Introduction

Optimizing Clinical Use of SSRIs: Theory and Practice

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Selective serotonin reuptake inhibitors (SSRIs) have been available for almost a decade, and in that period they have had a tremendous impact on pharmacotherapy. A number of SSRIs currently are available in the United States, including fluoxetine, paroxetine, and sertraline, and new ones, such as citalopram, soon will be added to the clinician's armamentarium. SSRIs have demonstrated a broad range of clinical applications. In addition to their usefulness in depression, SSRIs also have been shown to be of therapeutic benefit in the treatment of obsessive-compulsive disorder, panic disorder, bulimia nervosa, social phobia, and premenstrual dysphoric disorder. They also have been noted to decrease anger and rage attacks, as well as to have potential roles in autism and anorexia nervosa. SSRIs generally have established better safety and tolerability profiles compared with tricyclic antidepressants. However, optimal clinical use of these agents requires understanding of both the similarities and differences among the SSRIs, as well as the clinical dilemmas that often face clinicians in the selection of an appropriate therapeutic intervention. This supplement to *The Journal of Clinical Psychiatry*, based on papers presented at a roundtable symposium, explores some of the issues surrounding the use of the SSRIs, with the goal of providing the clinician a useful review of the data to help better understand and utilize the SSRIs in practice.

After years of study and clinical use, SSRIs are considered first-line agents for the treatment of depression. In clinical trials, patients treated with SSRIs suffer fewer adverse events, especially events that are cognitive or cardiovascular in nature, than do patients treated with tricyclic antidepressants. Particularly in overdose, the SSRIs have demonstrated improved safety compared with tricyclic antidepressants; few SSRI-only deaths have been recorded.

Despite what we have learned about SSRIs, a number of issues remain unresolved. We still are uncertain how inhibition of neuronal serotonin reuptake works to relieve signs and symptoms of disease. It also is unclear why patients may respond preferentially to one SSRI compared with another. When faced with a patient who is refractory to treatment, it is arguable whether augmentation or switch to another agent is a preferred strategy.

As a group, the SSRIs have been studied and used extensively around the world, but additional research is required to understand the breadth as well as the limitations of their usefulness. For example, further study to establish the safety and effectiveness of SSRIs in the treatment of patients with comorbid medical disorders—such as post-infarction—is needed. In addition, there are marked differences among the SSRIs in their effects on P450 isoenzymes (which are involved in the metabolism of many drugs) and thus the potential for causing clinically significant drug interactions. Since suicidal thoughts and acts are symptoms of major depression, a concern with the prescription of any medication is its margin of safety in overdose. Although the SSRIs are far safer than TCAs in overdose, clinicians need to appreciate the signs and symptoms of SSRI overdose, as well as the potential for toxicity when SSRIs are ingested with other drugs or alcohol.

This supplement contains 6 papers, each discussing a different aspect of SSRI use in the clinical setting. First, Dennis L. Murphy, M.D., and his colleagues review and update what is known about the mechanisms of serotonergic neurotransmission. Recognizing that depression and cardiovascular disease frequently co-occur, and that they may be pathologically related, my paper discusses the cardiovascular effects of antidepressant drugs. Next, David J. Greenblatt, M.D., and associates review the effects of SSRI antidepressants on the human cytochromes P450. Laurel E. S. Mayer, M.D., and B. Timothy Walsh, M.D., discuss the potential role SSRIs play in the treatment of patients with eating disorders. J. Craig Nelson, M.D., reviews the evidence supporting whether augmentation or switch to an alternative antidepressant medication is a preferred strategy among partial or nonresponders to an adequate course of SSRI therapy. Finally, Jean T. Barbey, M.D., and Steven P. Roose, M.D., describe the signs, symptoms, and risk of mortality associated with SSRI overdose.

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