Lamotrigine Use in Patients with Binge Eating and Purging, Significant Affect Dysregulation, and Poor Impulse Control

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ABSTRACT

Objective: Some patients with symptoms of binge eating and purging are successfully treated with specific serotonin reuptake inhibitors (SSRIs), but others experience only partial or no benefit. Significant affect dysregulation and poor impulse control may be characteristics that limit responsiveness.

Method: We report on the treatment of five patients with bulimia nervosa (BN), anorexia nervosa—binge/purge type (AN-B/P) or eating disorder not otherwise specified (EDNOS), using the anticonvulsant lamotrigine after inadequate response to SSRIs.

Results: Following addition of lamotrigine to an antidepressant in four cases, and switch from an antidepressant to lamotrigine in one case, patients experienced substantial improvement in mood reactivity and instability, impulsive drives and behaviors, and eating-disordered symptoms.

Discussion: These findings raise the possibility that lamotrigine, either as monotherapy or as an augmenting agent to antidepressants, may be useful in patients who binge eat and purge, and have significant affect dysregulation with poor impulse control. © 2013 Wiley Periodicals, Inc.

Keywords: lamotrigine; anticonvulsants; bulimia nervosa; anorexia nervosa; eating disorder; binge eating; impulsive behavior; self-injurious behavior; self-destructive behavior; dangerous behavior

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Introduction

Bulimia nervosa (BN) and anorexia nervosa—binge/purge type (AN-B/P) remain difficult-to-treat psychiatric illnesses in many cases, yet formal investigations into pharmacological treatment of binge/purge eating disorders have been almost non-existent during the past 20 years. In 1996, the US Food and Drug Administration granted its only approval of a medication to treat eating disorders, namely, use of the serotonin specific reuptake inhibitor (SSRI) fluoxetine in BN. Similar to earlier studies of a wide range of antidepressant medications, the fluoxetine double-blind, placebo-controlled trials showed many patients achieved short-term reductions of 50–75% in episodes of binge eating, purging, or both. Nonetheless, it is noteworthy that many of these patients who were considered “responders” continued to binge and purge at a frequency that still met criteria for BN at the end of the studies. Overall, the literature reveals that only a minority of patients achieve full remission of the binge/purge symptoms.

The reason for a limited or lack of response to antidepressants for binge/purge symptoms in a sizable number of patients is unknown. However, it has been noted that those eating-disordered individuals with the most dysregulated characteristics tend to have poor outcomes and are often less responsive to existing treatments. Likewise, in our clinical experience, patients with comorbid impulsive and dysregulated symptoms and behaviors such as self-harming, substance abuse, promiscuity, shoplifting, excessive risk-taking, and reactive, erratic mood shifts tend to achieve less benefit from antidepressant monotherapy. In fact, some of these patients appear to become more agitated and experience worsening of symptoms. Given the benefit of some anticonvulsant medications in unstable mood and behavioral states such as bipolar disorder and, in more recent literature, borderline

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personality disorder (BPD), \(^5\) we became interested in this medication class for particularly dysregulated BN and AN-B/P patients.

There is limited evidence for use of anticonvulsants in binge/purge eating disorders. The only randomized-controlled data stems from two trials, with a total of 129 patients, demonstrating effectiveness of topiramate in BN. Reduction in binge eating and purging was similar to that seen in antidepressant trials. Other dysregulated behaviors were not assessed. \(^6\)–\(^8\) Although generally well tolerated in these studies, topiramate is associated with side effects for many patients in clinical practice. In addition to oversedation and cognitive problems, side effects can include weight loss, which would be inappropriate in AN-B/P or low-weight BN. In our search for a better tolerated and weight-neutral anticonvulsant, we began using lamotrigine (often added to a partially-effective antidepressant) in BN and AN-B/P patients with significant affective instability and impulse dyscontrol.

**Method**

We describe five case reports (Table 1) of lamotrigine administration in patients with BN, AN-B/P or eating disorder not otherwise specified (EDNOS) who previously had not responded to conventional treatments. They comprise the good early responders for whom we had the longest-term follow-up data. Diagnoses were established by clinician interviews, and histories were recalled via chart reviews. Those in intensive programs (patients \#2–5) participated concurrently in a variety of psychotherapies, including dialectical behavior therapy.

**Case Reports**

**Patient \#1**

Fifteen-year-old female with history of AN (subsequently EDNOS), major depressive disorder (MDD), generalized anxiety disorder (GAD), and trichotillomania. She also displayed aggressive verbal behavior and impulsive features, but had never experienced mania or hypomania, and did not meet criteria for BPD. In outpatient family behavioral therapy she restored weight from a body mass index (BMI) of 15–19. During that time medication consisted of citalopram 60 mg/day and aripiprazole 5 mg/day. Although mood and aggressive verbal behaviors partially improved with weight restoration, she remained highly impulsive, engaging in sexual promiscuity, binge eating, shoplifting, and daily marijuana use. Social and family interactions suffered greatly. The patient remained moderately depressed, with occasional suicidal ideation and significant distress about her weight gain. Her BMI increased to 25, as she struggled with binge eating alternating with restrictive eating as compensation. With possible increased binge cravings, aripiprazole was discontinued, and citalopram was switched to escitalopram 20 mg/day. Lamotrigine was started and titrated to 100 mg/day, with this medication combination maintained for the next 1.5 years. Gradually she achieved full remission of depression, with a marked reduction in both frequency and intensity of mood swings. Her BMI settled at 20, with normal eating patterns and absence of bingeing. Substance use became sporadic, promiscuity and shoplifting ceased, and social relationships steadied. She was described by her parents as much calmer and able to tolerate conflicts without becoming highly agitated and verbally aggressive.

**Patient \#2**

Sixteen-year-old female with history of AN-B/P and MDD. Upon admission to an intensive outpatient ED program with a BMI of 17, she was quite depressed with intermittent suicidal ideation. The patient was treated with escitalopram 10 mg/day. Subsequently she experienced periods of “normal” mood, but these would be followed by severe crashes into depression with strong suicidal thinking, eventually leading to a first psychiatric hospitalization. Sleep remained normal, and she denied racing thoughts or other symptoms suggestive of a bipolar mixed state. She also began self-harming by cutting for the first time while on escitalopram monotherapy. Lamotrigine was added and titrated to 200 mg/day. Attempts were made to discontinue escitalopram, but the patient’s mood symptoms responded better to combination drug therapy. She now has been on escitalopram 10 mg/day and lamotrigine 200 mg/day for 4 years. Mood has been very stable, with appropriate reactions to life stressors. Her weight increased to and remained stable at a BMI of 22. She stopped cutting and has reported no suicidal ideation or binge/purge episodes since stabilized on lamotrigine.

**Patient \#3**

Seventeen-year-old female with history of AN-B/P and MDD. The patient was admitted to an ED day-treatment program with a BMI of 16, binge/purge episodes several times daily, depression, suicidal ideation, and self-harm by cutting. After an initial positive response to escitalopram 10 mg/day
<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Age and Gender</th>
<th>Diagnoses</th>
<th>BMI at Initiation of Lamotrigine</th>
<th>BMI Following Lamotrigine Treatment</th>
<th>Months on Lamotrigine</th>
<th>Daily Dose of Lamotrigine Following Titration</th>
<th>Other Medications and Daily Doses</th>
<th>Symptoms/Behaviors</th>
<th>Clinical Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>15, F</td>
<td>EDNOS (history of AN, now weight restored), MDD, GAD, trichotillomania, THC abuse</td>
<td>25</td>
<td>20</td>
<td>18</td>
<td>100 mg</td>
<td>escitalopram 20 mg</td>
<td>binging; food restriction; verbal aggression; promiscuity; shoplifting; daily THC use; suicidal ideation; depression; mood swings; anxiety; interpersonal problems</td>
<td>normal eating patterns; cessation of binging; shoplifting, promiscuity, infrequent substance use; full remission of depression/suicidal ideation; marked reduction in mood swings; calmer, able to tolerate conflict without aggression; improved relationships; weight restoration; cessation of binge eating, purging, cutting; remission of depression/suicidal ideation; mood stability; appropriate reactions to stressors; weight restoration; cessation of binge eating, purging, cutting; improved depression; rare suicidal ideation; mood stability; decreased distress intolerance; poor social boundaries; volatile relationships</td>
</tr>
<tr>
<td>2</td>
<td>16, F</td>
<td>AN-B/P, MDD</td>
<td>17</td>
<td>22</td>
<td>48</td>
<td>200 mg</td>
<td>escitalopram 10 mg</td>
<td>food restriction; binging; purging by vomiting; cutting; suicidal ideation; depression; mood swings</td>
<td>weight restoration; cessation of binge eating, purging, cutting; improved depression; rare suicidal ideation; mood stability; decreased distress intolerance; significantly decreased purging; sobriety; remission of depression; sense of calm; improved academic performance</td>
</tr>
<tr>
<td>3</td>
<td>17, F</td>
<td>AN-B/P, MDD</td>
<td>16</td>
<td>20.5</td>
<td>5</td>
<td>75 mg</td>
<td>escitalopram 5 mg</td>
<td>food restriction; binging; purging by vomiting; cutting; suicidal ideation; depression; mood swings; anxiety; agitation</td>
<td>weight restoration; cessation of binge eating, purging, cutting; improved depression; rare suicidal ideation; mood stability; decreased distress intolerance; significantly decreased purging; sobriety; remission of depression; sense of calm; improved academic performance</td>
</tr>
<tr>
<td>4</td>
<td>20, F</td>
<td>BN, MDD, GAD, intermittent alcohol &amp; cocaine abuse</td>
<td>21.3</td>
<td>21–22</td>
<td>5</td>
<td>350 mg</td>
<td>quetiapine 50–75 mg qhs</td>
<td>food restriction; binging; purging by vomiting; alcohol abuse; cocaine abuse; depression; mood swings; insomnia (chronic); anxiety; restlessness; impulsive thoughts declining academic performance</td>
<td>significantly decreased binging; sobriety; remission of depression; sense of calm; improved academic performance</td>
</tr>
<tr>
<td>5</td>
<td>21, F</td>
<td>BN, MDD, GAD, possible ADHD, PD cluster B traits</td>
<td>20.7</td>
<td>21.8</td>
<td>13</td>
<td>400 mg</td>
<td>venlafaxine XR 225 mg; topiramate 150 mg</td>
<td>binging; purging by vomiting; depression; suicidal ideation; anxiety; agitation; controlled substance misuse; poor medication adherence; impulsive medication changes; severe distress intolerance; poor social boundaries; volatile relationships</td>
<td>significantly decreased binging; rare purging; decreased depression/suicidal ideation; decreased anxiety; improved mood stability; improved organization; medication adherence; improved social function; return to school; improved performance</td>
</tr>
</tbody>
</table>

BMI, body mass index; AN, anorexia nervosa; AN-B/P, anorexia nervosa-binge-purge-type; BN, bulimia nervosa; EDNOS, eating disorder not otherwise specified; MDD, major depressive disorder; THC, tetrahydrocannabinol; GAD, generalized anxiety disorder; ADHD, attention deficit-hyperactivity disorder; PD, personality disorder; ED, eating disorder.
depression soon worsened, anxiety increased, and thoughts were consumed by ruminations of overdosing on pain medication. She never reported manic or hypomanic symptoms, though agitation was common. Aripiprazole 2 mg/day was added with some benefit, but the patient still had mood swings, depression and binge eating, and could not tolerate dose titration. Aripiprazole was discontinued and escitalopram was reduced to 5 mg/day. Lamotrigine was begun and titrated to 75 mg/day. During the next 5 months she restored weight to a BMI of 20.5, and binge/purge symptoms gradually ceased. She reported no self-harm urges and stopped cutting. The previously intense suicidal ideation became infrequent and fleeting. Both affective instability and subjective intensity of distress were much reduced.

**Patient #4**

Twenty-year-old female college student with history of BN, MDD, GAD, and intermittent drug and alcohol use, who admitted to an ED intensive outpatient program after 2 years of near-daily binge eating and purging. BMI was of 21.3. She had recently started fluoxetine, and at 60 mg/day, reported fewer depressive symptoms and a 50% decrease in binge/purge episodes. However, the patient complained of restlessness, excessive worries, insomnia, and impulsivity. Cocaine and alcohol use accelerated. Mood fluctuated between several weeks of lethargy and depression followed by several weeks of increased energy and motivation, though her “up” periods were not suggestive of hypomania or mania. She began missing classes and grades declined. She tried several SSRIs in combination with aripiprazole with partial improvement in depression and mood swings, but continued to feel anxious, stressed and overwhelmed. The patient then spent 30 days in a residential drug rehabilitation program, where she was switched to lamotrigine. Quetiapine 50–75 mg qhs was added for insomnia. During the next 4 months of outpatient care, lamotrigine was titrated to 350 mg/day. The patient remained sober and stopped binge eating. Purging decreased to several times per month. BMI was stable at 21–22. The patient reported feeling much calmer on lamotrigine, and depression fully remitted. She returned to college with improved performance.

**Patient #5**

Twenty-one-year-old female with history of BN, MDD, GAD, questionable attention deficit-hyperactivity disorder, and cluster B personality disorder traits. She presented for ED day-treatment after being required to leave college for suicidal ideation. She had experienced volatile relationships with peers, long episodes of depression, and periods of agitation, anxiety and poor impulse control that did not meet criteria for hypomania or mania. For 3 years, she had been binge eating and purging up to 4 days per week. BMI was 20.7. At admission the patient was taking escitalopram 20 mg/day. She had been discontinued from benzodiazepines and stimulants because of a tendency to misuse them. When feeling an urge to binge eat, she would contact her psychiatrist with lengthy, scattered voice messages and e-mails requesting urgent medication changes. She tinkered with doses and started and stopped medications impulsively. During the next 7 months she tried fluoxetine, venlafaxine XR, and low-dose aripiprazole. She also took varying doses of topiramate (average approximately 100 mg/day), which helped some with binge cravings. However, adherence with these medications was erratic. The one constant throughout the patient’s treatment was lamotrigine. She began 25 mg/day at admission, and was eventually titrated to 200 mg bid. Starting at 75 mg/day at discharge, the patient was able to return to college, on lamotrigine 200 mg bid, venlafaxine XR 225 mg/day, and topiramate 150 mg/day. Six months later the patient reported she was doing very well at school. She had consistently remained on the same dose of lamotrigine, which is highly significant given her history. Both the patient and her parents considered lamotrigine the key to her relative stability.

**Discussion**

Very limited previous data have suggested a role for lamotrigine in the treatment of some patients with binge-eating behaviors,9–11 and our cases support its potential efficacy in those characterized by significant affect dysregulation. Across different diagnoses (BN, AN-B/P; and EDNOS with history of AN) and comorbidities (MDD, GAD, anxiety NOS, substance abuse, trichotillomania, and personality disorder cluster B traits), we found this medication appeared to promote a “shared” positive response regarding mood stabilization, impulse regulation, and eating-disordered symptoms. All patients had MDD punctuated by anxious, irritable or labile moods, which significantly improved after adding lamotrigine. Poor impulse control, a common feature...
characterized by not only binge/purge eating symptoms, but also aggression, promiscuity and shoplifting (patient #1), self-harm urges and cutting (patients #2 and #3), substance abuse (patient #4), and interpersonal disinhibition and impulsive medication changes (patient #5), also greatly decreased following lamotrigine augmentation. All five patients had a substantial reduction in binge/purge behaviors, with three achieving full remission. Though there were no specific weight patterns in response to lamotrigine administration, the two patients with current AN obtained normal BMIs, and the other patients remained within a normal weight range. Of note, we did not have reason to believe that the AN patients gained weight as a direct effect of the medication. Rather, they described feeling less anxious about eating, and were able to establish more appropriate eating patterns.

It is important to emphasize that all our patients were concurrently treated with other medications, so it is not possible to isolate the effects of lamotrigine. However, lamotrigine was added after a period of clinical observation in which no further psychopathological improvement was achieved either with the current medications or with partial weight restoration. Patients #1, #2, and #3 were on low doses of SSRIs, patient #4 was on a very-low-dose atypical antipsychotic, and patient #5 was both on a serotonin and norepinephrine reuptake inhibitor (SNRI) and an anticonvulsant. While it appeared to be the addition of lamotrigine that led to improvement in each case, it is possible that the combination of medications was responsible.

An intriguing consideration is whether some ED patients with affect dysregulation and impulse dyscontrol would do better on lamotrigine alone. We found that some patients on antidepressant monotherapy experienced improved depression, but became more agitated and affectively unstable. Given the known potential of antidepressants to destabilize mood in bipolar disorder, it is possible that some of these over-activated young patients could have had early manifestations of bipolar symptoms that had not yet reached full-blown presentations. It is also possible, as some authors have speculated, that individuals with binge/purge-type eating disorders may have a type of bipolar syndrome. Such theories involve potentially shared phenomenological elements, biological and genetic underpinnings, aspects of illness course, and pharmacological response. Exploration of the complex overlap between eating disorders and bipolar disorder, as well as other dysregulated and impulsive states such as BPD, is beyond the scope of this paper but is an area worthy of further study.

The final dose of lamotrigine in our cases ranged from 75 to 400 mg/day. Although the target dose for bipolar disorder is considered 200 mg/day, higher doses are not uncommon (and in seizure disorders, dosing can reach 500 mg/day). In accordance with safety requirements, lamotrigine was initiated at 25 mg/day for 2 weeks and increased to 50 mg/day for the next 2 weeks. Formal recommendations in bipolar disorder call for increase to 100 mg/day in week 5, and to 200 mg/day in week 6. However, in clinical practice we often continue to titrate slowly after week 4, because some ED patients will have good responses at lower doses. A slow titration is recommended to minimize the risk of rash, which is related to the rate of dose escalation. As an additional dosing consideration, the patients in our sample were not taking oral contraceptives, but prescribers should remember that these medications can significantly decrease concentrations of lamotrigine. Moreover, lamotrigine may interact with several other psychotropic medications, such as aripiprazole, olanzapine, quetiapine, fluoxetine, sertraline, and escitalopram, to result in altered pharmacokinetics.

Though in one of the small series cited above two hypersensitivity reactions were noted, our patients reported no adverse events with lamotrigine, and it is known to have good tolerability in clinical practice, especially compared to other anticonvulsant medications. The most common potential side effects include benign rash (up to 10%), headache, nausea, insomnia, somnolence, fatigue, dizziness, blurred vision, ataxia, tremor, rhinitis, and abdominal pain. The most frequent cause of discontinuation of lamotrigine is benign rash. This is because if any skin eruption is suspected of being a drug-induced rash, the medication generally must be discontinued and should not be retried. Such precautions are taken because a rare but very serious adverse effect of lamotrigine is the rash of Stevens-Johnson syndrome and epidermal necrolysis. In studies with epilepsy patients, incidence of Stevens-Johnson syndrome varied between 0.08 and 0.3% in adults. Children showed a threefold risk of serious rash compared to adults. As previously noted, risk of rash is reduced by the standard slow titration used today for lamotrigine.

The patients in our cases reported feeling positive about taking lamotrigine, even where there were long histories of poor adherence with or intolerability of other medications. Major factors described were the low side-effect burden and reported weight neutrality of the medication. The weight-neutral profile of lamotrigine can be highly
relevant in improving adherence with treatment. In fact, many ED patients refuse any medication associated with weight gain, because of the intolerable fear of losing control over eating and weight. Therefore, lamotrigine could be perceived by patients as a “safe” way to lower anxiety and dysregulation levels.

Lamotrigine is a glutamate antagonist that inhibits the sodium-dependent release of glutamate from presynaptic neuron vesicles by blocking voltage-sensitive sodium channels. Its glutamatergic effects are of particular interest in eating disorders because this neurotransmitter appears to be a crucial element in regulation of food intake and reward processes. Glutamatergic receptors are ubiquitous in the brain and are also located in the hypothalamus, a well-known key regulatory region of eating behaviors. Glutamatergic projections to the lateral hypothalamus could be involved in the modification of both the commencement and duration of eating. The stimulation of this hypothalamic area provokes eating behavior, while glutamate antagonism might reduce food intake. Lamotrigine potentially may be effective in reducing binge eating based on the latter mechanism, as trials in binge eating disorder with associated obesity have aimed to clarify. Moreover, glutamate is involved in the modulation of the limbic components of the basal ganglia, with glutamatergic neurons projecting from the amygdala, hippocampus, and medial prefrontal cortex (MPFC) to the nucleus accumbens, and from the medial dorsal thalamus to the MPFC. This network is specifically involved in mirroring motivations and emotions in behaviors, and it also plays a major role in the modulation of the mesolimbic dopamine system, a key element in the neurobiology of eating disorders.

Conclusion

Individuals with eating disorders complicated by severe affective and impulse control problems tend to have poor outcomes. Therefore, it is necessary to develop new treatment approaches that take into account both eating symptomatology and broader behavioral pathology. The preliminary findings presented in this paper raise the possibility that lamotrigine might be useful in treating ED patients with significant impulse and affect dysregulation. Controlled trials are needed to answer the question of whether lamotrigine is effective as a monotherapy or in combination with antidepressant medication, as well as to assess the tolerability and safety of the medication in this patient population.

References