D.[8] Higher sensitivity and specificity are reported also in studies in which normal comparison groups are screened for a current disorder. For example, Zimmerman and Coryell,[9] using the CES-D, report a sensitivity of 88% and a specificity of 92% in a normal comparison group for a family study of mood disorders.

Methodological issues may have artifactually lowered the estimates of the sensitivity and specificity of the MDQ in our community survey.[2] There was often an interval of up to 6 months from the time of the mail-in MDQ screen and the follow-up Structured Clinical Interview for DSM-IV (SCID) diagnostic interview. If the SCID had been conducted at the same time as the screen, the results would likely have been much better. In fact, we did re-administer the MDQ immediately following the telephone SCID interview. The weighted sensitivity and specificity were 75% and 94%, respectively. This result strongly suggests that if we had been able to conduct the SCID interviews closer in time to the MDQ screen, the sensitivity and specificity would have been higher.

Zimmerman and colleagues[1] raised a question about the figure in the publication. They note that at an MDQ score of zero, "the sensitivity should have been close to 100% and the specificity close to 0%,"[1(p?)] which is not the case in the figure. In the figure, the score does not include the co-occurrence and psychosocial impairment items, which are critical to scoring MDQ positives. Therefore, the sensitivity is not 100% at an MDQ score of zero.

In conclusion, we acknowledge that there is much to be improved in the ability to screen for bipolar disorder in the community, and we agree that the MDQ has limitations. However, given the public health significance of bipolar disorder and its neglect in epidemiologic and primary care studies, having new tools for screening represents a step forward. The MDQ represents the current state of the art. We await the development of improved screening tools for bipolar disorder.

REFERENCES

1. Zimmerman M, Posternak MA, Chelminski I, et al. Using questionnaires to screen for psychiatric disorders: a comment on a study of screening for bipolar disorder in the community [commentary]. J Clin Psychiatry 2004;65:605–610
2. Hirschfeld RMA, Calabrese JR, Weissman MM, et al. Screening for bipolar disorder in the community. J Clin Psychiatry 2003;64:53–59
3. Eaton WW, Neufeld K, Chen L, et al. A comparison of self-report and clinical diagnostic interviews for depression: diagnostic interview schedule and schedules for clinical assessment in neuropsychiatry in the Baltimore Epidemiologic Catchment Area follow-up. Arch Gen Psychiatry 2000;57:217–222
4. Tuunainen A, Langer RD, Klauber MR, et al. Short version of the CES-D (Burnam screen) for depression in reference to the structured psychiatric interview. Psychiatry Res 2001;103:261–270
5. Roberts RE, Lewinsohn PM, Seeley JR. Screening for adolescent depression: a comparison of depression scales. J Am Acad Child Adolesc Psychiatry 1991;30:58–66
6. Murray RP, Barnes GE, Patton D. The relative performance of diverse measures of alcohol abuse and dependence in a community sample. J Stud Alcohol 1994;55:72–80
7. Beekman AT, Deeg DJ, Van Limbeek J, et al. Criterion validity of the Center for Epidemiologic Studies Depression scale (CES-D): results from a community-based sample of older subjects in the Netherlands. Psychol Med 1997;27:231–235
8. Garrison CZ, Addy CL, Jackson KL, et al. The CES-D as a screen for depression and other psychiatric disorders in adolescents. J Am Acad Child Adolesc Psychiatry 1991;30:636–641
9. Zimmerman M, Coryell W. Screening for major depressive disorder in the community: a comparison of measures. Psychol Assess 1994;6:71–74

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Schizophrenia as a Manifestation of X-Linked McLeod-Neuroacanthocytosis Syndrome

Sir: Neuroacanthocytosis syndromes represent a heterogeneous group of neurodegenerative disorders defined by the association of red blood cell (RBC) acanthocytosis and variable neurologic signs and symptoms.[1] A progressive chorea syndrome comparable to the prototype Huntington's disease represents the core clinical feature of a subgroup of neuroacanthocytosis syndromes, including the autosomal recessive choreoacanthocytosis (MIM #200150),[2] the autosomal dominant Huntington's disease–like disorder type 2 (MIM #606438),[3] and the X-linked McLeod syndrome (MIM #314850).[4]

The McLeod syndrome is defined by an abnormal expression of Kell and XK RBC antigens.[5,6] Affected males have RBC acanthocytosis and elevated serum creatine kinase levels and are prone to develop a progressive chorea syndrome with additional neuromuscular manifestations.[4,7,8] The disorder is caused by mutations of the *XK* gene encoding the XK protein, a ubiquitously expressed membrane transport protein.[9] The XK protein is linked to the Kell glycoprotein by a single disulfide bond, and the 2 proteins probably form a functional complex.[9–11] The Kell protein is an endothelin-3–converting enzyme generating the bioactive endothelin-3.[12] The XK protein shares important homologies with the ced-8 protein of the nematode *C. elegans*. Ced-8 acts as a cell death effector of the enzymatic apoptosis cascade that is initiated by the caspase ced-3.[13] The human homologue of ced-3, caspase-8, plays a crucial role in the pathogenesis of Huntington's disease.[14,15] Therefore, the striatal neurodegeneration in McLeod syndrome might be caused by XK-linked apoptosis dysregulation.

The patient described here belongs to a previously described McLeod family (individual IV-5 in Jung et al.[8]), and the following case report adds important psychiatric findings to the initial clinical description.

Case report. At the age of 48 years, Mr. A had normal neurologic examination results except for mild motor restlessness and absent deep tendon reflexes. Laboratory workup demonstrated RBC acanthocytosis (17%; normal, < 3%; Figure 1) and marked serum creatine kinase elevation (3100 U/L; normal, < 270 U/L). Cerebral magnetic resonance imaging findings were normal, but [18F]-FDG (2-fluoro-2-deoxy-glucose) positron emission tomography revealed severely impaired striatal glucose metabolism without abnormalities of the cerebral cortex.[8] Neuropsychological examination demonstrated mild impairment of the figural memory without deficits of verbal or executive functions.[8]

Mr. A's psychiatric status at the first neurologic visit in 1999 was normal, but his psychiatric history fulfilled the DSM-IV[16] criteria for schizophrenia. He had normal childhood psychomotor development and superior school achievement, and he received a university degree in Slavic languages and literature. At the age of 39 years, he was hospitalized with an initial schizophrenic episode manifesting with incoherent thoughts, paranoid delusions, verbal and visual hallucinations, and affective lability. Treatment with zuclopenthixol acetate led to a remission of the psychopathology. Three years later, after discontinuation of the neuroleptic medication, Mr. A presented again with a schizophrenic episode that remitted with clozapine treatment. During the following years, he had recurrent schizophrenic episodes that required several psychiatric hospitalizations. Clozapine and lithium treatment were combined, resulting in a reduced frequency of psychotic episodes during the 2 years preceding the first neurologic visit.

Figure 1. Peripheral Blood Smear of the Patient Showing Significant Acanthocytosis[a]
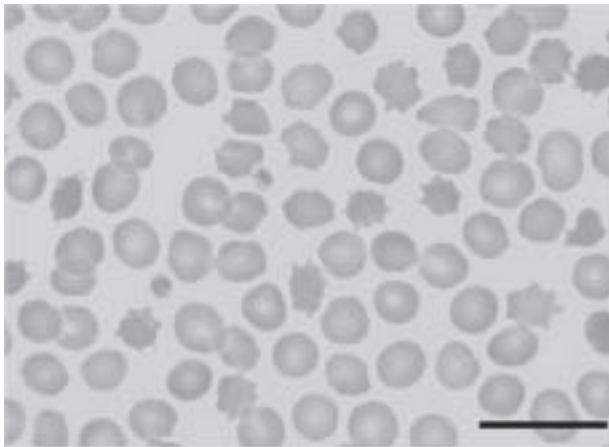
[a]May-Grunwald-Giemsa stain (Merck, Darmstadt, Germany); ×100; scale bar = 25 μm.

Over the course of 4 years of follow-up after the first visit, however, the patient's psychiatric state rapidly deteriorated. Psychotic episodes with more prominent affective symptoms such as severe depressive syndromes, delusion of impoverishment, and markedly incoherent thoughts frequently recurred. A combination of quetiapine, mirtazapine, and valproic acid was initiated. Nevertheless, the intervals between Mr. A's psychotic episodes shortened, and his psychiatric symptoms became persistent. In addition, his subcortical cognitive deficits deteriorated, and a choreiform movement disorder gradually developed. Presently, at the age of 52 years, the patient has significant psychiatric, cognitive, and neurologic impairment that makes him fully dependent on social welfare.

The symptoms of the patient described in our report fulfilled the DSM-IV[16] criteria for schizophrenia. Although we cannot absolutely rule out an independent psychiatric disease, the clinical findings, disease course, and neuroradiological findings strongly suggest that McLeod syndrome is the cause of the patient's psychopathology. Basal ganglia diseases may impair basal ganglia–prefrontal cortical circuits that are proposed to be a crucial factor in schizophrenia genesis.[17,18] Therefore, the McLeod syndrome might represent a model for the understanding of schizophrenia pathophysiology.

All McLeod patients reported to date had absent tendon reflexes of at least the ankle tendons, significant RBC acanthocytosis, and elevated serum creatine kinase levels.[4,7,8] It is worthy of note that a majority of McLeod patients developed psychiatric abnormalities during the disease course.[4] Psychiatric symptoms were heterogeneous, consisting of personality changes, depression, anxiety, paranoid delusions, and obsessive-compulsive disorder.[4,7,8,19] In addition, the association of schizophrenia-like symptoms and acanthocytosis was reported in 1 patient without further specification of the disease.[20]

Our case report demonstrates that schizophrenia-like symptoms may be the prominent initial clinical manifestation of a McLeod-neuroacanthocytosis syndrome. Consequently, we propose that a clinical examination for absent tendon reflexes as well as a laboratory screening for RBC acanthocytosis and elevated serum creatine kinase level should be included in the workup of patients with a first psychotic episode, particularly if a chorea syndrome or another movement disorder is present.

Because the discrimination of primary movement disorders and drug-induced dyskinesias may be difficult, and because patients with neurologic basal ganglia diseases may be more likely to develop extrapyramidal adverse effects, clinical and laboratory screening for neuroacanthocytosis is also suggested in patients with drug-induced dyskinesias.

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

REFERENCES

 1. Rampoldi L, Danek A, Monaco AP. Clinical features and molecular bases of neuroacanthocytosis. J Mol Med 2002;80:475–491
 2. Rampoldi L, Dobson-Stone C, Rubio JP, et al. A conserved sorting-associated protein is mutant in chorea-acanthocytosis. Nat Genet 2001;28:119–120
 3. Walker RH, Rasmussen A, Rudnicki D, et al. Huntington's disease–like 2 can present as chorea-acanthocytosis. Neurology 2003;61:1002–1004
 4. Danek A, Rubio JP, Rampoldi L, et al. McLeod neuroacanthocytosis: genotype and phenotype. Ann Neurol 2001;50:755–764
 5. Allen FH, Krabbe SMR, Corcoran PA. A new phenotype (McLeod) in the Kell blood-group system. Vox Sang 1961;6:555–560
 6. Wimer BM, Marsh WL, Taswell HF, et al. Haematological changes associated with the McLeod phenotype of the Kell blood group system. Br J Haematol 1977;36:219–224
 7. Hardie RJ, Pullon HW, Harding AE, et al. Neuroacanthocytosis: a clinical, haematological and pathological study of 19 cases. Brain 1991;114:13–49
 8. Jung HH, Hergersberg M, Kneifel S, et al. McLeod syndrome: a novel mutation, predominant psychiatric manifestations, and distinct striatal imaging findings. Ann Neurol 2001;49:384–392
 9. Ho M, Chelly J, Carter N, et al. Isolation of the gene for McLeod syndrome that encodes a novel membrane transport protein. Cell 1994;77:869–880
10. Russo D, Wu X, Redman CM, et al. Expression of Kell blood group protein in nonerythroid tissues. Blood 2000;96:340–346
11. Jung HH, Russo D, Redman C, et al. Kell and XK immunohistochemistry in McLeod myopathy. Muscle Nerve 2001;24:1346–1351
12. Lee S, Lin M, Mele A, et al. Proteolytic processing of big endothelin-3 by the Kell blood group protein. Blood 1999;94:1440–1450
13. Stanfield GM, Horvitz HR. The ced-8 gene controls the timing of programmed cell deaths in *C. elegans*. Mol Cell 2000;5:423–433
14. Hackam AS, Yassa AS, Singaraja R, et al. Huntingtin interacting protein 1 induces apoptosis via a novel caspase-dependent death effector domain. J Biol Chem 2000;275:41299–41308
15. Gervais FG, Singaraja R, Xanthoudakis S, et al. Recruitment and activation of caspase-8 by the Huntingtin-interacting protein Hip-1 and a novel partner Hippi. Nat Cell Biol 2002;4:95–105
16. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition. Washington, DC: American Psychiatric Association; 1994
17. Tsuang D, DiGiacomo L, Lipe H, et al. Familial aggregation of schizophrenia-like symptoms in Huntington's disease. Am J Med Genet 1998;81:323–327
18. Bunney WE, Bunney BG. Evidence for a compromised dorsolateral prefrontal cortical parallel circuit in schizophrenia. Brain Res Brain Res Rev 2000;31:138–146
19. Witt TN, Danek A, Reiter M, et al. McLeod syndrome: a distinct form of neuroacanthocytosis: report of two cases and literature review with emphasis on neuromuscular manifestations. J Neurol 1992;239:302–306
20. Rovito DA, Pirone FJ. Acanthocytosis associated with schizophrenia. Am J Psychiatry 1963;120:182–185

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Diabetic Ketoacidosis, Neuroleptic Malignant Syndrome, and Myocardial Infarction in a Patient Taking Risperidone and Lithium Carbonate

Sir: Atypical antipsychotic–induced hyperglycemia[1] and ketoacidosis[2,3] are well documented. We report the occurrence of hyperglycemic ketoacidosis, neuroleptic malignant syndrome, and myocardial infarction in a patient taking risperidone and lithium.

Case report. Mr. A, a 46-year-old man without family history of diabetes, had been treated in our psychiatric clinic since 1998 with lithium carbonate, 900 mg, and risperidone, 3 mg, daily. In August 1999, Mr. A's blood lithium level and all other laboratory data were within normal limits. On September 16, 2000, the patient was brought to the emergency room in an acute manic state.

In the emergency room (9:00 a.m.), the patient's temperature of 100.6°F, blood pressure of 162/82 mm Hg, and pulse of 108 were noted. All psychiatric medications were stopped. At 4:00 p.m., Mr. A was somnolent, with a temperature of 96.3°F, blood pressure of 148/110 mm Hg, and pulse rate of 130. At 8:00 p.m. on the psychiatric ward, a blood pressure of 162/100 mm Hg, temperature of 100.9°F, and pulse rate of 122 were recorded. The next morning, the patient's temperature was 103°F with a pulse of 152. He had a seizure followed by coma. His blood glucose level was 1201 mg/dL and blood urea nitrogen (BUN) level was 66 mg/dL, necessitating transfer to the intensive care unit.

He rapidly decompensated, requiring intubation and cooling measures. (See Table 1 for laboratory test results.) The patient's cerebrospinal fluid glucose level was 549 mg/dL. Cerebrospinal fluid and blood culture and toxicology screen results were negative. Intravenous dantrolene (140 mg as a loading dose and 70 mg 4 times daily), metoprolol for blood pressure, bicarbonate for alkalinization, ceftriaxone for infection, insulin for hyperglycemia, furosemide for preventing oliguria, isosorbide dinitrate for acute kidney failure, and heparin for preventing intravascular coagulation were instituted. Electrocardiogram results indicated nonspecific T wave abnormalities, and anterolateral subepicardial injury. With bromocriptine treatment, he started recovering, with laboratory values showing a trend toward improvement. On September 21, due to lack of supply, dantrolene was substituted with bromocriptine, 2.5 mg t.i.d. On September 23, his laboratory values were within normal limits, and he was extubated and transferred to the psychiatry unit for the treatment of bipolar disorder with lithium. On October 3, he was discharged on lithium treatment as improved. His laboratory results have been within normal limits for over 2 years on lithium treatment alone, without antidiabetic therapy.

Diabetes was likely to have been associated with risperidone treatment in this case, as reinstitution of lithium without risperidone resulted in its reversal. The ensuing dehydration and electrolyte imbalance predisposed the patient to neuroleptic malignant syndrome.[2–4] In animals, hyperglycemia can diminish dopaminergic transmission and increase postsynaptic dopaminergic supersensitivity.[5,6] Atypical antipsychotic–induced hyperglycemia should be recognized and treated promptly to prevent neuroleptic malignant syndrome.

Table 1. Laboratory Values for a Patient Treated With Risperidone and Lithium Carbonate Who Developed 3 Life-Threatening Medical Conditions

Component	Patient's Value	Reference Range
Serum/plasma levels		
White blood cell count	25,200/mm^3	4500–11,000/mm^3
Hemoglobin	16.2 g/dL	14.0–17.5 g/dL
Hematocrit	47.3%	41%–50%
Sodium	140 mmol/L	136–142 mmol/L
Potassium	4.6 mmol/L	3.5–5.0 mmol/L
Chloride	98 mmol/L	96–106 mmol/L
BUN	66 mg/dL	0.3–1.2 mg/dL
Glucose	1201 mg/dL	70–110 mg/dL
Troponin I	139 ng/dL	< 0.04 ng/dL
Creatine phosphokinase	66,559 IU/L	24–90 IU/L
Glutamic acid decarboxylase	< 1 U/L	0–30 U/L
Blood gases		
pH	7.579	7.35–7.45
P$_{CO_2}$	30.5 mm Hg	35–45 mm Hg
P$_{O_2}$	90.0 mm Hg	80–100 mm Hg
HCO$_3$	28.8 mmol/L	22–30 mmol/L
Standard bicarbonate	31.0 mmol/L	21–28 mmol/L
Base excess	+7.9	+7.45

REFERENCES

1. Ananth J, Venkatesh R, Burgoyne K, et al. Atypical antipsychotic drug use and diabetes. Psychother Psychosom 2002;71:244–254
2. Yang SH, McNealy MJ. Rhabdomyolysis, pancreatitis, hyperglycemia with ziprasidone [letter]. Am J Psychiatry 2002;159:1435
3. de Boer C, Gaete HP. Neuroleptic malignant syndrome and diabetic ketoacidosis. Br J Psychiatry 1992;161:856–858
4. Malyuk R, Gibson B, Procyshyn RM, et al. Olanzapine associated weight gain, hyperglycemia and neuroleptic malignant syndrome: case report. Int J Geriatr Psychiatry 2002;17:326–328
5. Chu PC, Lin MT, Shian LR, et al. Alterations in physiologic functions and in brain monoamine content in streptozocin-diabetic rats. Diabetes 1986;35:481–485
6. Saller CF, Kopin IJ. Glucose potentiates haloperidol induced catalepsy. Life Sci 1981;29:2337–2341

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Dosing Differences Between Valproic Acid Concentrate and Divalproex Sodium: A Case Report

Sir: Valproic acid concentrate is an immediate-release preparation of valproic acid with rapid absorption following oral administration.[1] Divalproex sodium tablets are a delayed-release formulation comprising valproate sodium and valproic acid in a 1:1 molar relationship.[2] Equivalent oral doses of divalproex sodium tablets and valproic acid concentrate deliver equivalent quantities of valproate ion systemically. The drug manufacturer recommends initiating the same total daily doses when converting a patient from valproic acid to valproex

sodium.[1,2] There is one report of a statistically significant decrease by 14.4% (p = .001) in plasma valproate concentrations upon switching dosage forms (from divalproex sodium to valproic acid); however, these changes were not found to be clinically significant, and investigators supported safely switching dosage forms in stabilized patients.[3] We will discuss a patient who displayed an unusual difference in bioavailability between valproic acid concentrate and divalproex sodium tablets.

Case report. Mr. A, a 35-year-old white man with an Axis I diagnosis of schizophrenia and an Axis III diagnosis of history of seizure disorder, was transferred to a treatment-refractory unit managed by the senior author (J.d.L.). He had been compliant with medications in the past 4 years, which was confirmed by adequate serial blood drug level concentrations. In May 1999, he was stabilized on valproic acid concentrate at a dose of 5250 mg/day with no seizure activity. His plasma valproate concentrations ranged from 55 to 100 mg/L (almost all within 60–90 mg/L, only 1 level was > 100 mg/L). The patient went through several unsuccessful antipsychotic trials before being started on clozapine treatment in December 2001. During the titration and stabilization of clozapine dosing, the patient's valproate levels remained in the range of 70 to 90 mg/L. His other medications included propranolol, 80 mg/day; benztropine, 1 mg/day; and docusate sodium, 250 mg/day. After being stabilized on clozapine, 700 mg/day, the patient's psychosis had improved significantly. He began to complain about the taste of valproic acid concentrate. With the assumption of bioequivalent formulations, we switched Mr. A to the exact total daily dose (5250 mg/day) of divalproex sodium in November 2002. No other changes were made to his concurrent medication regimen. Surprisingly, 4 weeks later, Mr. A's blood valproate level was 145 mg/L. Aside from slight drowsiness, which was difficult to distinguish from clozapine-associated sedation, there were no obvious signs of toxicity. The divalproex sodium dose was decreased to 3750 mg/day, with a resulting valproate level of 135 mg/L. The divalproex sodium dose was further decreased to 3000 mg/day, with a resulting level of 127 mg/L. Once again, the dose was further reduced to 2500 mg/day, with a resulting level of 120 mg/L. The patient was finally stabilized and discharged on divalproex sodium, 2000 mg/day. At this dose, serial blood valproate levels fell within the desired range (70–90 mg/L). Therefore, in this patient, the bioavailability of valproic acid concentrate appears to be at least 2 to 3 times lower than that of divalproex sodium tablets.

This is a truly unique case in our practice experience. During the time frame of this case, there were no other reports of unusual blood valproate levels. In our institution, all plasma valproate levels are drawn at approximately 8:00 a.m. The senior author (J.d.L.) has switched several patients between dosage formulations with no significant differences in blood valproate levels. Moreover, literature does not provide similar descriptions or possible explanations. One possible hypothesis may include changes in bioequivalency, possibly related to pharmacokinetic variability in absorption or metabolism of valproic acid concentrate compared with that of divalproex sodium in this patient for unknown reasons. Unfortunately, we cannot find evidence of literature support for this hypothesis. However, on the basis of this rare case, it may be advisable to closely monitor plasma valproate concentrations when switching between dosing formulations of valproic acid.

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

REFERENCES

1. Depakene [package insert]. Abbott Park, Ill: Abbott Laboratories; 2001
2. Depakote [package insert]. Abbott Park, Ill: Abbott Laboratories; 2002
3. Sherr JD, Kelly DL. Substitution of immediate-release valproic acid for divalproex sodium for adult psychiatric inpatients. Psychiatr Serv 1998;49:1355–1357

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A Case of Kleptomania Correlating With Premenstrual Dysphoria

Sir: Evidence suggesting efficacy of the serotonin reuptake inhibitors (SRIs) in the treatment of impulse-control disorders,[1–3] including kleptomania[4,5] and premenstrual dysphoric disorder (PMDD),[6] suggests that abnormal serotonin neurotransmission is implicated in their pathophysiology. If kleptomania is more common in women, although reporting bias clouds the data, then the periodic hormonal effects of estrogen on the serotonin system may be at play. We report on a patient with kleptomania and PMDD whose kleptomania symptoms varied consistently with the menstrual cycle, significantly worsening during the luteal phase. Treatment with escitalopram, 10 mg/day, for 4 weeks led to complete resolution of both kleptomania and PMDD symptoms.

Case report. Ms. A is a 48-year-old, college-educated, married, white woman who presented to our clinic for treatment of impulsive stealing. A diagnostic interview, including the Mini-International Neuropsychiatric Interview[7] and the Minnesota Impulse Control Disorders Questionnaire,[8] revealed a diagnosis of kleptomania with comorbid PMDD according to DSM-IV criteria[9] and a history of 1 brief major depressive episode 4 years prior to presentation. The patient reported a frequency of stealing that averaged 2.5 episodes a week and that involved unnecessary, inexpensive items she could easily afford. She reported that her preoccupation with stealing produced great stress on her family and her job as a travel advisor. She had no history of substance abuse or medical illnesses and no manifestations of antisocial or other pathological personality types. The patient had never been formally diagnosed with kleptomania or PMDD and had never received psychotherapy or medications for these conditions.

Ms. A's kleptomania symptoms began at age 14 years, 4 months after menarche. Since onset of her kleptomania, the patient has consistently noted a marked intensification of her urges to steal in the 10 to 14 days before menses; during that time, the frequency of her stealing usually increases to about 4 episodes weekly before decreasing again to about once weekly in the first 2 weeks of her cycle. The patient reported 4 kleptomania-related arrests, including one that led to a 5-day jail sentence and 3 additional apprehensions by store guards. All arrests and apprehensions occurred during the luteal phase of her cycle and were likely due to increased exposure from more reckless stealing. Her PMDD symptoms included depressed mood, affective lability, lack of energy, anger, and headaches;

these symptoms occurred exclusively during the luteal phase and remitted completely within a few days after the start of the follicular phase. The PMDD diagnosis was not confirmed prospectively with daily symptom ratings.

Given open-label reports of SRI success in treating kleptomania[4,5] and well-documented efficacy in the treatment of PMDD,[6,10,11] pharmacotherapy was initiated with escitalopram, 10 mg/day, given throughout the menstrual cycle. Excepting insomnia that resolved by day 7, no side effects were encountered. By week 4, the patient's kleptomania urges had completely subsided and her stealing had ceased. Her PMDD symptoms remitted, and no intensification of urges was noted during the following luteal phase. Two months after initiation of daily escitalopram, the patient remains continuously free of kleptomania urges and has no PMDD symptoms. Prior to treatment, her longest stealing-free period lasted 4 months, following her 5-day jail sentence on kleptomania-related charges 6 years prior to presentation. Given that PMDD and kleptomania have been in remission for only 2 months, we cannot be sure that remission will be sustained with continued treatment. Whether and how quickly the symptoms would recur if treatment were stopped also remains unknown.

REFERENCES

1. Bloch MR, Elliott M, Thompson H, et al. Fluoxetine in pathological skin-picking, open-label and double-blind results. Psychosomatics 2001;42:314–319
2. Kim SW, Grant JE, Adson DE, et al. A double-blind placebo-controlled study of the efficacy and safety of paroxetine in the treatment of pathological gambling. J Clin Psychiatry 2002;63:501–507
3. Koran LM, Chuong HW, Bullock KD, et al. Citalopram for compulsive shopping disorder: an open-label study followed by a double-blind discontinuation. J Clin Psychiatry 2003;64:793–798
4. McElroy SL, Pope HG, Hudson JL, et al. Kleptomania: a report of 20 cases. Am J Psychiatry 1991;48:652–657
5. Lepkifker E, Dannon PN, Ziv R, et al. The treatment of kleptomania with serotonin reuptake inhibitors. Clin Neuropharmacol 1999;22:40–43
6. Eriksson E, Hedberg MA, Abdersch B, et al. The serotonin reuptake inhibitor paroxetine is superior to the noradrenaline reuptake inhibitor maprotiline in the treatment of premenstrual syndrome. Neuropsychopharmacology 1995;12:167–176
7. Lecrubier Y, Sheehan D, Weiller E, et al. The Mini-International Neuropsychiatric Interview (MINI) short diagnostic structured interview: reliability and validity according to the CIDI. Eur Psychiatry 1997;12:224–231
8. Christenson GA, Faber RF, de Zwaan M, et al. Compulsive buying: descriptive characteristics and psychiatric comorbidity. J Clin Psychiatry 1994;55:5–11
9. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition. Washington, DC: American Psychiatric Association; 1994
10. Steiner M, Steinberg S, Stewart D, et al. Fluoxetine in the treatment of premenstrual dysphoria. N Engl J Med 1995;332:1529–1534
11. Yonkers KA, Halbreich U, Freeman E, et al. Symptomatic improvement of premenstrual dysphoric disorder with sertraline treatment: a randomized controlled trial. JAMA 1997;278:983–988

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Acetaminophen Preferable to Ibuprofen for Pretreatment of Electroconvulsive Therapy–Induced Headache

Sir: It is curious that Leung and colleagues[1] would promote first-line use of a nonsteroidal anti-inflammatory drug (NSAID), albeit the least problematic one, for pretreatment of electroconvulsive therapy (ECT)–induced headache. It is recommended that ibuprofen be given with food or milk, but pre-ECT medication must be given on an empty stomach, with a sip of water. The gastrointestinal complications of NSAID treatment are well documented.[2]

While the article[1] mentions other analgesics such as acetaminophen and narcotics for post-ECT headaches, the study compared only ibuprofen and placebo pretreatment. The implication was that ibuprofen was somehow superior to acetaminophen or other pretreatment analgesics. That is misleading, as acetaminophen is generally as good as or better than ibuprofen for analgesia for headache.[3] Ultimately, though, the added risk of gastrointestinal side effects from ibuprofen should make acetaminophen the first choice specifically in cases in which the medication must be given on an empty stomach.

REFERENCES

1. Leung M, Hollander Y, Brown GR. Pretreatment with ibuprofen to prevent electroconvulsive therapy–induced headache. J Clin Psychiatry 2003;64:551–553
2. Sandler RS, Bjorkman DJ, Laine LA. Risk Reduction and the GI Tract: From Theory to Reality [Medscape Web site]. June 5, 2003. Available at: http://www.medscape.com/viewprogram2416_pnt.1-44. Accessed Sept 1, 2003
3. Barclay L. Acetaminophen as effective as ibuprofen for high-altitude headache. J Emerg Med 2003;24:383–387

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