Preliminary Findings

BIPOLAR SPECTRUM IN CLUSTER HEADACHE PATIENTS

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Abstract. *Two hundred seventy-five consecutive cluster headache patients, seen over a period of 17 years, were evaluated. The age range was 20 to 78, with an average age of 49. There were 170 men and 105 women. Lifetime prevalence of the bipolar spectrum was assessed. Of the 275 cluster patients, 134 had episodic cluster, and 141 were chronic cluster sufferers. In the episodic cluster cohort, eight patients (6 %) fit the criteria for the bipolar spectrum. One patient was bipolar I, four were bipolar II, two were cyclothymic, while one was bipolar NOS. In the chronic cluster cohort, ten patients (7 %) were bipolar. Two were bipolar I, two were bipolar II, four were cyclothymic, while two were bipolar not-otherwise-specified (NOS). In all, 18 of 275 patients (6.6 %) fulfilled criteria for the bipolar spectrum; 1.1 % were bipolar I; 2.2 % were bipolar II; 2.2% were cyclothymic; and 1.1 % were bipolar NOS. This study indicates that, as with migraine, bipolar is seen with an increased frequency among cluster patients.*

Descriptors. *bipolar, cluster headache, depression, migraine*

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INTRODUCTION

Mood disorders, including anxiety, recurrent major depression, and dysthyma, have been noted to have an increased incidence in patients suffering from migraine (1-4). Conversely, individuals with bipolar illness have an increased incidence of migraine as well (5). However, the cluster headache population has not been as well studied with respect to bipolar disorders or any affective disorders for that matter. The purpose of the present study was to assess a large population of cluster headache sufferers with regard to the entire bipolar spectrum.

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METHODOLOGY

Two hundred seventy-five consecutive cluster headache patients, seen over a period of 17 years, were evaluated. The age range was 20 to 78, with an average age of 49. There were 170 men and 105 women. Chart review, mood disorder questionnaire administration, and interviews with patients and families were undertaken by the

treating neurologist/psychopharmacologist. All of the patients were evaluated at the Robbins Headache Clinic. Inclusion criteria included (*i*) age 20 or older and (*ii*) a history of cluster headache as defined by the International Headache Society (6). With these measures, the lifetime prevalence of bipolar illness in the cohort studied was assessed.

Bipolar illness was defined according to the criteria established by the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) (7). In addition, the modifications to DSM-IV by Akiskal were utilized in defining bipolar disorders (8,9).

Bipolar I disorder was defined according to the DSM-IV criteria; there had to be at least one episode, currently or in the past, of true mania.

Bipolar II was assessed according to DSM-IV. There had to have been one or more major depressive episode, at least one hypomanic episode; no mania or mixed episodes, and these episodes must have caused significant distress or impairment in patient functioning.

Cyclothymic disorder was defined according to DSM-IV criteria – at least two years of numerous periods of hypomania and numerous episodes of depressive symptoms that do not meet criteria for major depressive episode. During the two-year period, the patient could not have been without the symptoms for more than two months at a time, and no major depressive episode, manic episode, or mixed episode could have been present during the first two years of the disturbance. These symptoms had to cause clinically significant distress or impairment in functioning and were not due to substance abuse or a medical condition.

Bipolar disorder not otherwise specified (NOS) was defined according to DSM-IV, with additions according to Akiskal (8,9). Examples of patients included in this category are those with (*i*) rapid alterations between manic and depressive symptoms that do not meet minimal criteria for a full manic episode, or for a major depressive episode; (*ii*) recurrent hypomanic episodes without intercurrent depressive symptoms; (*iii*) a presence of a hyperthymic temperament as the prevalent, long-term functioning of the person[1]; (*iv*) a presence of a persistently agitated, angry, moody personality (temperamental instability), particularly with a strong family history of bipolar disorder and/or a hypomanic reaction to an antidepressant; and (*v*) the temperamental triad of increased energy, daydreaming, and lability of mood also was used as additional indicators of bipolarity.

RESULTS

Of the 275 cluster patients, 134 had episodic cluster, and 141 were chronic cluster sufferers. In the episodic cluster cohort, eight patients (6 %) fit the criteria for the bipolar spectrum. One patient was bipolar I, four were bipolar II, two were cyclothymic, while one was bipolar NOS. In the chronic cluster cohort, ten patients (7 %) were bipolar. Two were bipolar I, two were bipolar II, four were cyclothymic, while two were bipolar not-otherwise-specified (NOS). In all, 18 of 275 patients (6.6 %) fulfilled criteria for the bipolar spectrum; 1.1 % were bipolar I; 2.2 % were bipolar II; 2.2% were cyclothymic; and 1.1 % were bipolar NOS.

DISCUSSION

The comorbidity of migraine with anxiety, depression, and bipolar has been established (1-4). However, these comorbid conditions have not been studied extensively in the cluster headache population. In a previous study of 1,000 migraineurs, 8.6% were classified as fitting the bipolar spectrum (10). In the current study 6.6% of 275 cluster patients (combined episodic and chronic) were diagnosed as bipolar. For those with episodic cluster headache, 6% fit the bipolar spectrum, while 7% of the chronic cluster headache patients were determined to be bipolar.

1. In these patients, a strong family history of bipolar illness also aided in the diagnosis of bipolarity. Also, a hypomanic reaction to an antidepressant was considered an additional bipolar trait in these hyperthymic individuals. Hyperthymic temperament is defined, according to Akiskal (8,9), as habitual long-term functioning of the individual, with the following attributes: cheerful and exuberant; jocular and glib or articulate; overoptimistic and carefree; overconfident, boastful, and grandiose; extroverted and people seeking, high energy level; full of plans and activities; versatile with broad interests; tendency to be overinvolved and meddlesome; uninhibited and stimulus seeking (at least at certain times); and a short sleeper (usually less than 6 hours per night).

Table I. Lifetime prevalence of bipolar in cluster patients studied.

	Episodic cluster n = (134)	Chronic cluster n = (141)	Combined n = (275)
	Patients	Patients	Percent of total patients
Bipolar I	1	2	1.1%
Bipolar II	4	2	2.2%
Cyclothymia	2	4	2.2%
Bipolar NOS	1	2	1.1%
Total bipolar spectrum	8 (6%)	10 (7%)	6.6%

While it is possible that poorly controlled pain may exacerbate depression, it is more likely that shared genetic and environmental factors contribute to the cluster headaches, as well as to the affective disorder. The clinical spectrum of bipolar disorders is an evolving concept. Bipolar II is very conservatively defined in DSM-IV, and DSM-IV has inherent biases against diagnosing bipolar illness. In the current study, the investigators expanded the definition of bipolar disorder, not otherwise specified, to include those with hyperthymic temperaments (8,9). We also included those cluster sufferers who had persistently agitated, angry personalities, with a strong family history of bipolar, and/or a hypomanic reaction to an antidepressant. These patients, along with those who have "persistent temperamental instability", with a strong family history of bipolar illness, constitute part of the milder end of the bipolar spectrum. It is these milder bipolar patients who tend to be missed and underdiagnosed. The presence of mania, or even hypomania, is not absolutely necessary for the diagnosis of (mild) bipolar spectrum disorder.

The therapeutic implications for recognizing bipolarity are great. Certain medications may be helpful for both cluster headache, and for the prevention of bipolar. Divalproex sodium (Depakote®) has been utilized extensively for both cluster headache prevention and for bipolar illness (11,12), and it has been well studied for both bipolar illness and for migraine. Divalproex sodium has become one of the primary migraine and chronic daily headache preventives (13). It is often the first choice for those patients with concurrent bipolar and cluster headache.

Other anticonvulsants have been less well studied for cluster headache. While lamotrigine (Lamictal®) has been shown to have good utility in the bipolar population, its efficacy in headache is lacking. Topiramate (Topamax®) has been useful for chronic daily headache and migraine (14), and possibly for cluster headache as well. However, its efficacy in bipolar illness is not well established. Carbamazepine (Carbatrol®, Epitol®, Tegretol®) has no known efficacy for cluster headache.

Lithium carbonate (Eskalith®) has been utilized for both the prevention of bipolar and cluster headaches (15). In selected patients, lithium may be a good choice for both conditions. Lithium is not efficacious for migraine or for chronic daily headache. Side effects often

limit the use of lithium.

The recognition of bipolar illness in headache patients carries important therapeutic implications.

CONCLUSIONS

Headache medications should be chosen on the basis of the headache type and severity, as well as comorbidities. The psychiatric comorbidities, including bipolar illness, often help guide our medication use. This study indicates that bipolar illness is a comorbid condition in 6.6% of cluster headache patients. For those patients identified as having cluster headache with bipolar illness, medications including divalproex sodium and lithium may be beneficial.

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