A Pilot Open Series of Lamotrigine in Eating Disorders Characterized by Significant Affect Dysregulation and Poor Impulse Control

Tiffany Nakamura MA, Laura Berner PhD, Anne Cusack PsyD, Mary Ellen Trunko MD, Terry Schwartz MD, Ursula Bailey MD, Joanna Chen BS, & Walter Kaye MD

Department of Psychiatry, University of California – San Diego

INTRODUCTION

- First-line interventions (behavioral therapies and selective serotonin reuptake inhibitors - SSRI’s) are often ineffective for a large proportion of BN patients who have been described as multi-impulsive, and who struggle with affective instability and dysregulated behaviors (Halmi, 2013; Mitchell, 2007; Rossiter,1993; Wilson, 2007).
- Patients with the binge-eating/purging subtype of anorexia nervosa (AN-B/P) have been less studied, but authors link significant emotion regulation difficulties and impulsive behaviors, along with poor treatment response, to this group as well (Racine, 2013).
- Consistent with the literature, our clinical experience is that severely dysregulated eating disorder patients often have little or no response to antidepressant monotherapy, and in some cases, appear to become more agitated with this treatment. This led to speculation that medications with mood-stabilizing properties (Crawford, 2015; Reich; 2009; Tritt, 2005) may be a better alternative.
- We previously reported a positive response to lamotrigine, an antiepileptic drug, in five patients with BN and AN who had significant affect dysregulation and impulsivity (Trunko, 2014). Though encouraging, these case reports were based on personal observation and our desire to support potential future controlled trials with lamotrigine led to this current follow up.

METHODS & PROCEDURE

- Titration and Measures
  - Starting dose lamotrigine = 25 mg/day for two weeks, increased to 50mg/day for the next two weeks, subsequent rate of titration was variable, with a maximum increase of 50 mg/day every two weeks until reaching therapeutic dose (expected range 100mg/day to 300mg/day). Increases and maximum dose were determined by the psychiatrist based on tolerability and therapeutic response.
  - Questionnaires completed at intake and approximately every 2 weeks thereafter (mean time between assessments = 20.5 days, SD = 12.9 days).
  - Borderline Evaluation of Severity Over Time (Pfohl, 2009)
    - Subscales: 1) Cognitive and affective dysregulation; 2) Behavioral dysregulation; 3) Skillful behavioral regulation
  - Zanarini Rating Scale for Borderline Personality Disorder (Zanarini, 2003)
    - Subscales: 1) Affective dysregulation; 2) Impulsive behaviors; 3) Unstable interpersonal relationships
  - Secondary outcome measures given at treatment start and at final assessment
    - Eating Disorder Examination Questionnaire (Fairburn, 2008)
      - Subscales: 1) Restrain; 2) Shape Concern; 3) Weight Concern; 4) Eating Concern
    - State-Trait Anxiety Inventory (Spielberger, 1983)
    - Beck Depression Inventory (Beck, 1996)
    - 21 item self-report questionnaire, rated on a 4-point Likert-type scale ranging from 0-3, with higher scores indicating greater severity of depression.

OBJECTIVE

This current study aimed to confirm our observations of positive responses to lamotrigine, in a larger series of patients, utilizing standardized instruments (Pfohl, 2009; Zanarini) designed to assess changes in affect and behavioral dysregulation in response to treatment as well as mood and eating disorder symptomology.

RESULTS

- Multilevel Models Examining Change in ZAN-BPD and BEST Scores Over Time
  - Effect Estimate S.E. df F p
  - ZAN-BPD Score
    - Dose -0.01963 0.00575 14.5 11.6 0.0041
    - Days on lamotrigine -0.02712 0.01610 50.9 19.7 <.0001
    - BMI 0.6092 0.3819 8.9 2.5 0.1457
    - Age -0.2442 0.1637 9.2 2.2 0.1692
  - BEST Score
    - Days on lamotrigine -0.04573 0.00594 50.2 63.9 <.0001
    - BMI -0.2523 0.5138 9.2 0.2 0.6350
    - Age -0.2941 0.2185 9.1 1.7 0.2257

- Scores on Secondary Outcome Measures Before and After Lamotrigine Treatment

- EDE-Q Scores
  - Measure Pre Post M (SD) M (SD) p Cohen’s d
  - Restraint 2.8 (1.5) 2.3 (1.0) 0.058 0.11
  - Eating Concern 2.9 (1.7) 2.2 (1.4) 0.033 0.45
  - Shape Concern 4.7 (2.2) 3.3 (1.6) 0.093 0.99
  - Weight Concern 4.1 (2.8) 3.4 (1.5) 0.406 0.36
  - Global 3.7 (1.4) 2.7 (1.0) 0.051 0.82
  - BDII 30.7 (15.4) 24.2 (12.4) 0.314 0.36
  - STAI State 60.2 (11.4) 60.2 (12.1) 0.799 0
  - STAI Trait 54.9 (8.9) 56.1 (10.6) 0.373 0.21

- The above results are consistent with prior reports of lamotrigine treatment benefit for some AN-B/P and AN patients with BN and AN-B/P spectrum disorders (Trunko, 2014; Rybakowski, 2008; Marllov, 2010) and for some patients with binge-eating behaviors (Guerdijika, 2009).

- In addition to significant changes noted above, patients who had a history of mood instability and dysregulated behaviors exhibited a greater decrease in reactivity, irritability, anger, impulsivity, anxiety, depression, SI, and drives to purge and self harm.

ANALYSES

- Both ZAN-BPD and BEST scores decreased as dose and time on drug increased.
- At 1 month BEST score reduction was very large (d = 2.41), ZAN-BPD score reduction was moderate to large (d = 0.78) and continued improving several months into lamotrigine titration.
- Inclusion of age and BMI in models did not impact findings, and results reported included these covariates.
- 77.8% of patients showed significant treatment response (RCI > 1.96) as measured by ZAN-BPD (mean RCI = 4.46, SD = 3.34).
- 56.8% of patients showed significant treatment response as measured by BEST scores (mean RCI = 2.26, SD = 0.96).

DISCUSSION

- This is the first study to use standardized measures of affective and behavioral dysregulation to document lamotrigine response in eating-disordered patients over a substantial time period.
- Increasing dose and time on lamotrigine were associated with significant and moderate-to-large self-reported reductions in dysregulated emotions and problems with impulse control.
- Data from two additional patients suggested these symptoms worsened with lamotrigine dose reduction and improved after lamotrigine re-titration.
- We found preliminary evidence of reduced eating disorder symptoms and depression, but little change in anxiety measures.
- These results are consistent with prior reports of lamotrigine treatment benefit for some patients with BN and AN-B/P spectrum disorders (Trunko, 2014; Rybakowski, 2008; Marllov, 2010) and for some patients with binge-eating behaviors (Guerdijika, 2009).

- Lamotrigine is a glutamate antagonist, and its effectiveness is believed to be mediated by glutamate regulation.
- Our findings raise the question as to whether glutamatergic abnormalities play a role in affective and behavioral dysregulation in individuals with eating disorders, as they may in in-patient disorder and BPD (Eichler, 2015; Krause-Utz, 2014). This could help explain why traditionally used serotoninergic antidepressants have limited impact for many of these eating-disordered patients.

CONCLUSION & FUTURE DIRECTIONS

- Our preliminary data support further study of lamotrigine for the treatment of dysregulation in eating-disordered patients. A growing body of evidence suggests that dysregulated behaviors may be linked to emotional instability. Pervasive deficits in self-regulatory control may contribute to inadequate response to existing impulse control disorders, as powerful but only temporary relief of dysregulated and impulsive behaviors may reinforce maladaptive cycles. Data from our small sample must be interpreted with caution as it is premature to draw any conclusions regarding the therapeutic utility of lamotrigine.
- Our findings preliminarily suggest that directly targeting regulatory deficits may be key to more effective treatment and support the feasibility of studying lamotrigine efficacy in eating-disordered populations. Our pilot findings are perhaps most important in supporting the need for large scale, rigorously controlled investigations of lamotrigine, used with or without concurrent DBT or other therapies, to elucidate how these factors might interact to treat dysregulated behavior in eating disorders.

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