

CASE REPORT

Adjunctive Methylphenidate in the Treatment of Bulimia Nervosa Co-occurring with Bipolar Disorder and Substance Dependence

by ANNA I. GUERDJIKOVA, PhD, and SUSAN L. McELROY, MD

Dr. Guerdjikova is from the Lindner Center of HOPE in Mason, Ohio, and Dr. McElroy is from the Department of Psychiatry and Behavioral Neuroscience, University of Cincinnati College of Medicine in Cincinnati, Ohio.

Innov Clin Neurosci. 2013;10(2):30–33

FUNDING: No funding was received for this article.

FINANCIAL DISCLOSURES: The authors do not have conflicts of interest relevant to the content of this article.

ADDRESS CORRESPONDENCE TO: Anna I. Guerdjikova PhD, Lindner Center of HOPE, Research Institute, 4075 Old Western Row Rd., Mason, Ohio 45040. Phone: 513-536-0721, Fax: 513-536-0709;
E-mail: anna.guerdjikova@lindnercenter.org

KEY WORDS: methylphenidate, stimulant, bipolar disorder, bulimia nervosa

ABSTRACT

Bulimia nervosa is associated with bipolar disorder, substance dependence, attention-deficit hyperactivity disorder, and anxiety disorders. Few reports, however, have addressed the treatment of patients with all of these conditions. We describe a young woman with bulimia nervosa, bipolar I disorder, cocaine and alcohol dependence, attention-deficit hyperactivity disorder, and panic disorder who achieved a sustained (>1 year) remission of her bulimia nervosa symptoms and significant improvement of her attention-deficit hyperactivity disorder symptoms with adjunctive methylphenidate after her bipolar, substance use, and panic disorders were successfully treated with hospitalization, intensive psychotherapy, quetiapine, and lamotrigine. Further research into the use of stimulants in bulimia nervosa, including in patients with complex co-morbidity, is required.

INTRODUCTION

Bulimia nervosa (BN) is associated with bipolar disorder, substance dependence, attention-deficit hyperactivity disorder (ADHD), and anxiety disorders.[1,2] However, there are no empirical data regarding the treatment of patients with all of these conditions.

We describe the successful treatment of a patient with BN, bipolar I disorder, cocaine and alcohol dependence, ADHD, and panic disorder. Her BN symptoms remitted for a period of over one year and her ADHD symptoms significantly improved with the stimulant medication methylphenidate, after her bipolar, substance use, and panic disorders were successfully treated with hospitalization, intensive psychotherapy, quetiapine, and lamotrigine. Although there are case reports of binge eating and purging behaviors in patients with BN (with and without ADHD) responding to treatment with stimulants,[3-6] to our knowledge, no report has described the use of a stimulant to treat BN in a patient with bipolar disorder and/or substance dependence.

CASE REPORT

Ms. D was a 32-year-old single, white woman who came to our attention when she was hospitalized for the treatment of alcohol and cocaine dependence and bipolar I disorder in August of 2010. Psychiatric

assessment, which included the Structured Clinical Interview for DSM-IV-TR (SCID)[7] revealed BN, purging type; bipolar I disorder, current episode hypomanic; alcohol dependence, with physiological dependence, early partial remission; cocaine dependence, with physiological dependence, in a controlled environment; and panic disorder. As a child, she had been diagnosed with ADHD and treated intermittently with methylphenidate.

Ms. D's mood disorder symptoms began when she was eight years old. She described at least two manic episodes and numerous depressive and hypomanic episodes, but had only received paroxetine and mirtazapine for depression and anxiety. A trial of atomoxetine made her feel worse. She had cocaine and alcohol dependence between ages of 18 and 21. She sustained sobriety for more than nine years until the summer of 2010 when her substance dependence relapsed. Immediately before her hospitalization at our center she had completed a five-day detoxification program.

Ms. D reported binge eating episodes followed by self-induced vomiting up to three times a day from age 18 years until the age of 27 years, when she entered a residential eating disorders treatment program and her symptoms subsequently remitted for a period of nine months. By age 29 years, however, she had completely slipped back into her earlier binge-purge routine. Six months prior to her hospitalization with us, she was binge eating and vomiting daily, and she had begun to abuse laxatives. In the three months prior to her admission, she said she was binging and purging 50 percent of the time and abusing alcohol and cocaine the other 50 percent of the time.

During hospitalization, her hypomanic and anxiety symptoms improved with quetiapine (600mg/day) without emergence of depression or anxiety, and her substance use and BN symptoms responded to intensive psychosocial treatment. Quetiapine was chosen because of its efficacy in mania, bipolar depression, and anxiety.[8] Upon discharge, Ms. D received outpatient care in our center with intensive psychotherapy and medication management. Her body mass index (BMI) at that time was 19.7kg/m^2, decreased from 20.5kg/m^2 upon admission.

Several months into her outpatient treatment, lamotrigine (titrated to 300mg) was added for emergent depressive symptoms. Her mood quickly stabilized and she remained euthymic and alcohol and drug free for the next 24 months. Her BN, however, relapsed and progressed to daily binge-purge episodes, which would increase to 2 to 3 episodes per day under stress. Despite continued psychotherapy and trials with aripiprazole, topiramate, acamprosate, and ondansteron, she also reported ongoing impaired concentration, inability to focus, and difficulty maintaining attention on one task.

In the middle of August 2011, she was started on oral methylphenidate, 18mg/day, to target both BN and ADHD symptoms. In September 2011, her dose was increased to 36mg/day and then to 54mg/day. In late September 2011, within several days of increasing the methylphenidate from 54mg/day to 72mg/day, Ms.D achieved complete remission of her BN. Her urges to binge eat resolved, she was able to control her food intake without binge eating, she made healthier food choices, and her eating habits became regular (i.e., three meals and one snack daily). Her BMI and vital signs remained stable. She reported improved sleeping habits and no side effects. She denied any increase in urges to use alcohol or cocaine and remained sober. Moreover, she also denied any return of her anxiety symptoms. In addition, she reported much improved concentration and functioning, began volunteering, and started classes.

In February 2012, Ms.D was switched to a daily 20mg methylphenidate transdermal patch in order to help further improve her concentration, which she said fluctuated throughout the day. In March 2012, her methylphenidate dose was increased to the 30mg daily patch. Her BN symptoms remained in complete remission and she reported improved ability to focus, stay on track, and complete tasks. At her last visit in September 2012, she had been euthymic and sober for over two years and in complete sustained remission from her BN for over one year. She reported not being "codependent" on her boyfriend or parents for the first time in her life. She had gained 3.6kg since her discharge from the hospital a little over two years ago and had maintained a stable BMI of 21kg/m^2 in the last eight months.

DISCUSSION

We present the case of a 32-year old woman with BN in conjunction with bipolar I disorder, cocaine and alcohol dependence, ADHD, and panic disorder, which all remitted on the combination of quetiapine, lamotrigine and methylphenidate administered in conjunction with psychosocial treatment. While the first two medications controlled the patient's mood and anxiety symptoms, the adjunctive stimulant resulted in a greater than 12- month remission of BN symptoms along with improved concentration and focus without causing increased urges to use substances or in mood instability or anxiety. Of note, in this particular case, we chose methylphenidate rather than amphetamine because the former might be associated with reduced abuse liability. Although no control data are available to support this notion in humans, preclinical research has suggested that in ADHD rat models, methylphenidate administration is associated with less "liking" of the drug as compared to amphetamines.[9]

Methylphenidate is a psychostimulant drug approved by the United States Food and Drug Administration (FDA) for treatment of ADHD.[10] It acts as a norepinephrine and dopamine reuptake inhibitor, thus increasing the level of the dopamine in the brain.[11,12] Preliminary data suggest that methylphenidate might also affect serotonin metabolism.[13] While the neurobiology of BN is not completely understood, dysregulation of both

dopamine and serotonin neurotransmitter systems has been implicated in BN pathogenesis.[14–16] Dopamine transmission abnormalities, in particular, have been well documented in the literature in subjects with BN in genetic[17–20] and imaging studies,[21–23] and thus we hypothesized that by exerting its dopamine-modulating properties methylphenidate might improve BN symptoms in Mr.D's case. Furthermore, our case report is consistent with others describing reduction of binge eating and purging behaviors in patients with BN when treated with methylphenidate and other stimulants.[3-6]

Despite extensive data on the co-morbidity between BN and both bipolar disorder and substance dependence,[24,25] to our knowledge, only one previous report has described the pharmacotherapeutic treatment of a patient with all three conditions. In this case report, a 57-year-old woman with severe BN, bipolar II depression, and a past history of alcohol abuse responded to combination therapy with olanzepine (5mg/day) and topiramate (400mg/day).[26] Ms. D was given a trial of topiramate 100mg/day in the early stages of her outpatient treatment with us, but she discontinued the drug because of sedation and cognitive impairment.

Randomized, placebo-controlled trials have shown that stimulants can improve ADHD symptoms in children and adolescents with bipolar disorder when added to mood-stabilizing agents.[27,28] Additionally, stimulant augmentation was not associated with worsening of mood symptoms. Studies of stimulants for cocaine dependence, however, have been mixed.[29] Of two controlled trials of methylphenidate in the treatment of cocaine dependence co-occurring with ADHD,[30,31] one showed a significantly greater reduction in ADHD symptoms in the methylphenidate group but no group differences in cocaine use outcomes,[30] while the other found no significant between-group differences in ADHD symptom response but that ADHD treatment responders were more likely to have a reduction in cocaine use compared with non-ADHD responders.[31]

In adults with bipolar disorder, ADHD is best confirmed when typical symptoms occur during periods of sustained euthymia.[32] It has been suggested that individuals with bipolar disorder and ADHD, particularly those with bipolar I disorder, might be at risk for mood destabilization with stimulant monotherapy, and thus should be prescribed mood-stabilizing medications before initiating ADHD therapies. Moreover, antidepressant monotherapy is generally not recommended for bipolar I disorder, as it may cause worsening of mood symptomatology.[33] Effective mood stabilization with quetiapine and lamotrigine prior to methylphenidade augmentation appeared critical for Ms.D, because her BN and ADHD symptoms had not responded to earlier trials of antidepressants, methylphenidate, or atomoxetine when given alone.

To our knowledge, this is the first scientific report of a stimulant being successfully used to treat BN in a patient with co-occurring bipolar I disorder and substance dependence. It illustrates the potential benefit of methylphenidate in treating BN, including when it co-occurs with bipolar disorder and substance dependence. Further research exploring various therapeutic options for such patients is called for. Also, randomized, placebo-controlled studies of stimulants in BN may be warranted.

CONSENT

Ms.D signed a document allowing her treatment team to use her de-identified data to prepare this scientific report.

REFERENCES

1. Hudson JI, Hiripi E, Pope HG, Jr., et al. The prevalence and correlates of eating disorders in the National Comorbidity Survey Replication. *Biol Psychiatry.* 2007;613:348–58.
2. Swanson SA, Crow SJ, Le Grange D, et al. Prevalence and correlates of eating disorders in adolescents. Results from the national comorbidity survey replication adolescent supplement. *Arch Gen Psychiatry. 2011;*687:714–723.
3. Drimmer EJ. Stimulant treatment of bulimia nervosa with and without attention-deficit disorder: three case reports. *Nutrition.* 2003;191:76–77.
4. Schweickert LA, Strober M, Moskowitz A. Efficacy of methylphenidate in bulimia nervosa comorbid with attention-deficit hyperactivity disorder: a case report. *Int J Eat Disord.*1997;213:299–301.
5. Sokol MS, Gray NS, Goldstein A, et al. Methylphenidate treatment for bulimia nervosa associated with a cluster B personality disorder. *Int J Eat Disord.* 1999;252:233–237.
6. Dukarm CP. Bulimia nervosa and attention deficit hyperactivity disorder: a possible role for stimulant medication. *J Womens Health* (Larchmt). 2005;144:345–350.
7. First M, Spitzer R, Gibbon M, et al. *Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Research Version, Patient Edition (SCID-I/P).* New York, NY: Biometrics Research Department, New York State Psychiatric Institute; 2002.
8. Sheehan DV, Harnett-Sheehan K, Hidalgo RB, et al. Randomized, placebo-controlled trial of quetiapine XR and divalproex ER monotherapies in the treatment of the anxious bipolar patient. *J Affect Disord.* 2013;145(1):83–94.
9. dela Pena I, Lee JC, Lee HL, et al. Differential behavioral responses of the spontaneously hypertensive rat to methylphenidate and methamphetamine: lack of a rewarding effect of repeated methylphenidate treatment. *Neurosci Lett.* 2012;5142:189–193.
10. United States Food and Drug Administration. Ritalin. http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.DrugDetails. Accessed February 1, 2013.
11. Gottlieb S. Methylphenidate works by increasing dopamine levels. *BMJ.* 2001;3227281:259.
12. Volkow ND, Wang G, Fowler JS, et al.

Therapeutic doses of oral methylphenidate significantly increase extracellular dopamine in the human brain. *J Neurosci.* 2001;212:RC121.
13. Molina-Carballo A, Naranjo-Gomez A, Uberos J, et al. Methylphenidate effects on blood serotonin and melatonin levels may help to synchronise biological rhythms in children with ADHD. *J Psychiatr Res.* 2013;47(3):377–383.
14. Kaye WH, Wierenga CE, Bailer UF, et al. Does a shared neurobiology for foods and drugs of abuse contribute to extremes of food ingestion in anorexia and bulimia nervosa? *Biol Psychiatry.* 2013 Feb 1. [epub ahead of print].
15. Broft AI, Berner LA, Martinez D, et al. Bulimia nervosa and evidence for striatal dopamine dysregulation: a conceptual review. *Physiol Behav.* 2011;1041:122–127.
16. Kaye W. Neurobiology of anorexia and bulimia nervosa. *Physiol Behav.* 2008;941:121–135.
17. Thaler L, Groleau P, Badawi G, et al. Epistatic interactions implicating dopaminergic genes in bulimia nervosa (BN): relationships to eating- and personality-related psychopathology. *Prog Neuropsychopharmacol Biol Psychiatry.* 2012;39(1):120–128.
18. Levitan RD, Kaplan AS, Davis C, et al. A season-of-birth/DRD4 interaction predicts maximal body mass index in women with bulimia nervosa. *Neuropsychopharmacology.* 2010;358:1729–1733.
19. Yilmaz Z, Kaplan AS, Zai CC, et al. COMT Val158Met variant and functional haplotypes associated with childhood ADHD history in women with bulimia nervosa. *Prog Neuropsychopharmacol Biol Psychiatry.* 2011;354:948–952.
20. Frieling H, Romer KD, Scholz S, et al. Epigenetic dysregulation of dopaminergic genes in eating disorders. *Int J Eat Disord.* 2009;437:577–583.
21. Frank GK, Reynolds JR, Shott ME, et al. Altered temporal difference learning in bulimia nervosa. *Biol Psychiatry.* 2011;708:728–735.
22. Frank GK. Advances in the diagnosis of anorexia nervosa and bulimia nervosa using brain imaging. *Expert Opin Med Diagn.* 2012;63:235–244.
23. Broft A, Shingleton R, Kaufman J, et al. Striatal dopamine in bulimia nervosa: A pet imaging study. *Int J Eat Disord.* 2012;455:648–656.
24. Lunde AV, Fasmer OB, Akiskal KK, et al. The relationship of bulimia and anorexia nervosa with bipolar disorder and its temperamental foundations. *J Affect Disord.* 2009;1153:309–314.
25. McElroy SL, Kotwal R, Keck PE, Jr. Comorbidity of eating disorders with bipolar disorder and treatment implications. *Bipolar Disord.* 2006;86:686–695.
26. Barbee JG. Topiramate in the treatment of severe bulimia nervosa with comorbid mood disorders: a case series. *Int J Eat Disord.* 2003;334:468–472.
27. Findling RL, Short EJ, McNamara NK, et al. Methylphenidate in the treatment of children and adolescents with bipolar disorder and attention-deficit/hyperactivity disorder. *J Am Acad Child Adolesc Psychiatry.* 2007;4611:1445–1453.
28. Scheffer RE, Kowatch RA, Carmody T, et al. Randomized, placebo-controlled trial of mixed amphetamine salts for symptoms of comorbid ADHD in pediatric bipolar disorder after mood stabilization with divalproex sodium. *Am J Psychiatry.* 2005;1621:58–64.
29. Castells X, Casas M, Perez-Mana C, et al. Efficacy of psychostimulant drugs for cocaine dependence. *Cochrane Database Syst Rev.* 2:CD007380.
30. Schubiner H, Saules KK, Arfken CL, et al. Double-blind placebo-controlled trial of methylphenidate in the treatment of adult ADHD patients with comorbid cocaine dependence. *Exp Clin Psychopharmacol.* 2002;103:286–294.
31. Levin FR, Evans SM, Brooks DJ, et al. Treatment of cocaine dependent treatment seekers with adult ADHD: double-blind comparison of methylphenidate and placebo. *Drug Alcohol Depend.* 2007;871:20–29.
32. Bond DJ, Hadjipavlou G, Lam RW, et al. The Canadian Network for Mood and Anxiety Treatments (CANMAT) task force recommendations for the management of patients with mood disorders and comorbid attention-deficit/hyperactivity disorder. *Ann Clin Psychiatry.* 2012;24(1):23–37.
33. Fountoulakis KN, Kasper S, Andreassen O, et al. Efficacy of pharmacotherapy in bipolar disorder: a report by the WPA section on pharmacopsychiatry. *Eur Arch Psychiatry Clin Neurosci.* 2012;262 Suppl 1:1–48. ■