Oxcarbazepine in the Treatment of Borderline Personality Disorder: A Pilot Study

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Background: According to available studies concerning treatment of patients with borderline personality disorder, mood stabilizers have been found effective in controlling core symptoms of borderline pathology, in particular impulsive behavior and mood instability. Oxcarbazepine, an anticonvulsant structurally related to carbamazepine, has been tested in psychiatric settings for treating patients with bipolar disorders, substance abuse, resistant psychosis, and schizoaffective disorder. The present article is a pilot study on the efficacy and tolerability of oxcarbazepine in the treatment of borderline personality disorder.

Method: Seventeen outpatients diagnosed with DSM-IV-TR borderline personality disorder were included. Patients were administered oxcarbazepine, 1200 to 1500 mg/day supplied twice daily, and tested at baseline, week 4, and week 12 using the Clinical Global Impressions scale-Severity of Illness item (CGI-S), the Brief Psychiatric Rating Scale (BPRS), the Hamilton Rating Scales for Depression and Anxiety (HAM-D, HAM-A), the Social Occupational Functioning Assessment Scale, and the Borderline Personality Disorder Severity Index (BPDSI). Adverse effects were collected and serum sodium level was measured. Statistics were performed by using the analysis of variance for repeated measures.

Results: Four patients discontinued treatment in the first 4 weeks due to noncompliance. A statistically significant response to oxcarbazepine was observed according to CGI-S and BPRS mean score ($p = .001$), HAM-A mean score ($p = .002$), BPDSI total score ($p = .0005$), and 4 BPDSI items, including interpersonal relationships ($p = .0005$), impulsivity ($p = .0005$), affective instability ($p = .0005$), and outbursts of anger ($p = .045$). No cases of significant hyponatremia or severe adverse effects were reported. Mild to moderate adverse effects included sedation, dizziness, nausea, and headache. Seven patients reported no adverse effects.

Conclusion: Oxcarbazepine was found an effective and well-tolerated treatment in the management of borderline personality disorder patients.

(J Clin Psychiatry 2005;66:1111–1115)

Received Jan. 12, 2005; accepted Feb. 8, 2005. *From the Unit of Psychiatry, Department of Neuroscience, University of Turin, Turin, Italy.*

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The focus of pharmacotherapy for patients with borderline personality disorder is to manage vulnerability traits, symptoms, and crises. Treatment strategies for borderline personality disorder target different domains of pathology, such as cognitive-perceptual, affective, and impulsive-behavioral symptoms.

Mood stabilizers, particularly anticonvulsants, are often used in clinical practice and are indicated for treating patients with borderline personality disorder by the guidelines of the American Psychiatric Association (APA).[1] Several studies are available dealing with lithium,[2–6] valproate,[7–14] carbamazepine,[4,8,15–18] and lamotrigine.[19–21] These data supported the efficacy of mood stabilizers on core symptoms of borderline pathology, in particular on impulsive-aggressive behavior and mood instability.[2,5,6,8,10–16,18,20]

Oxcarbazepine is an anticonvulsant structurally related to carbamazepine, with the same mechanism of action of blocking voltage-gated sodium channels but fewer side effects and drug interactions.[22] A series of studies indicated the efficacy of oxcarbazepine in the treatment of bipolar disorder, mainly manic or mixed episodes, and of substance abuse, resistant psychosis, and schizoaffective disorder.[23–34] APA guidelines for the treatment of bipolar disorders[35] considered oxcarbazepine an alternative to lithium or valproate, and the Texas Consensus Conference Panel recommended the use of this agent instead of carbamazepine.[36] Recent data concern the use of oxcarbazepine in substance abuse disorder,[37] resistant psychosis,[32,38] and schizoaffective disorder.[26,30] No systematic study is yet available on the efficacy of this drug in borderline personality disorder patients.

The present investigation is a pilot open-label study, with the aim of testing the efficacy and tolerability of oxcarbazepine in the treatment of borderline personality disorder.

METHOD

Seventeen consecutive outpatients aged ≥ 18 years and ≤ 50 years who had a diagnosis of borderline personality disorder were included in this study. Patients attended the Service for Personality Disorders, Unit of Psychiatry, Department of Neuroscience, University of Turin, Turin, Italy. Diagnosis was made by an expert clinician (S.B.) according to DSM-IV-TR criteria[39] and confirmed

using the Structured Clinical Interview for DSM-IV Axis II Disorders.[40]

Subjects were excluded if they had a current or previous record of delirium, dementia, amnestic disorder, or other cognitive disorders; schizophrenia or other psychotic disorders; major depressive disorder or bipolar disorders; or eating disorders. Patients were also excluded if they had a current diagnosis of substance abuse disorder or if they had received psychotropic drugs and/or psychotherapy in the 3 months preceding the beginning of the study. Female patients of childbearing age were excluded if they were not using adequate birth control methods (according to the judgment of the clinician).

Each patient participated voluntarily in the study after providing written informed consent. Declaration of Helsinki guidelines were followed. Recruited patients were treated with open-label oxcarbazepine. Medication was started at 600 mg/day and was increased in 4 to 5 days up to a dose of 1200 to 1500 mg/day, supplied twice daily. Treatment was maintained for 12 weeks. No other psychotropic drug or psychological intervention was allowed during the treatment period.

Patients were repeatedly tested (at baseline, week 4, and week 12) using the following instruments: (1) the Clinical Global Impressions scale-Severity of Illness item (CGI-S)[41]; (2) the Brief Psychiatric Rating Scale (BPRS)[42]; (3) the Hamilton Rating Scales for Depression and Anxiety (HAM-D, HAM-A)[43,44]; (4) the Social Occupational Functioning Assessment Scale (SOFAS)[45]; and (5) the Borderline Personality Disorder Severity Index (BPDSI).[46]

Assessment was performed by an investigator (E.P.) who was blind to the treatment regimen. Prior to this study, this interviewer received training sessions on the BPDSI.

Serum sodium level was measured in all patients after 4 weeks of treatment, and drug administration was stopped if sodium level was ≤ 125 mmol/L.[47] Patients were interviewed at each visit to collect data about the occurrence and severity of adverse effects. Adverse effects were rated as severe when they were related to a significant impairment of patient's global functioning (according to the clinical judgment).

Statistics were performed on each rating scale by using the analysis of variance (ANOVA) for repeated measures (SPSS, version 11.0.0, Chicago, Ill.). p Values were considered significant when ≤ .05.

RESULTS

Seventeen subjects (mean ± SD age: 28.3 ± 6.1 years; 11 women and 6 men) were included. Four patients (23.5%) discontinued treatment in the first 4 weeks due to noncompliance. The 13 patients who completed treatment had a mean age of 28.7 ± 5.9 years; they were 8 women (61.5%) and 5 men (38.5%). The mean daily dose of oxcarbazepine was 1315.4 ± 151.9 mg.

Table 1. Results of Analysis of Variance for Repeated Measures Performed With Borderline Personality Disorder Symptom and Social Functioning Rating Scales in Patients Treated With Oxcarbazepine (N = 13)

	Score			
Measure	Baseline	Week 4	Week 12	p
CGI-S				
Mean	4.85	4.54	3.92	.001
SD	0.38	0.52	0.76	
SE	0.104	0.144	0.211	
BPRS				
Mean	43.69	39.15	33	.001
SD	4.25	7.02	8.41	
SE	1.179	1.948	2.332	
HAM-A				
Mean	15	12.92	9.38	.002
SD	3.83	3.45	3.88	
SE	1.062	0.957	1.077	
HAM-D				
Mean	12.46	11.46	9.77	NS
SD	0.98	2.37	2.92	
SE	0.268	0.656	0.810	
SOFAS				
Mean	48.08	53.31	56.62	NS
SD	3.57	5.94	10.31	
SE	0.990	1.646	2.859	

Abbreviations: BPRS = Brief Psychiatric Rating Scale, CGI-S = Clinical Global Impressions scale-Severity of Illness item, HAM-A = Hamilton Rating Scale for Anxiety, HAM-D = Hamilton Rating Scale for Depression, NS = nonsignificant, SOFAS = Social Occupational Functioning Assessment Scale.

Results of ANOVA applied to rating scales scores are reported in Tables 1–3. A statistically significant decrease was observed in CGI-S and BPRS mean scores (p = .001 each), HAM-A mean score (p = .002), BPDSI total score (p = .0005), and 4 BPDSI items, including interpersonal relationships (p = .0005), impulsivity (p = .0005), affective instability (p = .0005), and outbursts of anger (p = .045). In contrast, there were no significant changes in HAM-D and SOFAS scores or in BPDSI scores of abandonment, identity, parasuicidal behavior, emptiness, or dissociation and paranoid ideation.

Adverse effects in our patients were mild to moderate in severity. The most common adverse effect was sedation (3/13 patients, 23.1%). Other adverse effects included dizziness and nausea (2/13 each, 15.4%) and headache (1/13, 7.7%). Seven patients (53.9%) had no adverse effects. No case of clinically significant hyponatremia was reported. Dropouts were never due to side effects.

DISCUSSION

In this pilot study of oxcarbazepine treatment of borderline personality disorder, a significant improvement was found according to several rating scales: the CGI-S, the BPRS, the HAM-A, and the BPDSI (total score, affective instability, impulsivity, outbursts of anger, and interpersonal relationships).

Table 2. Results of Analysis of Variance for Repeated Measures Performed With Borderline Personality Disorder Severity Index (BPDSI) Total and Factor Scores in Patients Treated With Oxcarbazepine (N = 13)

	Score			
Measure	Baseline	Week 4	Week 12	p
BPDSI				
Total				
Mean	49.43	42.50	35.80	.0005
SD	4.32	4.76	6.85	
SE	1.197	1.321	1.899	
Abandonment				
Mean	6.78	6.05	5.49	NS
SD	1.50	1.52	1.37	
SE	0.415	0.423	0.381	
Interpersonal relationships				
Mean	6.85	5.74	4.91	.0005
SD	0.69	0.88	1.49	
SE	0.192	0.244	0.412	
Identity				
Mean	4.84	4.50	4.23	NS
SD	2.00	1.71	1.77	
SE	0.55	0.47	0.49	
Impulsivity				
Mean	6.08	4.96	4.06	.0005
SD	1.28	1.05	0.77	
SE	0.35	0.29	0.21	

Abbreviation: NS = nonsignificant.

Table 3. Results of Analysis of Variance for Repeated Measures Performed With Borderline Personality Disorder Severity Index (BPDSI) Factor Scores in Patients Treated With Oxcarbazepine (N = 13)

	Score			
BPDSI Factor	Baseline	Week 4	Week 12	p
Parasuicidal behavior				
Mean	1.93	1.66	1.23	NS
SD	0.73	0.74	0.44	
SE	0.203	0.207	0.121	
Affective instability				
Mean	7.80	6.51	4.58	.0005
SD	0.94	0.65	1.56	
SE	0.262	0.182	0.434	
Emptiness				
Mean	7.16	6.79	6.26	NS
SD	1.06	1.07	0.99	
SE	0.294	0.298	0.277	
Outbursts of anger				
Mean	5.66	4.44	3.84	.045
SD	1.81	1.59	2.02	
SE	0.501	0.440	0.559	
Dissociation and paranoid ideation				
Mean	2.33	1.85	1.51	NS
SD	1.37	1.55	1.67	
SE	0.381	0.430	0.465	

Abbreviation: NS = nonsignificant.

The decrease of CGI-S, BPRS, HAM-A, and BPDSI mean scores suggests the efficacy of oxcarbazepine on a broad spectrum of borderline personality disorder symptoms. The improvement of global psychopathology replicates previous findings concerning mood stabilizers, particularly valproate.[8,12,13] A decrease of anxiety was already reported by Cowdry and Gardner[16] in a sample of borderline patients treated with carbamazepine, a drug that is structurally related to oxcarbazepine.

As for single BPDSI factors, the efficacy of oxcarbazepine in reducing affective instability and controlling impulsivity is consistent with previous trials of carbamazepine, lithium, and valproate in groups of borderline personality disorder patients.[2,5,6,8,10–13,15,16,18] These are relevant findings to prove the therapeutic effects of oxcarbazepine, as mood instability and impulsivity are considered core biopsychological dimensions of borderline disorder.[48–50] In addition, the efficacy of oxcarbazepine on mood instability in both bipolar and borderline patients suggests the existence of common psychopathologic features in the 2 clinical conditions. Of course, these data are not sufficient to verify the hypothesis that borderline personality disorder can be categorized as an atypical, milder form of bipolar spectrum disorder.[51–54]

It is noticeable that the BPDSI factor "outbursts of anger" showed a significant response to oxcarbazepine, but the level of significance was much lower than for the factor "impulsivity" ($p = .045$ vs. $p = .0005$). This difference is not easy to explain, as we could consider the 2 factors as related to the same psychopathologic dimension of borderline personality disorder.[55–57] We could suggest that feelings of anger, which are not necessarily expressed by aggressive behavior, are related not only to impulsivity, but also to increased mood reactivity and to intolerance to frustration or abandonment.

The efficacy of oxcarbazepine in controlling affective instability and impulsivity (that is, in stabilizing patients' symptoms) may indirectly contribute to improvement of interpersonal relationships, by softening the trend of borderline patients to alternate between extremes of idealization and devaluation.

In conclusion, our data suggest that oxcarbazepine can be taken into account as an effective drug for pharmacotherapy of borderline personality disorder patients and can be considered as an option for monotherapy of this personality disorder.

Concerning tolerability, our patients reported slightly higher rates of adverse effects if compared with other investigations on oxcarbazepine,[28] probably due to different diagnoses and clinical pictures. Nevertheless, adverse effects were mild to moderate and never required treatment discontinuation. In particular, no cases of clinically significant hyponatremia were found, indicating that oxcarbazepine was a safe and well-accepted therapy in this group of patients.

Two major limitations of these results are the small sample size and the lack of a double-blind controlled design. This is in fact a pilot study, which can provide preliminary data and promote controlled trials of oxcarbazepine in borderline personality disorder. A relevant issue

for future investigations will be to identify which dimension of borderline personality disorder psychopathology is the primary target of oxcarbazepine therapeutic action, as this finding could help to propose a physiopathologic pathway related to the effects of this drug and perhaps other mood stabilizers in borderline patients.

Drug names: carbamazepine (Carbatrol, Equetro, and others), lamotrigine (Lamictal), lithium (Lithobid, Eskalith, and others), oxcarbazepine (Trileptal).

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