REVIEW

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Differentiating bipolar disorder from depression in primary care

ABSTRACT

Because patients with bipolar disorder spend more time in the depressed phase than in the manic phase, many receive an incorrect diagnosis of unipolar major depression and receive inadequate or improper treatment for it, leading to a dramatically increased risk of morbidity and suicide. Greater diagnostic accuracy is needed.

KEY POINTS

Clinicians can better recognize bipolar disorder by asking about any manic or hypomanic symptoms in the past and about family history. Screening questionnaires can be useful, as can talking to the patient's family.

Patients with bipolar disorder are more likely than their unipolar counterparts to have their first mood episode (usually depression) before age 25, to suffer more recurrent episodes, and to have shorter intervals of wellness between episodes. They may have mostly recurrent depression with only brief, subtle episodes of hypomania.

Patients with bipolar disorder have highly variable results with antidepressants, ranging from multiple drug treatment failures and resistance to either erratic responses or remarkably fast, sudden, brief relief of depression.

Lithium, lamotrigine, the olanzapine-fluoxetine combination, or quetiapine are currently recommended as initial options for acute bipolar depression even though they do not have FDA approval for this indication

WHEN PHYSICIANS encounter a patient who obviously is depressed, they should not assume that the patient has unipolar depression until they have ruled out bipolar disorder (formerly called "manic-depressive illness").

Missing the diagnosis of bipolar disorder in depressed outpatients can lead to treatment resistance, worsening symptoms and dysfunction, and increased risk of hospitalization and suicide. For example, some bipolar patients may not respond to antidepressant monotherapy. Others may have an exaggerated response to an antidepressant and enter into manic or unstable mood states.

This article highlights the need to consider bipolar disorder in the differential diagnosis of major depression, reviews the forms of bipolar disorder, and discusses how to initiate treatment for it.

PRIMARY CARE PHYSICIANS ON THE FRONT LINES

We are aiming our remarks at primary care physicians, mainly because they are the physicians who now deliver up to two thirds of all mental health services.[1]

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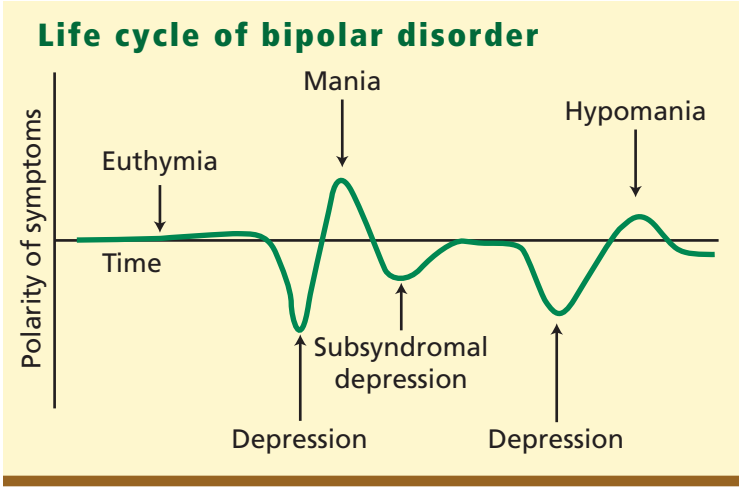

FIGURE 1

Many factors have moved primary care physicians to the front lines in the diagnosis and treatment of depression and other mood disorders. Newer antidepressants are thought to be more effective and safer than older ones and thus easier for primary care physicians to use. The government and industry have undertaken education programs about depression for primary care physicians and the general public. In many areas, mental health specialists are in short supply or access is limited.

Bipolar patients have symptoms (mostly depression) nearly half of their lives

MAJOR DEPRESSION IS A DIAGNOSIS OF EXCLUSION

The *Diagnostic and Statistical Manual of Mental Disorders, 4th Edition* (DSM-IV)[2] defines a depressive episode as a distinct period of at least 2 weeks during which there is either depressed mood or loss of interest or pleasure in nearly all activities, causing a marked impairment in occupational or social functioning. The patient must have at least five of the following symptoms:

- Depressed mood most of the day, nearly every day
- Markedly diminished interest or pleasure in all (or almost all) activities
- Significant weight loss when not dieting, or weight gain
- Insomnia or hypersomnia nearly every day
- Psychomotor agitation or retardation
- Fatigue or loss of energy
- Feelings of worthlessness or excessive guilt
- Diminished ability to think or concentrate
- Recurrent thoughts of death or suicide, or a suicide attempt.

Depression is not always unipolar

When a patient presents with these classic signs and symptoms, a busy clinician may be led to quickly diagnose major depression and begin treatment with a traditional antidepressant. However, as with all illnesses, it is critically important to go through the differential diagnosis.

Just as "all that wheezes is not asthma," all depression is not unipolar. In fact, unipolar major depression is a diagnosis of exclusion: one must first exclude depression due to a general medical problem (such as hypothyroidism) or to alcohol or medication use, adjustment disorders, grief, psychosocial factors, personality disorders, and perhaps most importantly, bipolar affective disorder in the depressed phase.

Only after these are ruled out should unipolar major depressive disorder be conclusively diagnosed and treated.[3]

BIPOLAR DISORDER USUALLY PRESENTS AS DEPRESSION

Bipolar disorder is characterized by dramatic mood swings—from euphoric, expansive, or irritable (mania) to extreme sadness and hopelessness (depression), with symptom-free periods (euthymia) in between.

The pattern isn't always so tidy. Between full-blown manic and depressive episodes, some bipolar patients experience subsyndromal episodes of depression or mania. Episodes of depression or mania can resolve (spontaneously or with treatment) to euthymia or switch from depression to mania or vice versa. Individual patients may experience some or all of these various phases of illness, and the time line for mood changes can be days, weeks, months, or years.

Complicating the picture, many patients present to their primary care physicians in relatively "mixed" states—experiencing both major depressive and manic symptoms simultaneously or in rapidly alternating fashion. Many have a mixed constellation of mood symptoms along with anxiety and multiple physical complaints. Some patients have psy-

TABLE 1

Clues that may differentiate bipolar from unipolar major depression

Both disorders

Recurrent major depressive episodes

Bipolar affective disorder

Depressive episodes that tend to be marked by hypersomnolence, anergia, and hyperphagia

Racing thoughts, irritability, or both

Brief, sudden, or paradoxical responses to traditional antidepressants

Earlier age of onset

Greater risk of suicide

Higher rates of bipolar disorder in family

Overall, less time spent well, and greater functional impairment

chotic symptoms such as hallucinations and delusions, more commonly seen in the manic phase than in the depressed phase.

FIGURE 1 shows how the mood of a patient with bipolar disorder can fluctuate over time. The presentation is usually depression rather than mania, because patients are "down" more of the time than they are "up." This is one of the reasons for misdiagnosis or lack of diagnosis of bipolar depression—a physician may not recognize bipolar disorder unless he or she asks about a history of mania. Even then, some patients may not recall these episodes or choose not to disclose them because they are embarrassed by behaviors that occurred while in a past manic state.

Of critical importance: the criteria for a major depressive episode are identical for major depressive disorder and for bipolar disorder in the depressed phase. Simply determining that the patient has a major depressive episode does not exclude bipolar disorder.

TABLE 1 highlights some clues that may help differentiate unipolar major depression from acute bipolar depression.

Subtypes of bipolar affective disorder

Furthermore, the DSM-IV[2] recognizes several subtypes of bipolar disorder.

Bipolar I disorder is the classic subtype: to qualify, patients must have had at least one major depressive episode and at least one manic or mixed episode.

A *manic episode* is a distinct period of abnormally and persistently elevated, expansive, or irritable mood, lasting at least 1 week, (or any duration if it is so severe that the patient must be hospitalized), that causes a marked impairment in occupational or social functioning. In addition, at least three of the following symptoms must be present (or four if the patient has an irritable mood):

- Inflated self-esteem or grandiosity
- Decreased need for sleep
- More talkative than usual, more rapid speech
- Flight of ideas or racing thoughts
- Distractibility
- Increased goal-directed activity or psychomotor agitation
- Excessive involvement in pleasurable activities with potentially painful consequences.

Bipolar II disorder is defined as one or more major depressive episodes and at least one *hypomanic* episode. Patients with bipolar II disorder have never experienced a full manic or mixed episode.

Hypomania is sometimes thought of as a milder form of mania, since it does not have to cause the marked impairment in functioning seen with full mania, but only a clear change in mood that is above the normal baseline. It is distinct from mania in several ways:

- General impairment is less severe in hypomania than in mania.
- Hypomanic patients may have fewer and milder lapses of judgment than manic patients do.
- Many patients with hypomania respond to outpatient treatment, whereas many

If a bipolar patient presents at all, he or she will most likely complain of depression

with mania need to be hospitalized for initial stabilization.

Cyclothymic disorder is a chronic, fluctuating mood disturbance. Patients experience numerous periods of hypomanic and depressive symptoms that may meet the criteria for hypomanic episodes but are not sufficient in number, severity, duration, or pervasiveness to satisfy the criteria for manic or major depressive episodes, as defined for bipolar I and II disorders.

The required duration of symptoms is 2 years (1 year in children and adolescents). Cyclothymic disorder usually has an insidious onset and a chronic course. An estimated 15% to 50% of patients subsequently develop bipolar I or II disorder.

Bipolar disorder not otherwise specified consists of bipolar features that do not meet the criteria for a particular bipolar disorder as outlined above. Examples:

- Recurrent depressive episodes plus hypomanic episodes that last less than the DSM-IV-required 4 days (the most common scenario)
- Recurrent hypomanic episodes without intercurrent depressive episodes
- A manic or mixed episode superimposed on schizophrenia, delusional disorder, or other psychotic disorder
- Situations in which the clinician concludes that bipolar disorder is present but cannot determine whether it is primary (idiopathic) or secondary to a medical condition or substance abuse.

Up to 15% of untreated or inadequately treated bipolar patients die by suicide

BIPOLAR DISORDER IS MORE COMMON THAN ONCE THOUGHT

In 1990, the World Health Organization cited bipolar disorder as the sixth leading cause of disability-adjusted life years worldwide among people age 15 to 44. The total lifetime cost for people with bipolar disorder with illness onset in 1998 was estimated at $24 billion.[4,5]

Bipolar disorder is more prevalent than previously thought. In a community-based screening study, Hirschfeld et al[6,7] sent the Mood Disorder Questionnaire (a validated screening tool, TABLE 2, **http://www.dbsalliance.org/questionnaire/screening_intro.asp**) to more than 125,000 adults in the United States. The adjusted prevalence of bipolar disorder was 3.7%, and about 31% of patients with bipolar disorder were misdiagnosed as having major depression.[7]

In 1,157 adult patients seeking primary care at an urban clinic in the United States, Das et al[8] found that the lifetime prevalence of bipolar disorder was about 10%.

In 187 patients at three primary care mood disorder clinics, the most common primary diagnosis was bipolar disorder (39%), followed by major depression (24%) and anxiety disorders that included obsessive-compulsive disorder, generalized anxiety disorder, panic disorder, and post-traumatic stress disorder (11.8%). Fifteen percent of these patients reported that they had attempted suicide.[9]

THE HUMAN SIDE OF THE ANALYSIS

Judd et al[10] followed 146 patients with bipolar I disorder every week for a mean of 12.8 years and found that they had symptoms at 47.3% of visits. Depression was the most frequent symptom (31.9%), followed by mania or hypomania (8.9%) and rapid cycling or mixed episodes (5.9%). The patients' symptomatic status changed an average of six times a year, and polarity changed more than three times a year.

Up to half of all people with bipolar disorder are estimated to make at least one suicide attempt in their lifetime, and 10% to 15% of untreated patients with bipolar disorder actually die by suicide.[11] Das et al[8] reported that nearly one fifth (18.8%) of their patients with bipolar disorder said they had thought about suicide during the 2 weeks prior to their visit.

The risk of suicidal behavior is highest during the acutely depressed phase of bipolar disorder.[12,13] In evaluating risk for suicide in any patient, his or her suffering may be the best indicator of heightened risk, and unfortunately, patients with bipolar disorder have symptoms (predominantly depression) nearly half of their lives and thus are at elevated risk of suicide.[10,14]

MANY ARE MISDIAGNOSED

Hirschfeld et al[15] surveyed US patients with bipolar disorder and found that 69% had been misdiagnosed, mostly as having unipolar

TABLE 2

Mood Disorder Questionnaire

1 Has there ever been a period of time when you were not your usual self and . . .

___ You felt so good or so hyper that other people thought you were not your normal self or you were so hyper that you got into trouble?

___ You were so irritable that you shouted at people or started fights or arguments?

___ You felt much more self-confident than usual?

___ You got much less sleep than usual and found you didn't really miss it?

___ You were much more talkative or spoke much faster than usual?

___ Thoughts raced through your head or you couldn't slow your mind down?

___ You were so easily distracted by things around you that you had trouble concentrating or staying on track?

___ You had much more energy than usual?

___ You were much more active or did many more things than usual?

___ You were much more social or outgoing than usual, for example, you telephoned friends in the middle of the night?

___ You were much more interested in sex than usual?

___ You did things that were unusual for you or that other people might have thought were excessive, foolish, or risky?

___ Spending money got you or your family into trouble?

2 If you checked "yes" to more than one of the above, have several of these ever happened during the same period of time?

_____

_____

3 How much of a problem did any of these cause you, like being unable to work; having family, money, or legal troubles; getting into arguments or fights? Please select one response only.

No problem Minor problem Moderate problem Serious problem

A positive screen requires 7 or more "yes" responses, symptom co-occurrence, and moderate-to-severe functional impairment as rated by the patient.

HIRSCHFELD RM, WILLIAMS JB, SPITZER RL, ET AL. DEVELOPMENT AND VALIDATION OF A SCREENING INSTRUMENT FOR BIPOLAR SPECTRUM DISORDER: THE MOOD DISORDER QUESTIONNAIRE. AM J PSYCHIATRY 2000; 157:1873–1875.

To recognize bipolar disorder, ask about a history of mania

depression. Thirty-five percent of them had symptoms for more than 10 years before receiving an accurate diagnosis; women were significantly more likely than men to be misdiagnosed. In 48%, the correct diagnosis had not been made until the third health professional was seen.[16]

Manning et al[17] similarly found that a bipolar disorder diagnosis may be missed for several years or more.

A study of 649 outpatients being treated with antidepressants for depression in a family medicine clinic also revealed a worrisome pattern of misdiagnosis—21.3% actually had bipolar disorder and had therefore likely been misdiagnosed as having unipolar major depression.[18]

Bipolar patients may represent 25% to 30% of difficult-to-treat depressed and anxious patients encountered in primary care.[17]

Ettinger et al[19] found bipolar symptoms in 12% of community-based epilepsy patients, and in 25% of cases the treating neurologist had not recognized the symptoms.

Misdiagnosis can prevent a patient with bipolar disorder from receiving focused treatment with medications thought more suitable and safer for them, namely mood stabilizers such as lithium (eg, Eskalith), divalproex (Depakote), lamotrigine (Lamictal), and atypical antipsychotics.

Patients with bipolar disorder have highly variable results with antidepressant medications

Even though effective treatments are available, only about 27% of patients with bipolar disorder receive treatment for it.[11] This is the lowest treatment rate of all the major psychiatric disorders. Approximately 20% of untreated or inadequately treated bipolar patients commit suicide.[11]

Simply diagnosing correctly and initiating a treatment relationship with a patient suffering with bipolar disorder may significantly improve outcomes and decrease morbidity and mortality. In addition, medicolegal risk is minimized through improved diagnostic accuracy.

DIFFERENTIATING UNIPOLAR FROM BIPOLAR DEPRESSION

Bipolar disorder can be difficult to recognize, even for psychiatrists. And unfortunately, until recently, little attention has been paid to learning how and why to distinguish bipolar affective disorder from major depressive disorder.

In bipolar I disorder, the depressed phase clearly accounts for more of the patient's time than the manic phase and carries a heavier burden, and even more so in the other subtypes, especially bipolar II disorder. Thus, primary care physicians must recognize that if a patient with bipolar disorder presents to the office at all, he or she will most likely complain of depression.

In making the differential diagnosis between unipolar and bipolar depression, it is important to assess the following:

History of mania. Ask the patient, family members, and significant others about a history of mania or hypomania. The Mood Disorder Questionnaire (TABLE 2) is simple and easy to use, or clinicians can use the mnemonic "DIGFAST" to cue their questions about these symptoms[20]:

- **D**istractibility: poorly focused, multitasking
- **I**nsomnia: decreased need for sleep
- **G**randiosity: inflated self-esteem
- **F**light of ideas: complaints of racing thoughts
- **A**ctivities: increased goal-directed activities
- **S**peech: pressured or more talkative
- **T**houghtlessness: risk-taking behaviors (sexual, financial, travel, driving).

The course of the illness may provide diagnostic clues. Patients with bipolar disorder are more likely than their unipolar counterparts to have their first mood episode (usually depression) at an earlier age (typically before age 25), to suffer more recurrent episodes overall, and to have shorter intervals of wellness between episodes. Remember that the pattern of illness may be mostly of highly recurrent depression with only brief, sometimes subtle episodes of hypomania, as in bipolar II disorder.

Response to past treatments. Patients with bipolar disorder have highly variable results with antidepressant medications, ranging from multiple drug treatment failures and resistance to either erratic responses or remarkably fast, sudden, brief relief of depressed mood (sometimes within days to 2 weeks of starting the antidepressant). Patients with treatment-refractory depression or erratic responses should be more carefully assessed for bipolar disorder.

A family history of bipolar disorder, other mood disorders, or schizophrenia is more common in patients with bipolar disorder than in those with unipolar major depression. A strong family history of bipolar disorder in a patient with major depression, even without prior mania or hypomania, should alert the clinician to the higher risk of bipolarity emerging later. More deliberate and careful treatment of depression is warranted in this type of patient.

A complicated life. In some depressed patients with heterogeneous and complicated histories in whom bipolar disorder cannot clearly be diagnosed on the basis of the DSM-IV criteria, a history of chaotic psychosocial events and development, multiple jobs, multiple marriages, multiple geographic relocations, bankruptcies, and overall unpredictability of behavior might suggest bipolar disorder more than unipolar illness, due to the highly recurring and chronic nature of bipolar disorder.

INITIATING TREATMENT FOR ACUTE BIPOLAR DEPRESSION

Treat or refer?

In general, one should consider consulting or referring the patient to a mental health specialist for the same reasons in bipolar disorder as in other illnesses. Patients who need immediate stabilization or who are a danger to themselves or others deserve consideration for immediate referral to a mental health specialist. For less acutely ill patients, primary care physicians may want to make a provisional diagnosis of bipolar illness and initiate appropriate treatment during the transition to specialty care.

Other patients may be treated entirely by their primary care physician, depending on the physician's training, experience, ability, and motivation. But even motivated primary care physicians with the proven ability to treat bipolar illness may choose to refer particular patients if a therapeutic alliance is problematic.

Similarly, the approach to enhancing care for patients with bipolar disorder follows the same general model applied to other illnesses managed in primary care settings, and is outlined below.

The therapeutic alliance

A structured and supportive relationship between the patient with bipolar disorder and his or her caregivers (medical professionals and family) is critical to achieving and maintaining health and quality of life. Taking time to listen and communicating clearly and frankly are key elements in building a therapeutic alliance. Medical professionals should aim to ask direct questions that are more likely to elicit specific information about aspects of the illness. Peer-to-peer support should also be encouraged.

'Meducation'

Doctors, other caregivers, and patients should be encouraged to educate themselves and each other about the different beliefs and experiences they bring to the therapeutic alliance. Information requested by the patient should be provided. Information about the seriousness of the illness and benefits of appropriate therapy should be made available and shared. This "meducation" can foster treatment adherence, destigmatize the disease, and help patients become active and informed participants in the management of their illness.

Patients should not make major decisions when in a depressive or manic episode

Enhance treatment adherence

One should discuss the patient's expectations about treatment, the treatment options, therapeutic effects, possible adverse effects, and likely need for long-term medication. Physicians should neither settle for partial benefit nor be dismayed by not achieving 100% control. Full functional recovery is likely to take several months. Physicians should foster an alliance with patients that helps them to express their treatment preferences.

Monitoring and managing symptoms and risk

One may be able to identify new episodes and high-risk situations early and manage them more effectively by knowing about the course and pattern of the patient's bipolar disorder. Different patients may have unique triggers and behavioral harbingers of poor control.

Solicit information from the patient's family and other third parties when assessing risk, especially suicide risk, substance use, and social isolation. Discuss the need to recognize

TABLE 3

Drugs for bipolar disorder: Approved indications

DRUG	MANIA	MAINTENANCE/ PROPHYLAXIS	BIPOLAR DEPRESSION
Aripiprazole (Abilify)	X	X	
Carbamazepine ER (Equetro)	X		
Chlorpromazine (Thorazine)	X		
Divalproex (Depakote)	X		
Lamotrigine (Lamictal)		X	
Lithium (Eskalith)	X	X	
Olanzapine (Zyprexa)	X	X	
Olanzapine-fluoxetine (Symbyax)			X
Quetiapine (Seroquel)	X		
Risperidone (Risperdal)	X		
Ziprasidone (Geodon)	X		

and manage risky behavior (eg, by limiting access to dangerous machinery, telephones, money). The family and other caregivers should be helped to recognize warning signs and risky situations. Patients should avoid making major or life-changing decisions when in a depressive or manic episode.

Encourage patients to monitor their mood, medication-taking, and sleep patterns. They should try to adhere to a consistent pattern of sleep and activities of daily living, including medication-taking.

MEDICATION OPTIONS

Detailed information on the medical management of bipolar disorder is beyond the scope of this article but can be found elsewhere.[21–23] Drugs approved by the US Food and Drug Administration (FDA) for treating bipolar disorder are listed in TABLE 3.

During the manic phase

Mania is generally more easily managed than depression, and many more approved options exist for mania, notably all of the atypical antipsychotics, lithium, and divalproex. Nevertheless, mania often requires psychiatric hospitalization.

There are no approved treatments for hypomania, although the same treatments used for mania are usually effective, sometimes at lower doses. Clinicians typically choose a single agent from TABLE 3 that has an antimanic indication to treat hypomania or mild mania, while two or more agents may be required for more severe cases of acute mania.

Mixed depressive-manic episodes can be challenging and are most often best approached either by first stabilizing the mania (eg, with an atypical antipsychotic agent or mood stabilizer) and then addressing any residual depression, or by using a combined pharmacologic approach from the outset of treatment (commonly with combinations of antipsychotics and mood stabilizers, or antidepressants with these agents).

Do not use a traditional antidepressant by itself to treat bipolar depression

During the depressed phase

Except for the combination formulation of olanzapine and fluoxetine (Symbyax), no agent is FDA-approved for acute bipolar depression. No traditional antidepressant by itself has ever demonstrated both safety and efficacy in bipolar depression, and these antidepressants are not formally indicated for such use by the FDA.

Long-term use of the olanzapine-fluoxetine combination can be complicated by weight gain and more serious metabolic risks (eg, type 2 diabetes and hyperlipidemia) associated with

TABLE 4

Initiating treatment of bipolar disorder

PHASE	STEP 1	STEP 2	STEP 3 AND BEYOND
Depressed	Lithium starting at 300–450 mg twice a day (target serum lithium level ≥ 0.8 mEq/L) Lamotrigine starting at 25 mg daily	Olanzapine-fluoxetine combination starting at 6 mg/25 mg at bedtime Quetiapine starting at 100 mg at bedtime; increase to 300 mg at bedtime by day 3	Combinations of lithium, lamotrigine, olanzapine-fluoxetine combination, quetiapine Addition of traditional antidepressant to one or more of above medications Electroconvulsive therapy
Manic	Lithium starting at 300–500 mg three times a day Valproic acid/divalproex starting at 500 mg three times a day; if using divalproex ER, 1,500 mg at bedtime Atypical antipsychotic, excluding olanzapine or clozapine (initial dosing varies; refer to prescribing information)	Two of the following in combination: • Lithium • Valproic acid/divalproex • Atypical antipsychotic, excluding clozapine or aripiprazole	Other two-drug combinations of lithium, valproic acid, atypical antipsychotics, carbamazepine, oxcarbazepine, topiramate Electroconvulsive therapy Clozapine Triple drug therapy

ADAPTED FROM GUIDELINES DEVELOPED BY SUPPES T, DENNEHY EB, HIRSCHFELD RM, ET AL; TEXAS CONSENSUS CONFERENCE PANEL ON MEDICATION TREATMENT OF BIPOLAR DISORDER. THE TEXAS IMPLEMENTATION OF MEDICATION ALGORITHMS: UPDATE TO THE ALGORITHMS FOR TREATMENT OF BIPOLAR I DISORDER. J CLIN PSYCHIATRY 2005; 66:870–886.

atypical antipsychotics such as olanzapine. Nonetheless, this agent should be considered the first-line treatment for acute bipolar depression, although the most recent practice guidelines suggest that lithium or lamotrigine or both in combination may be superior, and that other atypical antipsychotics—notably quetiapine (Seroquel)—might deserve equal consideration.[24]

Two large FDA registration trials of quetiapine as a monotherapy for acute bipolar depression had promising results and may lead to an FDA-approved indication in the near future for quetiapine in a dosage range of 300 to 600 mg at bedtime.

The safety issues of the atypical antipsychotics will be discussed in an upcoming article in this journal.

Off-label use of many agents, notably lithium, lamotrigine, and quetiapine, is a common strategy for the management of acute bipolar depression. Evidence in support of using these agents includes data from double-blind, placebo-controlled, randomized trials and considerable clinical experience. In this manner, lithium may be most effective at doses titrated to achieve serum blood levels of more than 0.8 mEq/L, while lamotrigine 50 to 200 mg daily (started at 25 mg daily and increased slowly every 1 to 2 weeks) may have antidepressant benefit in bipolar disorder.

TABLE 4 outlines the initial steps in the medical treatment of patients with bipolar disorder in the acute phases.[24]

The traditional antidepressants used for unipolar major depression are not considered first-line or second-line treatments for acute bipolar depression, and should never be used as monotherapy in this condition. Lithium, lamotrigine, the olanzapine-fluoxetine combination, or quetiapine are currently recommended as initial options, with traditional antide-

pressants used only in combination with a mood stabilizer that can protect against a switch to mania and may also treat core symptoms of depression.

Consultation or collaborative care with a psychiatrist may enhance the treatment for patients with bipolar disorder with the hope of improving outcomes and quality of life.

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