

Introduction

An Overview of the Issues Surrounding the Recognition and Management of Bipolar Disorder and Comorbid Anxiety

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In contrast to the relationship between substance abuse and bipolar disorder, the relationship between bipolar disorder and anxiety disorders is vastly underexplored, underappreciated, and certainly understudied. This inattention is surprising in light of the fact that anxiety disorders have the highest rate of comorbidity with bipolar disorder, exceeding the comorbidity rate even of substance abuse. In addition, the impact of this comorbidity on the clinical course of bipolar disorder is severe.

In response to this inattention, this set of articles will explore the relationship of bipolar disorders with anxiety symptoms and disorders. We will review data on the prevalence and impact of the relationship between these disorders. We will learn what is known about treatment in adults. We will examine and explore the comorbidity of anxiety disorders and bipolar disorder in youth. We will conclude with a discussion of the recognition and management of bipolar disorder and anxiety disorders in elderly populations.

Martin B. Keller, M.D., reviews the prevalence and impact of comorbid anxiety and bipolar disorder. He reports that over half of patients with bipolar disorder have at least one comorbid anxiety disorder, and nearly a third have multiple anxiety disorders. The most frequent comorbid anxiety disorder is generalized anxiety disorder. The impact of comorbid anxiety disorder on the course of bipolar disorder is substantial. Individuals with bipolar disorder and comorbid anxiety disorders, in general, have an age at onset of bipolar disorder 3 to 4 years earlier than those without anxiety disorders. Comorbidity predicts a more

pernicious course of bipolar disorder than in those patients without comorbid disorders in terms of increased prevalence of suicide, worse response to treatment, increased number of psychotic and mixed features, and increased rates of neuropsychological dysfunction, as well as other negative outcomes. In addition, patients with bipolar disorder and comorbid anxiety have a higher rate of substance abuse. Quality of life in those with bipolar disorder and comorbid anxiety is severely compromised. Such individuals generally fare significantly worse in terms of work, family, and social impairment, as well as increased health care costs and strains on family than do those with bipolar disorder alone.

Pharmacologic treatment considerations in comorbid and anxiety disorders in adults are addressed in the article by Paul E. Keck, Jr., M.D.; Jeffrey R. Strawn, M.D.; and Susan L. McElroy, M.D. Unfortunately, no randomized, controlled clinical trials have been conducted with patients with comorbid bipolar disorder and anxiety disorders. However, a number of studies have been done on medications used in the treatment of patients with bipolar disorder for several anxiety disorders. There is evidence that valproate is useful in the treatment of panic disorder. Lamotrigine, risperidone, and olanzapine have been found to be helpful in the management of patients with posttraumatic stress disorder. Adjunctive risperidone, olanzapine, and quetiapine were found to be effective in the treatment of SSRI-refractory obsessive-compulsive disorder.

Keck and colleagues conclude that, with the absence of controlled trials of the management of comorbid bipolar and anxiety disorders, clinicians should focus first on mood stabilization of comorbid patients, and that they should seek to use mood-stabilizing medications for which there has been some efficacy demonstrated in treatment of anxiety disorders.

In her article, Karen Dineen Wagner, M.D., Ph.D., explores the comorbidity of bipolar disorder and anxiety disorder in children and adolescents. In general, the prevalence of anxiety disorders in adolescents with bipolar disorder is in the range of 10% to 33%. Because there have been no large or nationwide community epidemiologic

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studies in children with psychiatric disorders, however, these rates must be considered estimates. In one study of adults, which included individuals with very early age at onset (less than 13 years old) with bipolar disorder, the prevalence rate of comorbid anxiety was nearly 70%. With regard to specific anxiety disorders, in one study¹ 44% of patients with bipolar disorder had comorbid obsessive-compulsive disorder. Comorbid social phobia was found in nearly 40% of the sample patients of children and adolescents with bipolar disorder. The rate of comorbid generalized anxiety disorder in these patients was somewhat lower (19%). Panic disorder was also frequent in patients with bipolar disorder. Fourteen percent of preschool-aged children with bipolar I disorder had comorbid posttraumatic stress disorder.

In terms of sequencing, anxiety disorders in general precede the onset of bipolar disorder by several years. From these data and studies, we can conclude that the occurrence of comorbid anxiety disorders is frequent and worsens the course of bipolar disorder in children and adolescents. The co-occurrence of bipolar disorder and anxiety disorders presents a number of diagnostic and management problems. First, symptoms of bipolar disorder may mask underlying anxiety symptoms. Treatment for anxiety symptoms may also, particularly with antidepressant medications, destabilize the course of bipolar disorder. In general, it is best to focus on controlling the bipolar disorder first and then managing the anxiety symptoms in youth.

Finally, Martha Sajatovic, M.D., and Helen C. Kales, M.D., address the issue of comorbidity in elderly populations. In general, geriatric patients with bipolar disorder have much in common with younger adult patients with

bipolar disorder, with the exception that increased rates of cognitive and functional impairment and “secondary mania” are found in elderly populations. Geriatric patients also seem at higher risk for relapse than younger adult patients, and suicide rates are higher in the elderly, as well. Unfortunately, we know relatively little about anxiety disorders in elderly populations. Prevalence rates appear to be somewhat lower than they are in younger adult populations.

With regard to management of older patients with bipolar disorder and comorbid anxiety, it is important to first assess and establish treatment for bipolar disorder. Use of lithium or valproate is encouraged. Although topiramate and gabapentin have been found to help in management of anxiety in geriatric populations, it is not clear if they would have utility in patients with bipolar disorder and anxiety. Use of atypical antipsychotics in the treatment of geriatric patients with bipolar disorder has not been well studied. Secondly, management of anxiety symptoms should be addressed.

In conclusion, the problem of comorbid anxiety in patients with bipolar disorders is substantial. Unfortunately, our knowledge of management of such patients from controlled research is minimal. The intent of these review articles is to be helpful in guiding the clinician when dealing with such patients. Hopefully, in the future there will be controlled studies that will inform the clinician on the management of bipolar patients with comorbid anxiety.

REFERENCE

1. Masi G, Toni C, Perugi G, et al. Anxiety disorders in children and adolescents with bipolar disorder: a neglected comorbidity. *Can J Psychiatry* 2001;46:797-802