

Overview

MORE THAN ONE-HALF OF A DECADE OF EXPERIENCE WITH VENLAFAXINE DUAL SEROTONIN-NOREPINEPHRINE REUPTAKE INHIBITOR

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There are many telling reasons to assemble a special issue of *Depression and Anxiety* at this time on venlafaxine, the dual serotonin-norepinephrine reuptake inhibitor, that is currently approved in the United States for the treatment of major depression and generalized anxiety disorder.

First, there has been increasing evidence largely compiled by Bech and his colleagues in Denmark that antidepressants that inhibit both norepinephrine and serotonin reuptake (SNRI) are more effective in severe and refractory depression than those that inhibit uptake of a single monoamine neurotransmitter. In addition, patients with major depression treated with dual reuptake inhibitors may achieve remission more frequently than those treated with single monoamine reuptake inhibitors. This is not a trivial point in view of the considerable morbidity associated with chronic depression. There is now convincing data not only of the potential suicide risk in partially treated depressed patients, but the emerging data base that suggests that depression is associated with a significantly increased risk for both the development of, and poor outcome after, both myocardial infarction and stroke.

The present volume reviews in a comprehensive fashion the neurobiology of depression with a focus on the pathophysiologic involvement of serotonergic and noreadrenergic systems, as well as the preclinical and clinical neuropharmacology of venlafaxine. Much emphasis is paid to summarize in a succinct manner the pharmacokinetics and drug-drug interaction profile of this agent, as well as its efficacy in the treatment of depression, severe depression, refractory depression, as well as geriatric depression. Moreover, particular consideration is given to the growing awareness of the remarkably high comorbidity of mood and anxiety disorders, and the efficacy of venlafaxine in these states. The use of venlafaxine in generalized anxiety disorder as well as in other psychiatric conditions is adequately reviewed, as is the use of this dual reuptake inhibitor in children and adolescents. Finally, the importance of measures of quality of life in assessing treatment response in mood and anxiety disorders is described, as well as pharmacoeconomic studies which seek to determine the cost utility of antidepressant treatment in this common and devastating set of conditions.

There is little doubt that the introduction of venlafaxine has had a remarkable impact on clinical practice. I

have had more than 25 patients who have failed multiple trials with virtually all of the antidepressants available who have responded to venlafaxine often with complete remission. One such case which may be worth recounting is that of the CEO of a major Atlanta company who had been admitted to the inpatient service with the diagnosis of early Alzheimer's disease and comorbid depression. He had a mini-mental state exam score of 20 and a past history of several severe depressions that had responded to either tricyclic antidepressant or electroconvulsive therapy. He failed treatment with two of the more modern antidepressants, and after eleven ECT treatments was considerably more confused and, of great concern, had no response whatsoever in terms of depression severity. Treatment was initiated with venlafaxine and after treatment with this agent for eight weeks at a dose of 375 mg per day, he not only achieved a complete remission of his depression, but his "dementia" completely resolved, with a mini-mental state score of 29 upon discharge. He, in fact, does not have Alzheimer's disease, but instead had a classic case of pseudodementia.

Discussing this case with my colleagues, it is clear that this is not an unusual outcome. It is my hope that this volume will communicate to clinicians in both academia and in the community the enthusiasm that the authors have for this dual reuptake inhibitor. Indeed, venlafaxine offers an important treatment option for both the psychiatrist and primary care physician for achieving a state of "wellness" in a broad spectrum of patients.

With the advent of new functional brain imaging techniques, particularly positron emission tomography, future developments in the field will likely allow for determination of which particular neurotransmitter system abnormality exists in a given patient, and the rational prescribing of antidepressants to target such abnormalities. This would finally allow for long awaited biological predictors of antidepressant drug responsiveness.

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