Multicenter Double-blind Comparison of Sertraline and Desipramine for Concurrent Obsessive-Compulsive and Major Depressive Disorders

Rudolf Hoehn-Saric, MD; Philip Ninan, MD; Donald W. Black, MD; Stephen Stahl, MD; John H. Greist, MD; Bruce Lydiard, MD; Susan McElroy, MD; John Zajecka, MD; Douglass Chapman, MS; Cathryn Clary, MD; Wilma Harrison, MD

Background: Serotonin reuptake inhibitors (SRIs) have demonstrated consistent efficacy in the treatment of obsessive-compulsive disorder (OCD), while agents that are primarily norepinephrine reuptake inhibitors have not. Comparable efficacy has been demonstrated for SRI and non-SRI antidepressants in uncomplicated major depressive disorder (MDD). This multicenter trial is the first comparison of an SRI (sertraline) and a non-SRI antidepressant (desipramine) in the treatment of OCD with concurrent MDD.

Methods: One hundred sixty-six patients diagnosed using structured clinical interviews and recruited from 16 treatment sites were randomly assigned to double-blind treatment with either sertraline (up to 200 mg/d) or desipramine (up to 300 mg/d) over 12 weeks. Measures of severity of OCD and MDD symptoms, as well as adverse effects of the medications, were monitored over the course of the treatment period.

Results: Patients assigned to sertraline responded significantly better at end point on measures of OCD and MDD symptoms compared with patients assigned to desipramine. Sertraline was also associated with a significantly greater number of patients who achieved a "robust" improvement in OCD symptoms (≥40% reduction) compared with desipramine. More patients receiving desipramine than sertraline discontinued treatment because of adverse events.

Conclusions: The SRI sertraline was more effective in reducing MDD and OCD symptoms than the primarily norepinephrine reuptake inhibitor desipramine for patients with concurrent OCD and MDD.

Arch Gen Psychiatry. 2000;57:76-82

DATA OBTAINED from epidemiological and clinical studies indicate that obsessive-compulsive disorder (OCD) and major depressive disorder (MDD) co-occur much more often than expected by chance alone. In clinical samples, about 60% of patients with OCD have a lifetime diagnosis of MDD. Lower but still substantial rates (ie, about 30%) of lifetime occurrence of MDD in patients with OCD have been found in population-based epidemiological studies.

Because most treatment studies of OCD have typically excluded patients with high levels of depressive symptoms or MDD (unless the MDD was judged to be secondary to the OCD), little is known about whether concurrent MDD influences the course of pharmacological treatment of OCD. A number of smaller studies have reported that subsyndromal baseline levels of MDD symptoms failed to predict the outcome of OCD treatment; however, a large, multicenter trial examining clomipramine treatment for OCD found that higher levels of initial depression were generally associated with diminished efficacy.

Furthermore, OCD symptoms have been associated with longer time to recovery among women with MDD. Thus, patients with OCD and concurrent MDD need to be targeted as a special population for treatment studies. Identification of the most efficacious treatment for this substantial subgroup of patients with OCD would potentially lead to a refinement of clinical decision making that might reduce patient suffering and complications resulting from the MDD (eg, suicidality, hospitalization, impaired work functioning).

Sertraline has been shown to be efficacious in the treatment of OCD, as have other serotonin reuptake inhibitors (SRIs), including the tricyclic clomipramine, and other selective serotonin reuptake inhibitors (SSRIs), such as fluvoxamine and fluoxetine. Studies comparing SRIs with one another in the treatment of OCD have generally found equivalent efficacy, while SRIs have been shown to be superior to desipramine (a non-SRI antidepressant) in treating OCD.

In the treatment of MDD, sertraline has been shown to be efficacious in sev-
eral placebo-controlled trials. Moreover, SSRIs and tricyclic antidepressants, such as desipramine, have been shown to have equivalent efficacy in the treatment of MDD. This raises the question of which type of medication would have superior efficacy in the context of patients with concurrent MDD and OCD, and whether an SRI like sertraline would improve symptoms of MDD in the context of OCD more than a non-SRI like desipramine. It may be that in the context of a full MDD episode, a predominantly noradrenergic agent like desipramine would be as effective as an SRI in treating the depression, but less effective in treating OCD. However, desipramine may also be effective in treating OCD, since desipramine may have some spillover effects on the serotonergic system. Indeed, microdialysis studies have indicated that desipramine can alter extracellular levels of serotonin.

The purpose of the current study was to compare the relative efficacy of sertraline and desipramine for patients with OCD and concurrent MDD in a multicenter, double-blind, randomized trial. Efficacy was assessed for degree of reduction of both OCD and MDD, in addition to the examination of the relative response and remission rates of the treatments. We also compared the adverse effects of both medications.

PATIENTS AND METHODS

PATIENTS

A group of 166 patients 18 years or older who met the DSM-III-R criteria for both current OCD and current MDD using the Structured Clinical Interview for DSM-III-R were recruited at 16 university-affiliated treatment centers that specialized in the treatment of OCD and other anxiety disorders.

In addition to meeting the full diagnostic criteria for OCD and MDD, patients had to meet severity criteria for both OCD and MDD symptoms at the assessments conducted at the beginning and end of a screening (washout) phase. To be included, patients needed to score 20 or higher on the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) 18 or higher on the 24-item Hamilton Rating Scale for Depression (HAM-D), and 2 or higher on item 1 (depressed mood) of the 24-item HAM-D, at both the screening and baseline assessments. A Clinical Global Impression (CGI) scale severity score of at least 4 for both MDD and OCD, indicating moderate to severe illness on each, was also needed at the screening and baseline assessments to qualify for the study.

Exclusion criteria consisted of (1) current or past DSM-III-R diagnosis of Tourette syndrome, bipolar disorder, schizophrenia, delusional disorder, psychotic disorder not elsewhere classified, or paraphilia; (2) principal diagnosis within the past 6 months of agoraphobia, generalized anxiety disorder, or posttraumatic stress disorder; (3) diagnosis of panic disorder within the past 6 months, any spontaneous panic attacks within the last month, or 4 or more spontaneous panic attacks in the past 4 months; (4) diagnosis of acute or chronic organic mental syndrome (eg, delirium, dementia, amnestic disorder); (5) diagnosis of schizotypal, antisocial, paranoid, or borderline personality disorder; (6) abuse or dependence on alcohol or any drug within the past 6 months; (7) any medical contraindications to antidepressant therapy as determined by medical history or physical examination; (8) evidence or history of significant hematological, endocrine, cardiovascular, pulmonary, renal, gastrointestinal, or neurological disease; (9) currently taking any psychotropic drug or receiving behavior therapy; (10) a CGI improvement rating of 1 or 2 for either MDD or OCD at the end of the baseline period; (11) current suicidality; (12) received electroconvulsive therapy within the past 3 months; and (13) any previous psychosurgery. Women were excluded if currently pregnant, nursing, or not practicing an effective method of birth control.

One hundred sixty-six patients were randomized; 2 patients failed to return for follow-up care (1 in each treatment group), leaving 85 patients given desipramine and 79 given sertraline to evaluate efficacy and safety. Double-blind treatment was provided for 12 weeks. The protocol and informed consent documents were approved by the institutional review boards associated with the 16 participating sites, and each patient provided written informed consent prior to study participation.

METHODS

All patients who were screened as meeting eligibility criteria for the study were placed on a 1-week single-blind pill placebo washout period, during which assessments were performed. During this screening phase, patients were given placebo capsules identical in appearance to the sertraline and desipramine capsules. Patients were instructed to take 4 placebo capsules daily; after the washout period, desipramine and sertraline were also administered as 4 capsules daily to maintain the blind.

For patients randomized to sertraline, dosages were titrated to 50 to 200 mg/d. All patients received 50 mg/d during the first 2 weeks; after this, in the absence of a satisfactory clinical response and no dose-limiting side effects, the dosage could be titrated to 100 mg/d any time between weeks 2 and 4, to 150 mg/d at week 4, and to 200 mg/d at week 5. Changes in dosage were always made in increments of 50 mg/d. All capsules (placebo, sertraline, and desipramine) were identical in appearance, and a blister card system was used during the 12-week treatment period to maintain the double-blind.

A similar stepwise flexible titration of desipramine was conducted. Beginning with 50 mg/d, dosages could be titrated by 50 mg/wk up to a maximum of 300 mg/d. If a patient was receiving 250 or 300 mg/d, capsules with 100 mg of desipramine were used in addition to 50-mg capsules, so that only 4 capsules per day were taken. Dosage was increased or decreased at any time on the basis of the patient’s clinical response or dose-limiting adverse events; the minimum sustained dosage allowed for either active agent was 50 mg/d or 4 capsules per day of placebo.

Medical screening, including laboratory tests, electrocardiogram, and physical examination, a Structured Clinical

Continued on next page
Interview for the DSM-III-R, and screening efficacy measures, was performed on the first day of the placebo washout period and again at the end of the washout to determine ongoing eligibility for randomization. After randomization, the patients were evaluated for efficacy from weeks 1 through 8, then every other week until either week 12 or discontinuation from the study; safety assessments were repeated at week 12 or at the last patient visit. Plasma samples to assess sertraline and desipramine levels were obtained at the first day of baseline and at 12 weeks or the last patient visit.

Randomization was performed centrally using a computer-generated randomization scheme.

OUTCOME MEASURES

The following efficacy measures were completed at each of the assessment visits: the Y-BOCS; the National Institute of Mental Health (NIMH) Global Obsessive-Compulsive Scale; CGI severity ratings for OCD, MDD, and overall assessment, as well as overall CGI improvement ratings; and the 24-item HAM-D. These ratings were performed by the treating physician or by a trained evaluator with established interrater reliability. The HAM-D and Y-BOCS were specified a priori as the primary outcome measures, while the single-item NIMH Global Obsessive-Compulsive Scale and the CGI ratings were designated as secondary outcome measures. In addition, the Bech melancholia subscale of the HAM-D and the Patient Global Improvement scale (assessed at baseline and week 12 only) for MDD, OCD, and overall were examined in secondary analyses.

The criterion for defining clinical response in MDD was at least a 50% decrease from baseline in the 24-item HAM-D score; following a commonly used convention in other studies, remission was defined as a 17-item HAM-D score of 7 or lower. For OCD, a clinical response was defined a priori as a decrease in the Y-BOCS total score of 40% or greater.

Patients were evaluated for adverse events at the end of baseline and at all weekly assessments during the treatment phase using the general inquiry section of the Systematic Assessment for Treatment Emergent Events, administered by the treating physician.

STATISTICAL ANALYSES

All efficacy analyses were conducted on end-point data (ie, at week 12 for completers) and at the last available visit for patients who did not complete the study (ie, intention to treat with the last observation carried forward).

The 16 investigative centers in this study varied in patient enrollment from 1 to 29. To ensure stable estimates, the following pooling algorithm was used for all analyses: centers were ranked in order of size and pooled, starting with the smallest, until the resulting pseudocenter reached the maximum size that was smaller than the largest actual center. The 6 smallest actual centers were combined into 1 pseudocenter (n = 24); all analyses were based on 10 actual centers and 1 pseudocenter.

Baseline comparability of the 2 treatment groups for demographic and clinical characteristics was assessed by analysis of variance for continuous variables and by the Cochran-Mantel-Haenszel test for categorical variables. Analysis of variance models included treatment and center terms; treatment × center interaction terms were also examined but were consistently nonsignificant and were therefore dropped from the models. The Cochran-Mantel-Haenszel tests included center as the stratification variable. For categorical variables, when stratification by center resulted in 3 or more sparse subtables (ie, any marginal total of 0), then the Pearson χ² test or the Fisher exact test was used as appropriate to include all available data.

Efficacy analyses were performed using analysis of covariance for continuous and multivalued ordinal categorical variables for which a baseline measurement existed; other variables (CGI improvement and PGI) were analyzed using analysis of variance models, as above. Binary variables were analyzed by the Cochran-Mantel-Haenszel test, as above. Analysis of covariance models used change from baseline to end point as the dependent variable and included treatment, center, and treatment × center interaction terms, with baseline measurement as the covariate. Interaction terms were consistently nonsignificant and were therefore dropped from all models. All hypotheses were tested using type III sums of squares with SAS version 6.11 (PROC GLM).

Safety analyses were performed using the Fisher exact test for incidence of adverse events and the Pearson χ² test for proportion of discontinuations. Adverse events were coded according to the World Health Organization dictionary.

All statistical tests were 2-sided, and significance was declared at α = .03, with the sole exception of treatment × center interaction effects, which were considered significant at α = .10.

RESULTS

BASELINE CLINICAL AND DEMOGRAPHIC CHARACTERISTICS

The average duration of the current episode of MDD was 24 months for the 79 patients assigned to sertraline and 29 months for the 85 patients assigned to desipramine (Table 1). The duration of OCD symptoms was more than 17 years for patients in both treatment groups. The current MDD episode was determined to be of moderate or severe intensity for all patients enrolled. The most common Axis I comorbid diagnosis other than MDD was generalized anxiety disorder (16% of patients).

There were no significant differences in any baseline clinical or demographic characteristics between the patients treated with sertraline and those treated with desipramine.

ADVERSE EVENTS AND PATIENT DISCONTINuations

Patients taking sertraline were significantly more likely to complete treatment than those taking desipramine (84% [66/79] vs 62% [53/85]; χ² = 9.2, P = .002). Discontinuations caused by adverse events were also significantly dif-
different between treatment groups (10% [8/79] for sertraline vs 26% [22/85] for desipramine; \( \chi^2 = 6.8; P = .009 \)). Overall, all patients taking sertraline (100% \( n = 79 \)) and almost all taking desipramine (99% \( n = 84 \)) reported at least 1 adverse event. However, most were mild to moderate and did not result in treatment discontinuation. Significantly more patients taking desipramine vs sertraline reported constipation (34% \( n = 29 \) vs 18% \( n = 14 \); \( P = .02 \)), dizziness (35% \( n = 30 \) vs 20% \( n = 16 \); \( P = .04 \)), micturition disorder (14% \( n = 12 \) vs 0% \( n = 0 \); \( P < .001 \)), and dry mouth (76% \( n = 65 \) vs 37% \( n = 29 \); \( P < .001 \)). Significantly more patients treated with sertraline reported diarrhea (28% \( n = 22 \) vs 9% \( n = 8 \); \( P = .002 \)) and headache (65% \( n = 51 \) vs 46% \( n = 39 \); \( P = .02 \)).

**DOSAGE**

The mean (SD) dosage of sertraline at end point for the intention-to-treat sample was 160.1 (50) mg/d; for desipramine, it was 193.5 (90) mg/d.

**EFFECTICITY RESULTS AND CLINICAL RESPONSE**

Sertraline was demonstrated to be more effective than desipramine, as measured by the mean change from baseline to end point on almost all measures (Table 2). Significant differences favoring sertraline were demonstrated on the 24-item HAM-D \( (P = .03) \) and the Y-BOCS \( (P = .05) \). Significant differences between the treatments were also found on a number of the secondary outcome measures, including the NIMH Global Obsessive-Compulsive Scale \( (P = .01) \), the Y-BOCS obsession scale \( (P = .04) \), the CGI melancholia subscale of the HAM-D \( (P = .03) \), the CGI severity depression scale \( (P = .004) \), the overall CGI severity scale \( (P = .03) \), and the CGI improvement scale \( (P = .02) \). Significant differences favoring sertraline were also found on the overall CGI rating \( (P = .004) \) and the CGI rating for MDD \( (P = .003) \). Significant main effects for center were apparent on 2 measures, including the Y-BOCS obsession scale.

**Table 1. Patient Characteristics**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Sertraline (n = 79)</th>
<th>Desipramine (n = 85)</th>
<th>Test Statistic†</th>
<th>df</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD) age, y</td>
<td>37.6 (12.4)</td>
<td>37.6 (10.0)</td>
<td>0.04</td>
<td>1.152</td>
<td>.85</td>
</tr>
<tr>
<td>Male, No. (%)</td>
<td>32 (41)</td>
<td>34 (40)</td>
<td>0.02</td>
<td>1</td>
<td>.89</td>
</tr>
<tr>
<td>White, No. (%)</td>
<td>77 (97)</td>
<td>77 (91)</td>
<td>3.18</td>
<td>1</td>
<td>.08</td>
</tr>
<tr>
<td>Married, No. (%)</td>
<td>31 (39)</td>
<td>40 (46)</td>
<td>0.85</td>
<td>1</td>
<td>.36</td>
</tr>
<tr>
<td>Employed, No. (%)</td>
<td>53 (67)</td>
<td>51 (60)</td>
<td>0.99</td>
<td>1</td>
<td>.32</td>
</tr>
<tr>
<td>Mean (SD) duration of OCD symptoms, mo</td>
<td>214 (161)</td>
<td>212 (130)</td>
<td>0.02</td>
<td>1.152</td>
<td>.89</td>
</tr>
<tr>
<td>Mean (SD) duration of MDD, mo</td>
<td>23.7 (46)</td>
<td>29.0 (55)</td>
<td>0.31</td>
<td>1.148</td>
<td>.58</td>
</tr>
</tbody>
</table>

*OCD indicates obsessive-compulsive disorder; MDD, major depressive disorder.
†The test statistics were the analysis of variance F ratio for continuous variables and the Cochran-Mantel-Haenszel \( \chi^2 \) test for categorical variables.

**Table 2. Change From Baseline to Week 12 on Primary and Secondary Efficacy Measures**

<table>
<thead>
<tr>
<th>Measures</th>
<th>Baseline Mean (SD)</th>
<th>Adjusted Change (SE) From Baseline to Week 12†</th>
<th>Analysis of Covariance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sertraline (n = 79)</td>
<td>Desipramine (n = 85)</td>
<td>Sertraline (n = 79)</td>
</tr>
<tr>
<td><strong>Primary</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HAM-D (24 item)</td>
<td>27.8 (5.6)</td>
<td>27.4 (5.5)</td>
<td>-14.8 (1.1)</td>
</tr>
<tr>
<td>Y-BOCS total</td>
<td>26.1 (3.8)</td>
<td>25.6 (3.9)</td>
<td>-8.4 (0.9)</td>
</tr>
<tr>
<td><strong>Secondary</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NIMH Global OC Scale</td>
<td>9.3 (1.4)</td>
<td>9.0 (1.4)</td>
<td>-2.7 (0.3)</td>
</tr>
<tr>
<td>Bech melancholia subscale (HAM-D)</td>
<td>9.6 (2.4)</td>
<td>9.6 (2.6)</td>
<td>-5.1 (0.4)</td>
</tr>
<tr>
<td>Y-BOCS obsessions scale</td>
<td>13.3 (2.0)</td>
<td>12.8 (2.0)</td>
<td>-4.3 (0.5)</td>
</tr>
<tr>
<td>Y-BOCS compulsion scale</td>
<td>12.8 (2.6)</td>
<td>12.8 (2.6)</td>
<td>-4.0 (0.5)</td>
</tr>
<tr>
<td>CGI-severity overall</td>
<td>4.8 (0.7)</td>
<td>4.8 (0.7)</td>
<td>-1.4 (0.1)</td>
</tr>
<tr>
<td>CGI-severity OCD</td>
<td>4.9 (0.8)</td>
<td>4.8 (0.7)</td>
<td>-1.2 (0.1)</td>
</tr>
<tr>
<td>CGI-severity depression</td>
<td>4.4 (0.7)</td>
<td>4.5 (0.7)</td>
<td>-2.0 (0.2)</td>
</tr>
<tr>
<td>CGI-improvement overall</td>
<td>2.4 (0.1)</td>
<td>2.9 (0.1)</td>
<td>5.39</td>
</tr>
<tr>
<td>CGI overall</td>
<td>2.3 (0.2)</td>
<td>3.1 (0.2)</td>
<td>8.63</td>
</tr>
<tr>
<td>CGI OCD</td>
<td>2.6 (0.2)</td>
<td>3.1 (0.2)</td>
<td>3.58</td>
</tr>
<tr>
<td>CGI depression</td>
<td>2.0 (0.2)</td>
<td>2.7 (0.2)</td>
<td>9.40</td>
</tr>
</tbody>
</table>

*HAM-D indicates Hamilton Rating Scale for Depression; Y-BOCS, Yale-Brown Obsessive Compulsive Scale; NIMH, National Institute of Mental Health; OC, obsessive-compulsive; CGI, Clinical Global Impression; OCD, obsessive-compulsive disorder; and PGI, Patient Global Improvement.
†Change scores are adjusted for baseline level and center. Last observation carried forward was used when 12-week scores were not available. The CGI-improvement overall and PGI means at 12 weeks are adjusted for site.

©2000 American Medical Association. All rights reserved.

 Downloaded From: http://archpsyc.jamanetwork.com/pdfaccess.ashx?url=data/journals/psych/11803/ on 06/17/2017
To our knowledge, this is the first study to examine treatment efficacy among a sample of patients selected to have concurrent OCD and MDD. The results demonstrated that sertraline, an SSRI, was more efficacious than desipramine, a predominantly norepinephrine reuptake inhibitor, in reducing both OCD and MDD symptoms in this population. A significantly greater number of patients achieved remission of their MDD with sertraline than with desipramine. Sertraline was also associated with a significantly greater number of patients who achieved a robust improvement (≥40% reduction) in OCD symptoms compared with desipramine. Overall PGI scores and PGI ratings of improvement in MDD confirmed the superiority of sertraline to desipramine that was apparent in the total scores on the HAM-D and Y-BOCS.

Our findings extend those from previous studies comparing SSRIs and non-SRIs for OCD. Previous investigations did not provide information on the comparison of these classes of medications in patients with concurrent MDD and OCD. Our results suggest that SRI treatment is appropriate for the relatively large proportion of patients with OCD and concurrent MDD who have often been excluded from previous trials of SRIs with OCD because of their MDD.

The improvements in patients treated with sertraline are particularly noteworthy because of the severity and chronicity of illness in this patient population. At baseline, patients had a mean duration of MDD of about 2 years and OCD symptoms of more than 17 years. This chronicity, evaluated with reports of depression predicting poor response to OCD treatment and OCD symptoms slowing recovery from MDD, suggests that the population of patients with OCD and concurrent MDD might be expected to demonstrate less treatment response compared with OCD samples without MDD comorbidity. However, the percentage change at end point in Y-BOCS scores for patients treated with sertraline in the current study compares favorably with results from a previous, large-scale study of sertraline treatment of OCD without concurrent depression (32.7% reduction compared with 23.4% reduction).

A substantially lower rate of treatment discontinuation caused by adverse effects was evident with sertraline compared with desipramine. This is consistent with the well-documented superior adverse-effect profiles of SSRIs compared with tricyclic antidepressants. Selective serotonin reuptake inhibitors have also been found to result in fewer adverse events and lower attrition rates compared with clomipramine in some OCD treatment studies but not others. Although the difference in adverse events between sertraline and desipramine was expected, its demonstration in this understudied population of patients with concurrent MDD and OCD provides further important information regarding treatment decisions for these patients.

The relatively higher dropout rate for desipramine vs sertraline was likely to have influenced the analysis of end-point efficacy scores. It may be that if these patients who discontinued desipramine therapy because of adverse effects had stayed in treatment longer, they would have achieved a greater response in both their MDD and OCD symptoms. However, the fact that a significantly greater number of patients were unable to complete desipramine treatment compared with sertraline treatment is obviously an important clinical consideration in choosing medications.

A limitation of the current study is the lack of a placebo control. The expected placebo response in patients with both OCD and concurrent MDD is unknown since there are no published studies demonstrating it. Although the improvement rates found in the current study are greater than those found for placebo in other treatment studies of patients with OCD, it is possible but unlikely that there would be a higher placebo response rate for patients with OCD and concurrent MDD.

It is also important to consider that there is overlap in symptoms in the assessment of OCD and MDD. In particular, there are items on the HAM-D scale that refer to anxiety or obsessionality. Sertraline’s greater influence, relative to desipramine, on OCD symptoms may have resulted in changes in HAM-D scores in part because of the HAM-D items that overlap with OCD.
symptoms. However, the advantage of sertraline over desipramine on other measures of depression (eg, CGI, patient global improvement) that do not involve specific OCD items provides some assurance that the superiority of sertraline is not a measurement artifact related to item overlap.

A further limitation of the current study is the use of multiple secondary efficacy measures without any statistical adjustment for the number of significance tests performed. It is therefore possible that some of the effects seen on secondary measures may have been obtained by chance. However, the effects were largely consistent in direction across measures. Moreover, while some measures did display main effects for center, indicating that some centers achieved better outcomes than other centers, there were no significant treatment × center interactions, suggesting that the superiority of sertraline over desipramine has some degree of generalizability.

We can speculate on the possible reasons why a non-SRI does not affect symptoms of MDD to the degree that an SRI does in the context of OCD. One explanation would be that MDD in the context of OCD is different than MDD without OCD. It may be that the serotonin system is more involved in OCD-related depression compared with MDD without OCD. Alternatively, as others have speculated, it seems possible that MDD is often secondary to the impairment from OCD (ie, the MDD is being maintained by demoralization related to ongoing severe OCD symptoms and the associated negative impact of such symptoms on social and work functioning). Reduction of the obsessive-compulsive symptoms would reduce one of the factors contributing to the depression. Treatment with a medication less efficacious for OCD would permit continuing OCD symptoms that would contribute to demoralization of patients at risk for MDD. Regardless of the explanation, the current study suggests that the serotoninergic antidepressant sertraline produces greater efficacy than the noradrenergic antidepressant desipramine for both OCD and MDD patients with obsessive-compulsive disorder. Arch Gen Psychiatry. 1991;46:730-738.

Accepted for publication September 28, 1999.

From the Departments of Psychiatry and Behavioral Sciences, The Johns Hopkins University School of Medicine, Baltimore, Md (Dr Hoehn-Saric), Emory University, Atlanta, Ga (Dr Ninan), and Medical University of South Carolina, Charleston (Dr Lydiard); Departments of Psychiatry, University of Iowa, Iowa City (Dr Black), University of California at San Diego (Dr Stahl), University of Cincinnati College of Medicine, Cincinnati, Ohio (Dr McElroy), and Rush-Presbyterian/St Luke’s Medical Center, Chicago, Ill (Dr Zajecka); Madison Institute of Medicine, Madison, Wis (Dr Griest); and Pfizer Inc, New York, NY (Mr Chapman and Drs Clary and Harrison). This research was supported by Pfizer Inc, New York, NY.

Portions of this study were presented at the European College on Neuropsychopharmacology, Vienna, Austria, September 14, 1997; the American College of Neuropsychopharmacology, Kamuela, Hawaii, December 10, 1997; and the American Psychiatric Association Meeting, Toronto, Ontario; June 2, 1998.

Corresponding author: Rudolf Hoehn-Saric, MD, Department of Psychiatry and Behavioral Sciences, The Henry Phipps Psychiatry Service, The Johns Hopkins University School of Medicine, 600 N Wolfe St, Meyer 144, Baltimore, MD 21287-7144.
Reviewed articles:


