

Topiramate Use in Refractory Bipolar Disorder

Abstract

Methods: Charts of outpatients with a DSM-IV diagnosis of bipolar disorder treated with adjunctive topiramate were reviewed retrospectively. Clinical assessments included Clinical Global Impression of Severity (CGIS) and Improvement Scales (CGI-I). Data on length of treatment, patient weight, and side effects were also analyzed.

Results: Two hundred sixty-eight patients were identified, of these 215 were treated with topiramate ≥ 1 month and served as the study population. Diagnoses included bipolar I (62%), bipolar II (27%) and bipolar NOS (11%). Topiramate treatment duration ranged from 1–25 months with a mean dose of 167 ± 113 mg/day. Mean CGI-S at baseline was 4.4 ± 0.8 and changed significantly by last visit (mean CGI-S: 3.7 ± 0.9 ; $p < 0.001$). Mean CGI-I at last visit was 3.1 ± 0.8 (range: 1-5). 53% of patients experienced mild improvement, with 21% much or very much improved based on CGI-I scores. Mean weight change from baseline was -7.5 ± 20 lbs ($p < 0.05$). The most common adverse events were CNS-related symptoms, and none were serious. Data stratified by treatment duration revealed long-term effects as measured by CGIS.

Conclusion: Many patients experience significant improvement in bipolar symptoms with add-on topiramate therapy in clinical practice.

Introduction

Bipolar disorder (BPD), a serious chronic psychiatric illness, occurs in approximately 2% of the adult population and in 1% of adolescents and children.¹ Treatment failure with commonly prescribed agents and drug-induced weight gain are two major issues that complicate the management of this disorder.^{2,3} Weight gain not only affects patient compliance, but also poses a health risk for many patients. Recent clinical evidence suggests that topiramate may be an effective therapeutic option for the treatment of bipolar disorder refractory to other agents.^{6,7} Additionally, data indicate that topiramate does not promote weight gain and may induce weight loss in overweight patients.^{8,9}

Objective

To assess the clinical utility of adjunctive topiramate in patients with refractory BPD and to investigate its effect on patient weight.

Methods

Study Design

- Retrospective review of 268 outpatient charts
- Patient inclusion criteria
 - Patients (n = 215) with a DSM-IV diagnosis of bipolar disorder who were treated with topiramate ≥ 1 month at Red Oak Psychiatry Association, PA, Houston, TX
- Duration of treatment ranged from 1-25 months

Table 1. Patient Characteristics (N = 268)

Age	Mean \pm SD	36.3 \pm 12.6 years
	Range	8-73 years
	Gender	209 (78%) females 59 (22%) males
Race	Caucasian	239 (89%)
	African American	12 (4%)
	Hispanic	10 (4%)
	Asian	2 (1%)
	Missing data	5 (2%)
Diagnoses	BPD I	165 (62%)
	BPD II	73 (27%)
	BPD NOS	29 (11%)
	Cyclothymia	1 (0.4%)
	Comorbid Diagnoses*	No comorbidity
	Panic disorder	29 (11%)
	Generalized anxiety disorder	25 (9%)
	Substance abuse	19 (7%)
	ADHD	19 (7%)
	Other	37 (13%)

*Patients may have more than 1 comorbid diagnosis

Treatment with Topiramate

- Mean dose: 167 ± 113 mg/day
- Dose range: 25-675 mg/day

Clinical Assessments

- Clinical Global Impression of Severity Scale (CGIS)
 - scale of 1-7; 1 = not mentally ill to 7 = among the most severely ill
 - performed at baseline, every 3 months thereafter,
- Clinical Global Improvement Scale (CGI-I)
 - scale of 1-7; 1 = very much improved to 7 = very much worse
 - calculated at last visit
- Patient weight
 - measured at baseline and at last visit

Statistical Analyses

- Sign tests were performed to evaluate changes in CGIS, weight, and number of hospitalizations from baseline to last visit. Differences in the incidence of symptoms of bipolar disorder from baseline to last visit were also compared.

Table 2. Concomitant Medications (n = 215)

Drug Class	Number of Patients
Antidepressants	166 (77%)
Mood stabilizers	98 (46%)
Antipsychotics	50 (23%)
Thyroid Medications	17 (8%)

Results

Number of evaluable patients: 215

Efficacy

- Mean CGIS decreased significantly from 4.4 ± 0.8 at baseline to 3.7 ± 0.9 at last visit ($p < 0.001$)
- Forty-five patients (21%) had a CGI-I score equal to 2 and 114 (53%) had a score of 3 (mean CGI-I score for entire group = 3.1 ± 0.9); 41 (19%) experienced no change, while 12 (6%) were minimally worse
- BPD symptomatology improved significantly ($p < .01$) for the symptoms of irritability, racing thoughts, distractibility, hyperactivity, risky behavior, and excessive spending

Figure 1. Severity of Illness (CGIS) (n = 215)

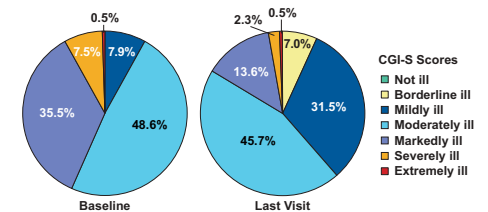


Figure 2. Change in CGI-S from Baseline (n = 215)

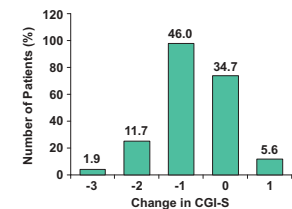


Figure 3a. Change in Severity of Illness (CGI-S) by BPD Diagnosis: BPD I (n = 131)*

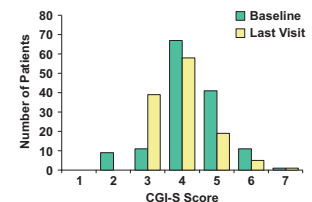


Figure 3b. Change in Severity of Illness (CGI-S) by BPD
Diagnosis: BPD II (n = 61)*

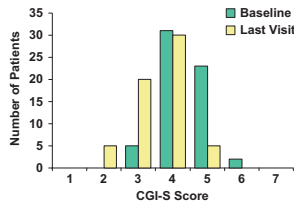


Figure 3c. Change in Severity of Illness (CGI-S) by BPD
Diagnosis: BPD NOS (n = 21)*

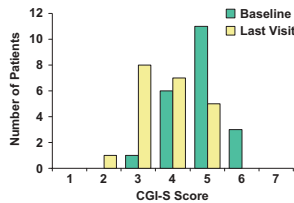


Figure 4a. Change in Severity of Illness (CGI-S) by Treatment
Duration: 1-6 months (n = 125)*

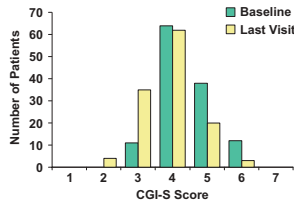


Figure 4b. Change in Severity of Illness (CGI-S) by Treatment
Duration: 6-12 months (n = 48)*

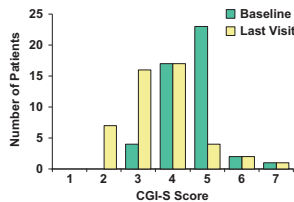


Figure 4c. Change in Severity of Illness (CGI-S) by Treatment
Duration: >12 months (n = 42)

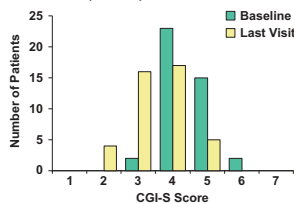


Figure 5. Overall Response to Topiramate Treatment
(CGI-I) (n = 215)

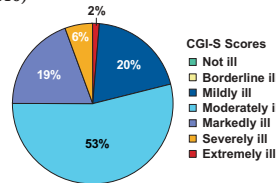
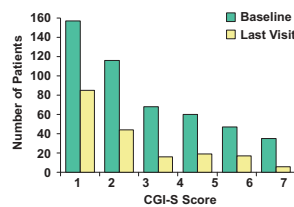


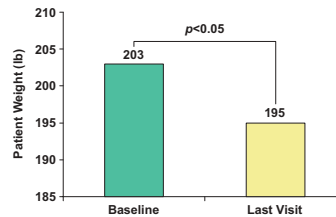
Figure 6. Symptoms Before and After Topiramate
Treatment (n = 215)



Changes in Weight

- Mean weight changed from 203 ± 60 lbs at baseline to 195 ± 57 lbs by last visit
- Mean change was -7.5 ± 20 lbs (range: -69 to +58 lbs; p<0.05)

Figure 7. Mean Weight Before and After Topiramate
Treatment (n = 84)*



Adverse Events

- The most commonly reported adverse event was cognitive effects, experienced by 19% of patients

Table 3. Adverse Events (n = 215)

Cognitive disturbance	40 (19%)
Paresthesia	31 (14%)
Dysphoric state	13 (6%)

*Smaller sample size is due to missing data

Conclusions

- Despite the significant burden of illness in this population, patients demonstrated a favorable response to adjunctive topiramate therapy, with the mean CGI-I score at the end of treatment indicating a shift from moderately to mildly ill
- The mean CGI-I score indicated that 74% of patients experienced at least minimal improvement with topiramate therapy
- Topiramate was found to be beneficial for all BPD diagnosis
- Significant reductions in symptoms of BPD occurred with topiramate therapy
- Topiramate was generally well tolerated, and on average, an 8 lbs weight loss was observed across patients
- In this patient population, topiramate is not associated with the weight gain seen with many other psychotropic drugs
- These findings suggest that topiramate was a beneficial mood stabilizer when used as adjunctive therapy in an outpatient setting

References

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