ABSTRACT

The lifetime prevalence of bipolar I disorder in the United States is reported to be between 1% and 1.6%; the prevalence of bipolar II disorder is estimated to be 0.5%. A more recent study, however, demonstrated an overall rate of 3.4%. Bipolar disorder is a lifelong debilitating and potentially fatal illness characterized by changes in mood, cognition, energy levels, behavior, and perception and is difficult to diagnose.

The primary goal of treatment for bipolar disorder is to prevent subsequent episodes, thus limiting morbidity and mortality. Comprehensive nursing management includes more than just treating the acute phase of illness. Identifying effective maintenance therapies that are both efficacious and tolerable is a central challenge in the management of patients with bipolar disorder. The use of mood stabilizers and antipsychotic medications may provide more effective stabilization and help reduce the frequency and severity of episodes, therefore improving outcomes and quality of life in these patients. Advanced practice psychiatric nurses, clinically trained to provide care from a holistic approach, are in an optimal position to weigh the benefits and risks of antipsychotic therapy and individualize care to better meet patient needs and overall treatment goals.

Atypical antipsychotic agents have been shown to be effective for acute manic episodes associated with bipolar disorder and some have been demonstrated to have mood-stabilizing properties. In this article, the data supporting the individual atypical agents used to treat this debilitating disorder are reviewed. (Adv Stud Nurs. 2004;2(1):24-32)

Bipolar disorder is a lifelong debilitating and potentially fatal illness characterized by changes in mood, cognition, energy levels, behavior, and perception. The essential feature of bipolar I disorder is the occurrence of one or more manic episodes or mixed episodes (episodes meeting criteria for both mania and major depression). Often, these patients have also experienced one or more major depressive episodes. A review of studies indicates that more than one half of bipolar patients may experience a major depressive episode prior to a manic episode and that they are likely to present in clinical settings with depression. Bipolar II disorder is characterized by the occurrence of one or more major depressive episodes accompanied by at least one hypomanic episode.

Studies published in 2001 and 2002 estimated the lifetime prevalence of bipolar I disorder in the United States to be between 1% and 1.6%; the prevalence of bipolar II disorder was estimated to be 0.5%.
recent study by Hirschfeld and colleagues, however, demonstrated an overall rate of 3.4%—3 times higher than previous estimates. When study results were adjusted for the nonresponse bias (66.8% of 127 800 subjects responded), the rate increased to 3.7%. The investigators also found that misdiagnosis of bipolar disorder appears to be extraordinarily common. Only 19.8% of the subjects who were positively screened for bipolar I or II disorders reported a previous diagnosis of bipolar disorder, whereas 31.2% reported receiving a diagnosis of unipolar depression. An additional 49.0% in this group noted that they had never been diagnosed with bipolar disorder or unipolar depression. The significant conclusion of this study was that nearly 4% of American adults may suffer from bipolar I and II disorders.

A survey sponsored by the National Depressive and Manic-Depressive Illness Association (NDMDA) determined that the peak age at onset of bipolar disorder was the middle to late teens, between 15 and 19 years of age. According to the NDMDA survey and the Epidemiologic Catchment Area (ECA) survey, the mean age of individuals with bipolar disorder is 21 years. One half of the respondents in the NDMDA study reported that they received no treatment within the first 5 years after the first episode of illness. Data from these studies underscore the fact that many patients with bipolar disorder remain untreated due to the lack of financial resources, housing, or social support or due to the effects of the disorder itself, which often pose significant barriers to treatment. For example, people with bipolar disorder who are experiencing a manic episode might not recognize that they are ill and might be unwilling to seek treatment.

Appropriate management of bipolar disorder is essential. Keck and colleagues estimate that 25% of patients with bipolar disorder attempt suicide. A high rate of comorbidity is also present in patients with bipolar disorder. Drug and alcohol abuse is common and worsens the underlying disorder. Patients who abuse alcohol and/or drugs are at higher risk for rapid cycling, mixed symptoms, and intractable disease compared with individuals who do not use drugs or alcohol in excess. In addition, patients with comorbid substance abuse often have a longer recovery period when treated.

**TREATMENT OF PSYCHOSIS IN BIPOLAR DISORDER**

Psychotic symptoms are common in bipolar disorder and are more common in mania than in depression. Goodwin and Jamison report that 58% of patients with bipolar disorder have at least one psychotic symptom; however, patient self-reports indicate that 90% of patients experience psychosis on a periodic basis. Delusions appear to be more common than hallucinations in manic patients.

In general, bipolar patients with psychotic symptoms tend to have a more severe course of illness, especially when these symptoms present with the first manic episode. Stabilized patients with bipolar disorder and a history of psychotic features have relapse rates 2 to 3 times greater than relapse rates in patients without psychosis. Tóhen and colleagues report that patients with "mood-congruent" psychosis (ie, delusions or hallucinations entirely consistent with the typical themes of a depressed or manic mood) tend to relapse less frequently than patients with "mood-incongruent" psychosis (ie, delusions without a perceivable connection to mood, such as those typically experienced in schizophrenia). It is therefore important to note mood congruency at the time of diagnosis.

The treatment of bipolar illness often involves a combination of therapies, including mood stabilizers and antipsychotic agents (Table). The American Psychiatric Association (APA) Practice Guidelines for Bipolar Disorder recommend that antipsychotic drugs be used in conjunction with mood stabilizers (eg, lithi-
um or valproate) for more severe acute manic or mixed episodes. For less ill patients in this category, either monotherapy with a mood stabilizer or an atypical antipsychotic agent is recommended. For patients with breakthrough symptoms of psychosis, antipsychotic medication should be added after mood stabilizer treatment has been optimized. For treatment-resistant patients with acute manic or mixed episodes, adding or changing the antipsychotic medication should be considered. However, the nurse will want to assess the patient's previous response and recent history of adherence to the current therapy before making significant changes. For maintenance treatment, the long-term use of an atypical antipsychotic agent may be beneficial in patients with persistent psychosis and in patients whose psychosis tends to recur.

**Conventional Antipsychotic Agents**

The primary disadvantage of conventional antipsychotic agents is their side-effect profile. Adverse effects include extrapyramidal symptoms (EPS), tardive dyskinesia, hyperprolactinemia, weight gain, sedation, and impaired sexual function. Some reports indicate that patients with bipolar disorder have a greater vulnerability to EPS and tardive dyskinesia compared with patients with schizophrenia. Conventional antipsychotic agents can also cause neuroleptic malignant syndrome, a rare but serious and potentially life-threatening condition. Patients taking conventional antipsychotic drugs often complain about cognitive side effects that can be more disturbing than the cognitive symptoms of psychosis. These adverse effects often lead to nonadherence and disruption of treatment with concomitant recurrence or relapse, rehospitalization, impaired personal relationships, occupational difficulties, suicide, and violence.

When used in conjunction with mood stabilizers, conventional antipsychotic drugs can have a negative impact on long-term treatment by causing neuroleptic dysphoria or increasing the frequency of depressive episodes. The long-term use of conventional antipsychotic drugs may protect against mood elevation and psychosis but do not alter the underlying cyclicity or protect against recurrent depression. In addition, they can induce rapid cycling in some patients. Despite these major drawbacks and recent evidence showing the advantages of atypical antipsychotic drugs, conventional agents continue to be routinely prescribed in patients with bipolar disorder. Cost and available formulation are important considerations when choosing pharmacotherapy; however, continued evaluation of existing evidence regarding the risk/benefit ratio is crucial.

**Advantages of Atypical Antipsychotic Agents**

The atypical antipsychotic agents may play a unique role in bipolar disorder by controlling symptoms of mania without the significant adverse effects of the conventional antipsychotic agents. Because of this improved side-effect profile, atypical agents are preferred for long-term treatment of bipolar disorder. The risk for EPS and tardive dyskinesia is lower with atypical antipsychotic drugs compared with conventional agents but may be dose dependent (increased risk with higher dosages). There is also a reduced risk of hyperprolactinemia (except with risperidone).

Atypical antipsychotic agents differ from conventional agents in their efficacy profile and in the types of symptoms they target. Data with clozapine, risperidone, olanzapine, quetiapine, ziprasidone, and aripiprazole in patients with acute bipolar mania are presented below.

**Clozapine**

No double-blind placebo-controlled studies of clozapine in the treatment of acute bipolar mania have been published. However, several open-label studies with small numbers of patients support clozapine as an effective agent for the short- and long-term control of acute mania and psychosis in patients with bipolar disorder. Effectiveness was shown in patients with pure and mixed type, rapid and nonrapid cycling, and with or without psychosis, as well as in patients who were refractory to treatment with mood stabilizers, conventional antipsychotic drugs, and electroconvulsive therapy.

Calabrese and colleagues showed that 13 weeks of clozapine treatment was effective in 25 acute manic patients with either bipolar disorder or schizoaffective disorder–bipolar subtype who were resistant or intolerant to lithium, anticonvulsants, and conventional neuroleptic agents. In this study, patients with bipolar disorder showed better improvement compared with those with schizoaffective disorder. In addition, nonrapid cyclers responded better than rapid cyclers. Suppes and colleagues conducted a randomized open-label study of clozapine add-on therapy versus treatment as usual for patients with...
treatment-resistant schizoaffective or bipolar disorder. The results demonstrated that clozapine had mood-stabilizing properties over 1 year of treatment, although patients with schizoaffective disorder required higher doses.

In a recent study, Ciapparelli and colleagues conducted a naturalistic 48-month follow-up of clozapine treatment in 101 patients with treatment-resistant schizophrenia, schizoaffective disorder, or bipolar disorder. More patients with schizoaffective disorder and bipolar disorder responded to clozapine compared with patients with schizophrenia (90.0%, 83.8%, and 64.7%, respectively). Those with bipolar disorder had the shortest response time and the highest psychosocial and occupational functioning levels throughout the 48 months. Incidentally, patients with schizoaffective disorder had the lowest treatment discontinuation rate.

**Risperidone**

Risperidone was approved by the US Food and Drug Administration (FDA) in December 2003 as monotherapy or combination therapy (with lithium or valproate) for the short-term treatment of acute manic or mixed episodes. Three recent studies support its usefulness in this disorder. Vieta and colleagues assessed the combination of risperidone and topiramate for mania in a 12-month, multicenter open-label study in 58 patients with bipolar disorder and a manic episode. In an analysis of 41 patients completing the study, combination treatment was associated with significant improvement in mania symptoms (P < .005) and long-term outcomes (P < .005). Relapse rates were significantly lower during the 12-month study period compared with the preceding year (P < .001). There was no increase in depressive symptoms and no weight gain among participants.

Yatham and colleagues conducted a 3-week study in 151 patients to determine the efficacy of risperidone added to a mood stabilizer (lithium or valproate) in patients with bipolar disorder. Patients treated with combination therapy experienced rapid improvement in mania with greater reductions at week 1 in the risperidone group compared with those not taking risperidone. Yatham and colleagues confirmed these findings in a 12-week prospective study in which risperidone was added to mood stabilizers in patients with bipolar disorder with either manic or mixed episodes. The combination resulted in a highly significant decrease in mania compared with baseline (-22.6 points on the Young Mania Rating Scale [YMRS]; P < .001). When the response was defined as a 50% or greater reduction in YMRS scores from baseline, 32%, 68%, and 90% of patients met the criteria at week 1, week 3, and week 12, respectively, illustrating the rapid onset of response. Significant decreases in depression rating scores were also reported.

**Olanzapine**

Olanzapine—both as monotherapy and in combination with lithium or valproate—is also approved by the FDA for the short-term treatment of acute mania in bipolar disorder. Tohen and colleagues studied the efficacy and safety of olanzapine versus placebo in a double-blind, 3-week, open-label trial involving 139 patients with acute mania associated with bipolar disorder. Patients taking olanzapine had greater improvement in mania measured by YMRS compared with those taking placebo. Significantly more patients taking olanzapine (48.6%) responded compared with those taking placebo (24.2%; P < .01). The starting dose of olanzapine was 10 mg daily with study investigators having the flexibility to titrate the dose based on response. The mean modal dose in this study was 14.9 mg. There were no statistically significant differences between olanzapine and placebo with respect to measures of Parkinsonism, akathisia, and dyskinesia.

In another study, Tohen and colleagues compared olanzapine with placebo in a 4-week, double-blind, parallel study in 115 patients with bipolar disorder. Again, patients taking olanzapine showed a significantly greater improvement in YMRS total score compared with those taking placebo (-14.8 ± 12.5 vs -8.1 ± 12.7; P < .001). Patients taking olanzapine also had a higher response rate compared with those taking placebo (65% vs 43%; P = .02). Although patients taking olanzapine did not show signs of EPS, they experienced more weight gain and somnolence compared with patients taking placebo. In this study, the starting dose was 15 mg, and again, study investigators had the flexibility to titrate the dose based on response. The mean modal dose in this study was 16.4 mg. The recommended starting dose of olanzapine for the treatment of acute manic episodes is 15 mg daily.

Rendell and colleagues examined 6 trials of monotherapy or combination therapy with olanzapine in patients with bipolar mania (n = 1422). They concluded that monotherapy and combination therapy with olanzapine was superior to placebo for reducing
the symptoms of mania; however, there was a high rate of failure to complete treatment with all treatments in the trials, which may have biased the estimates of relative efficacy. Olanzapine was also superior to placebo for reducing psychotic symptoms and was superior to divalproex for reducing manic symptoms. Olanzapine had the same rate of clinical response as haloperidol; however, fewer patients taking olanzapine compared with haloperidol discontinued treatment. Olanzapine caused greater weight gain and somnolence compared with placebo, but depressive symptoms and movement disorder were similar to those with placebo. Olanzapine also caused more prolactin elevation compared with placebo and more weight gain compared with haloperidol.

In January 2004, olanzapine received approval as maintenance therapy for the long-term treatment of bipolar disorder. Two studies evaluating the long-term effectiveness of olanzapine in bipolar disorder were submitted to the FDA for consideration for a maintenance indication. The first study was a randomized double-blind trial of olanzapine versus placebo to evaluate relapse prevention in bipolar disorder. Patients who met criteria for symptomatic remission while being treated in an open-label trial of olanzapine for 6 to 12 weeks were enrolled and randomized to treatment with either olanzapine or placebo. At endpoint, patients taking olanzapine had a significantly prolonged time to relapse compared with those taking placebo. Patients taking olanzapine had a 46.7% rate of relapse compared with 80.1% in patients taking placebo.

The second study submitted to the FDA was a randomized, double-blind, 52-week trial comparing the effectiveness of olanzapine with lithium. Prior to study enrollment, patients were treated with an open-label combination of olanzapine and lithium for 6 to 12 weeks. Patients achieving symptomatic remission were then randomized to treatment with either olanzapine or lithium. The olanzapine group had a significantly lower rate of manic relapse compared with the lithium group (P < .001). Both treatments had comparable efficacy in preventing a depressive episode. More patients in the olanzapine group completed the 52-week trial compared with patients in the lithium group (P = .004).

Quetiapine

In January 2004, quetiapine received FDA approval for the short-term treatment of acute manic episodes associated with bipolar I disorder either alone (monotherapy) or as adjunctive therapy when added to lithium or divalproex. The efficacy of quetiapine in the treatment of acute manic episodes was established in 3 placebo-controlled trials (2 monotherapy and 1 adjunct therapy) in patients who met Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, criteria for bipolar disorder with manic episodes. The primary outcome in all 3 studies was change from baseline in the YMRS total score after 3 weeks.

A pooled analysis of data from 2 double-blind, randomized, placebo-controlled trials assessed the efficacy and safety of quetiapine monotherapy for the treatment of acute manic episodes in adults with bipolar I disorder. After 3 weeks of treatment, significantly more patients taking quetiapine achieved a response (350% decrease from baseline YMRS score) compared with patients taking placebo (48.1% vs 31.3%; P < .0006) and a statistically significant change in YMRS total score was observed from day 4 onward in the quetiapine group versus placebo (P = .021). In a separate study, 190 inpatients were randomized to treatment with either quetiapine (n = 90) or placebo (n = 100) as adjunctive therapy to a mood stabilizer (lithium or divalproex). Of the patients who completed the study, 56 were taking quetiapine and 49 were taking placebo. Patients taking quetiapine as adjunctive therapy had a significantly greater change in YMRS compared with those taking placebo (mean change, –13.76 and –9.93, respectively; P = .021). Significantly more patients in the quetiapine group achieved a 50% reduction in YMRS scores (54.3% vs 32.6%; P = .005). Change in Clinical Global Impression Scale for Bipolar (CGI-BP) severity score was also significantly greater for the quetiapine group (–13.8 vs –0.78; P < .001). Quetiapine is generally well tolerated; the most common adverse events with quetiapine were somnolence, dry mouth, asthenia, and orthostatic hypotension. Discontinuation due to adverse events with quetiapine was similar to that with placebo (5.6% vs 6.0%).

Earlier studies with quetiapine showed similar results. Delbello and colleagues conducted a randomized, double-blind, placebo-controlled, 6-week study of quetiapine in combination with divalproex for the treatment of mania in adolescents (n = 30) with bipolar disorder and observed that the combination was superior to divalproex alone in reducing YMRS scores (P = .03). More patients taking combination treatment compared with divalproex monotherapy responded to therapy (87% vs 53%; P = .05), and there were no significant differences between groups.
on safety measures. Patients taking combination therapy had more mild-to-moderate sedation compared with patients taking divalproex alone.

In a similar study involving adult patients, Sachs and colleagues showed that quetiapine plus a mood stabilizer (lithium or divalproex) resulted in a 53% response rate compared with 32% for mood stabilizers alone (P < .005). Vieta and colleagues studied quetiapine as an add-on to mood stabilizers in 14 patients with bipolar disorder and rapid cycling symptoms. Combination therapy significantly reduced scores on the general CGI-BP (−1.8; P = .013), the mania subscale of the CGI-BP (−1.3; P = .016), and the YMRS (−1.01; P = .025); however, depression was not significantly affected. The most common side effect was sedation.

In a 12-month preliminary open-label study, Altamura and colleagues examined quetiapine versus mood stabilizers in the maintenance treatment for bipolar disorder (n = 28). All patients experienced a significant improvement on several scales (Brief Psychiatric Rating Scale, CGI, Hamilton Depression Rating Scale) with no significant side effects and good compliance.

ZIPRASIDONE

Data with ziprasidone for bipolar disorder are limited; however, a randomized, double-blind study published in 2003 suggests its value. In this trial, 210 patients with bipolar I disorder and a current manic or mixed episode were treated with ziprasidone (40-80 mg twice daily) or placebo for 3 weeks. Ziprasidone produced rapid, sustained improvements compared with baseline and placebo on all primary and most secondary efficacy measures (Figure 1). Significant improvements were observed within 2 days of treatment and were maintained throughout the 3 weeks. The authors reported that ziprasidone was generally well tolerated, associated with a low rate of EPS, and did not cause weight gain.

ARIPIPRAZOLE

Four controlled trials with aripiprazole in bipolar disorder have been completed. Keck et al studied 262 patients with bipolar disorder who were treated with aripiprazole (30 mg daily, reduced to 15 mg daily if necessary for tolerability) or placebo for 3 weeks. Aripiprazole produced statistically significant mean improvements in the YMRS total score compared with
placebo (--8.2 vs -3.4; P < .01) and a significantly higher response rate (40% vs 19%). Response to aripiprazole was rapid and as early as day 4, with 15% responding at day 4 compared with 4% of those taking placebo (P < .01; Figure 2). By day 4, aripiprazole had separated from placebo on key efficacy variables (response per YMRS; CGI-BP scores for severity of illness [mania] and change from preceding phase [mania]). The completion rate was significantly higher with aripiprazole compared with placebo (42% vs 21%). Discontinuation rates due to adverse events did not differ significantly between treatments. There were no significant changes in body weight with aripiprazole versus placebo, and aripiprazole was not associated with elevated serum prolactin or QTc prolongation.

In a 3-week, double-blind, placebo-controlled trial of 272 inpatients with bipolar disorder experiencing an acute manic episode, patients were randomized to receive either placebo or a starting dose of 30 mg daily of aripiprazole, with the option to decrease the dosage to 15 mg daily (mean dose, 27.6 mg daily). Aripiprazole produced significantly greater improvements in YMRS score by day 4 compared with placebo (–8.17 vs –5.37; P < .002); the separation increased throughout the 3-week treatment period (week 3: –12.52 vs –7.19; P < .001). Significantly more patients responded to treatment with aripiprazole compared with placebo (53% vs 32%, P < .001) at week 3. Aripiprazole produced significant improvements compared with placebo in the CGI-BP (P = .009 at week 3), Positive and Negative Syndrome Scale (PANSS) Total (P = .011) and PANSS Hostility Subscale (P = .002) scores. The number of patients who experienced clinically significant weight gain (defined as ≥7% weight gain) was comparable between treatment groups. There was no significant difference in the rate of EPS between aripiprazole and placebo, and discontinuation rates due to adverse events were similar. In this study, the most commonly reported adverse events for aripiprazole were akathisia, dyspepsia, and constipation.

In a separate 12-week, multicenter, double-blind study of 338 inpatients or outpatients with acute mania, a significantly greater percentage of patients responded to treatment with aripiprazole compared with haloperidol at week 12 (49.7% vs 28.4%; P < .001). Patients were randomized to receive aripiprazole 15 mg daily or haloperidol 10 mg daily, with the option to increase doses to a maximum of 30 mg daily for aripiprazole (mean dose, 21.6 mg daily) or 15 mg daily for haloperidol (mean dose, 11 mg daily). Although both drugs produced similar improvement in mean YMRS and CGI severity scores, significantly more patients taking aripiprazole remained in the trial compared with those taking haloperidol (50.9% vs 29.1%; P < .001). Response rates were better with aripiprazole compared with haloperidol at 3 weeks (51% vs 43%) and 12 weeks (50% vs 28%, P < .001). Discontinuations due to adverse events were 49.1% in the haloperidol group compared to 18.9% in the aripiprazole group. Patients taking haloperidol also experienced significantly more EPS compared with those taking aripiprazole, as measured by mean change from baseline to endpoint in the Simpson-Angus Scale (1.02 vs 5.70; P < .001), the Barnes Akathisia Scale (0.32 vs 0.80; P < .001) and the Abnormal Involuntary Movement Scale (0.14 vs 0.81; P < .002). Patients taking haloperidol also had a significant increase in prolactin levels compared with a decrease for patients taking aripiprazole (P < .001). Weight change associated with aripiprazole and haloperidol was 0.27 kg and –0.10 kg, respectively, and no patients in either treatment group had clinically significant increases in QTc interval. The high tolerability of aripiprazole was noted with the most commonly observed side effects reported in this study (incidence rate >10%) being insomnia, depression, akathisia, and headache. The most common side effects with haloperidol were EPS, akathisia, depression, headache, and tremor.

Clinical Implications

Because 90% of patients who experience a manic episode will develop additional affective episodes, the primary goal of treatment for bipolar disorder is to prevent subsequent episodes, thus limiting morbidity and mortality. Pharmacologic management of bipolar disorder includes more than just treating the acute phase of illness. Identifying effective maintenance therapies that are both efficacious and well tolerated is a central challenge in the management of patients with bipolar disorder. The use of mood stabilizers and antipsychotic therapy may provide more effective stabilization and help reduce the frequency and severity of episodes, therefore improving functional outcomes and quality of life in these patients.

Advanced practice psychiatric nurses are in an optimal position to be knowledgeable about the benefits
and risks of antipsychotic therapy and to individualize care to better meet patient needs and overall treatment goals. Minimizing sedation due to therapy is important in facilitating the resumption of daily activities and reintegration into society. In addition, establishing and maintaining a supportive and therapeutic relationship and monitoring treatment response is critical to the proper understanding and management of an individual patient. A crucial element of this alliance is the knowledge gained about the course of the patient’s illness that allows careful monitoring of the patient’s psychiatric status so that new episodes can be identified as early as possible. Educating patients and their families regarding the seriousness of bipolar disorder and the expected effects of its treatment are critical to enhancing treatment adherence and reinforcing the patient’s collaborative role in achieving recovery. In addition, the psychiatric nurse can assist the patient in anticipating stressors and determining ways to cope so the impact of those stressors is minimized. Assisting the patient to develop a schedule that aims to regulate sleep and activity is another crucial intervention, considering that disrupted circadian rhythms may exacerbate or trigger a mood episode.

Detailed information on implementing an effective treatment plan as well as the adverse effects and dosing recommendations for combination therapies can be found in the APA clinical practice guidelines devoted to the treatment of bipolar disorder, available at http://www.psych.org/psych_pract/tpggm/bipolar_revisebook_index.cfm. The APA guidelines list many resources for patients and caregivers to help manage this difficult disorder (see sidebar) 14.

With 4 atypical antipsychotic agents now being indicated for the treatment of acute mania, and 2 additional agents (ziprasidone and aripiprazole) seeking indications in the treatment of bipolar disorder, the role of atypical antipsychotic agents in treating this complicated illness and the available options continue to expand.

**REFERENCES**


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**Educational Resources for Depression and Bipolar Disorder**

Internet Mental Health
www.mentalhealth.org

National Foundation For Depressive Illness, Inc.
www.depression.org

National Alliance for the Mentally Ill
www.nami.org

National Institute of Mental Health Public Inquiries
www.nimh.nih.gov

National Mental Health Association
www.nmha.org

National Depressive and Manic Depressive Association
www.ndmia.org

Data from the American Psychiatric Association.14