Prevalence and Impact of Comorbid Anxiety and Bipolar Disorder

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Comorbid conditions pose a serious risk to patients with bipolar disorder, but anxiety comorbidity poses a specific hazard due to the increased negative impact of anxiety on illness course and treatment. Anxiety comorbidity appears to be highly prevalent and is associated with intensified symptoms of bipolar disorder and additional comorbid disorders, resulting in a negative impact on the patient and on the course of the illness. The presence of anxiety in bipolar patients is also associated with a lowered age at onset, hampered patient response to treatment such as lithium, increased rates of suicide and substance abuse, and decreased quality of life. Patients can experience work, family, and social impairment and be made to contend with increased health care costs and strains on family support. Studies are few and have a limited scope, and many have failed to consider the clinical significance of comorbid anxiety and bipolar disorder. Because the degree to which anxiety impacts patients with bipolar disorder is not fully known, more information is needed about the relationship between bipolar disorder and anxiety. *(J Clin Psychiatry 2006;67[suppl 1]:5–7)*

In patients with bipolar disorder, comorbid anxiety is highly prevalent and is associated with worsened illness course and functional outcome. Anxiety lowers the age at onset of bipolar disorder, has a negative impact on bipolar treatment, exacerbates associated conditions such as suicidal behavior and substance abuse, and is associated with diminished quality of life.

PREVALENCE OF COMORBID ANXIETY AND BIPOLAR DISORDER

Comorbid conditions pose a serious risk to patients with bipolar disorder, but anxiety comorbidity poses a specific hazard due to the increased negative impact of anxiety on illness course and treatment. Comorbid anxiety also appears to be highly prevalent in patients with bipolar disorder, making anxiety a major aspect of treatment that physicians need to address. Several studies[1–10] of patients with bipolar disorder have found high rates of comorbidity in general and comorbid anxiety in particular. In addition, patients with comorbid anxiety often have multiple anxiety disorders.

Psychiatric Comorbidity

Comorbidity in patients with bipolar disorder has been suggested to be part of the normal course of the illness because a high proportion of patients with bipolar disorder have serious comorbid conditions.[1] According to the findings of the National Comorbidity Survey, 95.5% of the study's patients with bipolar I disorder met criteria for 3 or more additional psychiatric disorders, the most common of which were anxiety, substance abuse, and conduct disorders.[2] The Stanley Foundation Bipolar Treatment Outcome Network[3] found that, of 288 patients with bipolar disorder, 65% had at least 1 comorbid Axis I disorder in their lifetimes, most commonly an anxiety disorder or substance disorder.

Anxiety Comorbidity

Research[4] also shows that patients with bipolar disorder have higher rates of anxiety than the general population. Boylan et al.[5] found that of patients with bipolar disorder, 55.8% had at least 1 comorbid anxiety disorder and 31.8% had multiple disorders. In their literature review, Boylan et al. noted that patients with bipolar disorder had a 20.8% rate of panic disorder compared with a 10% rate of major depressive disorder. Other rates they noted were that 30% of patients with bipolar disorder were found to have generalized anxiety disorder, between 7.8% and 47.2% had social phobia, between 3.2% and 35% had obsessive-compulsive disorder, and up to 40% may have had posttraumatic stress disorder.[5] The Systematic Treatment En-

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hancement Program for Bipolar Disorder (STEP-BD), a national longitudinal public health initiative funded by the National Institute of Mental Health (NIMH), also showed high prevalence rates for a lifetime anxiety disorder (51.2%) and for a current anxiety disorder (30.5%).[6] Anxiety comorbidity was found to be higher for patients with bipolar I than for patients with bipolar II disorder.

While patients with bipolar disorder are prone to a high prevalence of anxiety, patients with panic disorder, conversely, are prone to a high prevalence of bipolar disorder.[4] Panic disorder appears to be the anxiety disorder most commonly comorbid in patients with bipolar disorder. Onset of panic has been noted during episodes of hypomania and depressive mania (mixed states).[7] Patients with bipolar disorder may have a higher sensitivity to anxiety than the general population.[7,8] Anxiety sensitivity has been found to be higher among patients with bipolar disorder compared with patients with unipolar depression, and the risk of panic may be pointedly higher during manic states, i.e., mania, hypomania, and mixed episodes.[8]

Research[9] has found that the relatives of children with bipolar disorder and comorbid anxiety have high rates of both bipolar disorder and anxiety. Data[10] from the NIMH Bipolar Disorder Genetics Initiative also indicate a genetic relationship; family members with bipolar disorder had an increased risk for developing panic disorder if subjects with bipolar disorder had panic attacks or panic disorder.

IMPACT OF COMORBID ANXIETY ON COURSE OF BIPOLAR DISEASE

Anxiety in patients with bipolar disorder tends to have an adverse effect by intensifying symptoms of bipolar disorder and other comorbid disorders, which consequently has a negative impact on the patient and on the course of the bipolar illness. The presence of anxiety in bipolar patients is associated with a lowered age at onset of bipolar disorder, hampered patient response to treatment, increased rates of suicide and substance abuse, and decreased quality of life.

Age at Onset

Patients with anxiety tend to experience much earlier age at onset of bipolar disorder,[3] which is associated with a more severe disease course and poorer outcome.[11] STEP-BD participants with a lifetime anxiety disorder were found to have a significantly lower age at onset (mean = 15.6 years) than subjects without anxiety (mean = 19.4 years).[6] Earlier age at onset could itself be associated with more severe disease course, or it could indicate a predisposition to other traits that worsen disease course, such as increased prevalence of suicide, poor response to lithium, increased number of psychotic features and mixed episodes, increased rates of neuropsychological dysfunction, increased likelihood of panic disorder comorbidity, and increased incidence of substance abuse.[11]

Because anxiety is a risk factor for a lower onset age of bipolar disorder, children with either disorder should be monitored for the other. Although research[12] suggests that diagnoses of bipolar disorder in children should be based on the same DSM-IV criteria as diagnoses of bipolar disorder in adults, children with bipolar disorder present in a way that is atypical compared with adults with bipolar disorder. Children have been found to have an extremely high prevalence of rapid cycling and increased rates of mixed states as opposed to the euphoric or grandiose presentations found in adult patients. Childhood bipolar disorder may be a chronic and mixed variant of bipolar disorder and, like adult bipolar disorder, have a reduced response to mood stabilizers like lithium.

Treatment Response

Studies[2,6,9,13] have noted that patients with bipolar disorder and comorbid anxiety have poor prognoses, increased severity and chronicity of symptoms, and reduced response to pharmacologic and psychotherapeutic treatments. STEP-BD research[6] found that few studies have investigated the efficacy of anxiety-specific pharmacologic therapies for bipolar patients with comorbid anxiety disorders. However, antidepressants may be prescribed by physicians for most anxiety comorbidities, despite the danger of antidepressant-induced manic switch. Many patients (59%) with a comorbid anxiety disorder were not taking an anxiety-specific pharmacologic treatment.[6]

Although research indicates that treatment for bipolar depression should begin with lithium,[1] anxiety symptoms decrease the effectiveness of lithium and anticonvulsants.[5,14] Combination therapies to treat both anxiety and bipolar depression are preferred. Atypical antipsychotics such as risperidone, olanzapine, and quetiapine have been found to have efficacy in treating bipolar depressive symptoms without manic switch.[15] Likewise, atypical antipsychotics appear to have a beneficial effect on anxiety disorders.[8,15]

Substance Abuse and Suicidal Behavior

Patients with bipolar disorder and comorbid anxiety have an increased prevalence of substance abuse and suicide. Substance abuse among patients with bipolar disorder and no anxiety is associated with complications such as increased rates of mixed or rapid-cycling mania, extended time of recovery, increased prevalence of medical disorders, and increased prevalence of suicide.[16] The presence of anxiety tends to exacerbate symptoms and increase these rates and is associated with a major increase in the likelihood of substance abuse.[4,15–18] STEP-BD data[6] suggested that alcohol and substance abuse are common among patients with bipolar disorder but that the rate of alcohol dependency was doubled in the presence of

an associated anxiety disorder. Thirty-two percent of the STEP-BD participants were found to have an anxiety disorder, and 48% were found to have a lifetime substance use disorder. Alcohol and substance abuse are also associated with other negative factors such as increased use of health care, impairment of function, risk for violent behavior, and negative treatment outcome.[17]

Patients with bipolar depression and comorbid substance abuse or anxiety have been found to have increased rates of suicide compared with bipolar depression without a comorbid disorder.[19] Suicide attempts were also found to be more frequent among STEP-BD participants with a lifetime anxiety disorder.[6]

Quality of Life

Comorbid anxiety disorders with bipolar disorder are associated with diminished quality of life and poorer functioning with each additional anxiety disorder.[6] Mood episodes can be longer, more frequent, and much more difficult to treat.[5] In addition, bipolar disorder and comorbid anxiety can have a major economic and social impact on patients, their families, and social associations. Patients can experience work, family, and social impairment and be made to contend with increased health care costs and strains on family support.[20]

CONCLUSION

Anxiety frequently affects patients with bipolar disorder, but clinical information regarding the extent of impact and treatment considerations for comorbid bipolar disorder and anxiety are lacking. Small sample sizes, a scarcity of consistent standards for making assessments across multiple studies, and study groups that are too heterogeneous confound the interpretation of data that do exist. A lack of information regarding acutely ill patients or pharmacologic therapies is problematic. Clearly, anxiety frequently occurs in patients with bipolar disorder and impacts treatment outcome. Further study of possible treatments is needed in patients with both disorders.

Drug names: lithium (Eskalith, Lithobid, and others), olanzapine (Zyprexa), quetiapine (Seroquel), risperidone (Risperdal).

Disclosure of off-label usage: The author has determined that, to the best of his knowledge, lithium, olanzapine, quetiapine, and risperidone are not approved by the U.S. Food and Drug Administration for the treatment of bipolar disorder and comorbid anxiety or other disorders.

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