Summary

Defining Remission in Patients Treated With Antidepressants

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These review articles reflect the presentations that were given at a conference held in Dallas, Texas, in January 1999. Both the conference and this series sought to establish the criteria necessary for measuring remission, or wellness, in patients with depression, anxiety, or comorbid depression with anxiety and to evaluate the pharmacotherapeutic options best suited to meet these new standards.

Today, depression and anxiety are viewed as two ends of a continuum, with a significant degree of comorbidity occurring between them; two thirds of patients with depression have experienced a previous anxiety disorder. The highest rate of anxiety comorbid with depression occurs with generalized anxiety disorder (GAD). Anxiety and depression are generally treated as separate entities; the serotonergic drugs are better anxiolytics than noradrenergic agents, and noradrenergic agents may have some advantages for treatment of severe depression.

The ultimate goal of treatment is complete remission. Remission is more than just the absence of psychopathology; it is the presence of normality. As Dr. Ninan suggests, normality is the capacity to vary, choose, and control the emotional, behavioral, cognitive, and interpersonal response to a given situation. Psychopathology is the limitation of that choice. Achieving full remission should be the objective for most patients.

While a 50% improvement from baseline scores on the Hamilton Rating Scale for Depression (HAM-D) or Hamilton Rating Scale for Anxiety (HAM-A) is acceptable for short-term comorbid depression and anxiety, it is not acceptable for long-term benefit; a 50% improvement is not a predictor of sustained remission, and symptoms will most likely reappear. The goal of antidepressant/anxiolytic treatment should be complete elimination of symptoms, as remission can emerge from symptomatic control. Increasingly aggressive treatment should continue until this goal is achieved.

In the traditional approach to therapy (i.e., treating depression or anxiety as separate entities), the agents used generally act through different mechanisms and are complicated by high relapse and discontinuation rates, as well as incomplete or inadequate response. Benzodiazepines can be effective in the short-term management of anxiety or panic, but they are not as effective as antidepressants in managing depression. Buspirone is somewhat effective in treating anxiety (with the exception of panic disorder); however, its antidepressant activity is observable only at high doses and, therefore, its clinical use has been limited to augmenting the effects of other antidepressant agents.

The selective serotonin reuptake inhibitors have significant anxiolytic activity, including activity in GAD. There have not yet been controlled studies of activity of mirtazapine or nefazodone in GAD or other anxiety disorders. The tricyclic antidepressants have anxiolytic and antipanic characteristics, but few studies show activity of the monoamine oxidase inhibitors in GAD or other anxiety disorders. Initial studies of bupropion revealed little in the way of specific anxiolytic effects, although the literature is relatively meager.

Treatment of anxiety and depression as separate entities does not address the current evidence that they occur together as comorbidities with greater frequency than previously thought. Thus, treatment with more than one agent or with an agent that has a dual mechanism of action may facilitate remission. Venlafaxine extended release (XR) is one of a class of antidepressant agents that has both serotonergic and noradrenergic mechanisms of action, and it has both antidepressant and anxiolytic activities. In fact, venlafaxine XR is now the most extensively studied antidepressant for GAD without comorbid major depressive disorder. Among such patients, it has a significant anxiolytic effect and demonstrates both short- and long-term efficacy, being superior to buspirone in both efficacy and tolerability. A drug that treats both anxiety and depression can have a particular advantage in the patient experiencing comorbidities.

According to the consensus guidelines, achieving remission means that the patient gets better and stays well,
and the symptoms do not reappear.\textsuperscript{12–14} Successful treatment implies patient and physician satisfaction with a response that falls in the remission range with the patient having sustained, optimal functioning.

On the basis of these endpoints, Dr. Ballenger suggests specific guidelines and gauges for remission of depression, panic disorder, social phobia, GAD, and all anxiety disorders. The treatment regimen most likely to achieve these guidelines will be the one most likely to provide sustained remission. Newer agents having dual mechanisms of action will help achieve these goals and will have the potential for effecting remission in the highest number of patients.

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