Introduction

Recent Developments in Achieving Depression Remission

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This special issue of *The Journal of Clinical Psychiatry* explores recent developments in antidepressant therapy. The selective serotonin reuptake inhibitors (SSRIs) have had a major impact on the treatment of depressed patients. These agents are effective in a wide range of depressive and anxiety disorders and are generally well tolerated. Still, there are some investigators who believe these agents are not as effective, particularly in more severely depressed patients, compared with the older tricyclic antidepressants (TCAs) or the newer serotonin-norepinephrine reuptake inhibitors (SNRIs). This supplement explores various issues related to the potential added benefit of so-called dual-action agents, such as SNRIs, in treating depressed patients.

Richelson reviews differential pharmacology of available antidepressants and those in development. He compares the relative effects on blocking the reuptake of monoamines (i.e., serotonin) or specific receptors (i.e., muscarinic). He reports on the relative effects of dual-action agents, such as duloxetine, as compared with SSRIs.

Stahl and Grady review key pharmacologic mechanisms of available antidepressants and contrast these with a number of unique mechanisms under study. For example, their review addresses such effects as glucocorticoid receptor antagonism, corticotropin-releasing hormone antagonism, and neurokinin-1 antagonism. The developmental status of these approaches is reviewed.

Thase addresses the ever-increasing importance of remission as a goal of treatment. He differentiates between *response* and *remission* or between "better" and "well," particularly with regard to long-term outcome and psychosocial function. He cites studies on comparable efficacy of specific classes of agents.

Fava reviews studies on physical symptoms, including pain, in major depression. He reports a recent study from his group pointing to greater residual somatic symptoms in patients who had "responded" but had not "remitted" on fluoxetine therapy compared with those who had "remitted." He raises the possibility that treating patients to remission of somatic symptoms, such as pain, may also be associated with higher rates of remission of depressive symptoms. Fava also discusses the possible advantage of dual-uptake effects on norepinephrine and serotonin in alleviating somatic symptoms in depression, particularly pain.

Lastly, recent reports on the efficacy and tolerability of duloxetine in major depression are reviewed in the article by Schatzberg. Duloxetine appears to exert potent effects on both norepinephrine and serotonin. Reports indicate that duloxetine is significantly more effective than placebo in patients with major depression. Side effects are as expected for an SNRI; however, there is little effect on the electrocardiogram, heart rate, or blood pressure. In one study, a visual analog scale for pain was used. Duloxetine appears to reduce pain symptoms in depressed patients. Thus, this drug may help reduce key noxious symptoms and increase the likelihood of achieving remission. The drug was recently given an approvable letter by the U.S. Food and Drug Administration.

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