Clinical Predictors of Drug Nonresponse in Obsessive-Compulsive Disorder

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Objective: Obsessive-compulsive disorder (OCD) is often a chronic and disabling illness with high comorbidity. Serotonin reuptake inhibitors (SRIs) are effective in treating OCD. However, 40% to 60% of patients with OCD do not respond adequately to SRIs. This study aims to identify the clinical predictors of nonresponse to SRIs in OCD by comparing SRI responders and nonresponders.

Method: 122 subjects with a diagnosis of DSM-IV OCD of at least 1 year's duration and with treatment history of adequate trials with at least 2 SRIs were recruited from December 2002 to March 2004. Of these, 67 were SRI responders and 55 were SRI nonresponders; they were compared on various clinical parameters. Nonresponse was defined as a score of ≥ 3 on the Clinical Global Impressions-Improvement subscale (CGI-I) after at least 2 adequate trials with SRIs. Response was defined as a score of 1 or 2 on the CGI-I.

Results: In regression analysis, baseline severity of OCD (p = .049), comorbid major depressive disorder (p = .005), presence of sexual obsessions (p = .002), and washing (p = .008) and miscellaneous compulsions (p = .013) were identified as predictors of nonresponse to SRIs. Early age at onset showed a trend toward prediction of nonresponse (p = .056). In the univariate analysis, mixed OCD (p = .001) and poor insight (p = .023) were associated with nonresponse.

Conclusion: This study has identified clinical predictors of nonresponse to SRIs. These predictors may have to be taken into consideration and assessed carefully when SRIs are prescribed to treat OCD. Future studies should aim at identifying treatment modalities that are effective in SRI nonresponders.

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Meta-analytical studies have shown serotonin reuptake inhibitors (SRIs) to be effective in the treatment of obsessive-compulsive disorder (OCD), but 40% to 60% of patients do not respond adequately.[1–6] Several studies have looked into demographic and clinical characteristics that have predictive value in the outcome of OCD. Earlier age at onset[5,7,8]; longer duration of illness and a continuous course[8–10]; a higher frequency of compulsive behaviors, particularly cleaning rituals[8] and somatic obsessions[7]; poor insight[7,11]; and the presence of comorbid tic disorders and Axis II disorders, particularly schizotypal, avoidant, and borderline personality disorders,[12–14] have been associated with poor response to antiobsessional drugs. In earlier studies, comorbid depression was reported to predict good response.[15,16] However, some recent studies have reported depression as a poor prognostic factor,[11,17] and many others[18–21] have reported response to be independent of comorbid depression.

Most of the available data on predictors of treatment response are from drug efficacy reports, which typically examine the treatment of patients with a particular drug for a predefined period to assess the effectiveness of the drug. However, poor response to one SRI does not necessarily mean nonresponse to another SRI or all SRIs. There are few data on the characteristics of patients who have failed to respond to 2 or more trials of SRIs.[22] In addition, there is lack of consensus about the definitions of response/nonresponse.[23] There is no clear consensus as to how many SRI trials are necessary to consider a patient to be a nonresponder. However, poor response to adequate trials with at least 2 SRIs may be needed before considering a patient to be an SRI nonresponder.

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We present here the demographic and clinical characteristics of SRI nonresponders compared to responders. The aim is to identify the clinical predictors of nonresponse to SRIs in OCD by comparing SRI responders and nonresponders. In this study, treatment with any 2 SRIs (clomipramine, fluoxetine, fluvoxamine, paroxetine, sertraline, citalopram, or escitalopram) in adequate doses for a period of at least 10 weeks each was considered essential before classifying a patient as a nonresponder. Similarly, treatment with an adequate dose for an adequate duration was required before a decision was made about response. Additionally, to be considered an SRI responder, patients should have been treated with only SRIs and should never have received cognitive-behavioral therapy or any other form of psychotherapeutic interventions.

METHOD

One hundred twenty-two consecutive subjects who met the inclusion criteria were recruited from the specialty OCD clinic and inpatients of the National Institute of Mental Health and Neurosciences (NIMHANS), Bangalore, India, from December 2002 to March 2004. The subjects selected were previously evaluated in detail by using a specific pro forma checklist developed to evaluate OCD subjects. Initial diagnostic evaluations were done by postgraduate junior residents in psychiatry and subsequently confirmed by a senior consultant (Y.C.J.R.) experienced in evaluating OCD patients. The study was conducted in compliance with the ethical guidelines of the Ethics Committee of the NIMHANS, and the subjects were recruited after giving written informed consent.

Inclusion criteria were a primary diagnosis of OCD per DSM-IV,[24] a Yale-Brown Obsessive Compulsive Scale (YBOCS) severity score of greater than 15 for those with mixed OCD (presence of equally prominent obsessions and compulsions) and greater than 8 for those with predominantly obsessions or compulsions,[25,26] illness duration of at least 1 year, and adequate trials with at least 2 SRIs. Primary diagnosis was defined as the dominant disorder for which treatment was sought. An adequate trial was defined as treatment with an SRI in adequate dose (fluoxetine, 40–80 mg/day; sertraline, 150–300 mg/day; citalopram, 40–80 mg/day; escitalopram, 20–40 mg/day; fluvoxamine, 200–300 mg/day; paroxetine, 40–80 mg/day; clomipramine, 150–250 mg/day) for a period of at least 10 weeks. The OCD subjects were subtyped into those with "predominantly obsessions," "predominantly compulsions," or "mixed," based on the ICD-10 definitions.[27] We also added an additional criterion: to be classified "predominantly obsessive," the YBOCS score on "compulsions" should not be greater than 5, and to be classified "predominantly compulsive," the YBOCS score on "obsessions" should not exceed 5. The additional criterion was added because the ICD-10 definitions of OCD subtypes are not strictly operationalized, and therefore subtyping could become highly subjective and vary across the raters.

The subjects who satisfied inclusion criteria (N = 122) were evaluated using the Structured Clinical Interview for DSM-IV Axis I Disorders, Patient Edition (SCID-I/P),[28] the Structured Clinical Interview for DSM-IV Axis II Personality Disorders (SCID-II),[29] the tic disorder subsection of the Schedule for Tourette and Other Behavioral Syndromes,[30] the YBOCS,[25] the Brown Assessment of Beliefs Scale (BABS),[31] the 16-item version of the Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q),[32] and the scale for Global Assessment of Functioning (GAF).[24] Higher scores on Q-LES-Q and GAF indicate higher quality of life and better global functioning, respectively. Subjects were also rated at baseline with the Clinical Global Impressions-Severity of Illness subscale (CGI-S).[33] All the evaluations were performed by the psychiatrists working in the OCD clinic who had considerable expertise in administering the instruments and were extensively trained by the senior consultant (Y.C.J.R.) of the clinic.

The YBOCS is a reliable and valid clinician-administered instrument that assesses current severity of OCD. The tic disorder checklist helps in checking for a variety of motor and vocal tics, both present and past. It assesses the severity of tics based on forcefulness, disruptiveness, and longest tic-free period. The BABS is a semi-structured, clinician-administered 7-item scale with specific probes and anchors designed to assess insight. It is based on the premise that insight exists on a continuum consisting of the following dimensions: conviction, perception of others' view of beliefs, explanation of differing views, fixity of ideas, attempts to disprove beliefs, insight, and ideas/delusions of reference. Each item is scored from 0 (nondelusional or least pathological) to 4 (delusional or most pathological). Total score ranges from 0 to 24, and the seventh item is not included in the total score because the item is not relevant to OCD, whereas it is more relevant to disorders such as body dysmorphic disorder, olfactory reference syndrome, and other types of delusional disorder.[31] The BABS cannot be administered to those who do not report associated consequences underlying obsessions; therefore, it was administered to only 53 nonresponders and 63 responders. Poor insight is indicated by a total BABS score of ≥ 12 (mean score of 2 for each item) and a score of ≥ 3 for the conviction item (fairly or completely convinced that belief/worry is true).[34]

Treatment response was assessed with the Clinical Global Impressions-Improvement subscale (CGI-I),[33] which has a rating of 1 to 7. Subjects with a score of 1 (very much improved) or 2 (much improved) were considered to be responders. Those subjects with a score of 3 (minimally improved), 4 (no change), 5 (mildly worse), 6 (moderately worse), or 7 (much worse) were considered to be nonre-

Table 1. Sociodemographic Profile of SRI Responders and Nonresponders With OCD

Characteristic	Responders (N = 67)	Nonresponders (N = 55)	χ^2/t Value	Significance
Age, mean (SD), y	31.16 (9.76)	26.92 (8.89)	2.48	.014
Gender, male, N (%)	41 (61)	31 (56)	0.291	.589
Marital status, N (%)			5.814	.016
Married	36 (54)	17 (31)		
Single	30 (45)	37 (67)		
Separated/divorced	1 (1)	1 (2)		
Residence, N (%)			8.319	.004
Rural	27 (40)	9 (16)		
Urban	40 (60)	46 (84)		
Occupation, N (%)			0.772	.380
Student	9 (13)	16 (29)		
Housewife	19 (28)	16 (29)		
Government employee	19 (28)	5 (9)		
Self-employed	17 (25)	10 (18)		
Unemployed	2 (3)	8 (15)		
Retired	1 (1)	0		
Age at OCD onset, mean (SD), y	22.55 (8.47)	18.24 (7.56)	2.93	.004
Duration of OCD, mean (SD), y	8.67 (6.43)	8.70 (6.45)	–0.022	.983

Abbreviations: OCD = obsessive-compulsive disorder, SRI = serotonin reuptake inhibitor.

sponders. We preferred the CGI-I over the YBOCS to measure improvement because the YBOCS may not be sensitive to subtle changes, such as a decrease from 5 hours to 3 hours per day of rituals and a decrease in avoidant behavior. The CGI-I is considered effective in capturing both the larger clinical psychopathology and subtle changes. Patients with a score of 1 or 2 on the CGI-I are usually considered responders.[23] The CGI-I was rated independently by 2 psychiatrists experienced in assessing OCD subjects after reviewing the treatment history with the subjects and the clinical charts. Subsequently, responder/nonresponder status was determined by the consensus opinion of the 2 psychiatrists.

Statistical Analysis

The statistical analysis was done using SPSS version 11 package (SPSS Inc., Chicago, Ill.). Chi-square/Fisher exact test was used to analyze categorical variables, and the independent sample t test/paired t test was used to analyze continuous variables. Multiple logistic stepwise forward regression analysis was performed to identify predictors of response/nonresponse to SRIs. The variables selected for inclusion in the regression analysis were those that were significant in the univariate analysis.

RESULTS

The sample of patients with OCD had 67 (55%) responders and 55 (45%) nonresponders. Of the nonresponders, 14 subjects (25%) had a history of treatment with cognitive-behavioral therapy, but none had responded to the treatment. None of the responders had received any form of psychotherapeutic intervention. The sociodemographic details are shown in Table 1. The clinical profile and comorbidity are described in Tables 2 and 3, respectively. The SRI nonresponders were significantly younger, had earlier onset of illness, and had more severe illness according to the baseline YBOCS score and CGI-S subscale compared to the responders. However, the mean duration of illness was similar in both groups. There was significant reduction in the total YBOCS score from baseline in responders (18.96 ± 9.41 vs. 9.41 ± 7.66, t = –7.837, p < .001), whereas in nonresponders there was no significant fall in the YBOCS score (25.30 ± 7.73 vs. 25.70 ± 8.36, t = 0.289, p = .774). Similarly, there was a significant fall in the CGI-S score from baseline in responders (4.04 ± 1.28 vs. 2.66 ± 0.88, t = 9.439, p < .001) but not in nonresponders (5.07 ± 1.02 vs. 4.80 ± 1.17, t = 1.476, p = .146). Understandably, the number of medication trials was higher in nonresponders compared to responders (2.6 ± 1.18 vs. 1.41 ± 0.67, t = –6.590, p < .001).

The subjects who were categorized as nonresponders had significantly higher rates of contamination and sexual obsessions. Similarly, compulsions such as washing, repeating, and miscellaneous compulsions (cognitive rituals, need to confess, and reassurance seeking) were significantly overrepresented in the nonresponders (Table 2). It was also found that mixed OCD was more common in nonresponders. When assessed for comorbidity, subjects who had not responded had higher rates of any Axis I comorbidity, tic disorder, major depressive disorder, and dysthymia. However, no difference was found in comorbid anxiety and personality disorders. Patients with poor insight were overrepresented in nonresponders compared to responders (7/53, 13% vs. 1/63, 2%; p = .023). Total BABS score was also higher in the nonresponders compared to responders (6.5 ± 5.26 vs. 4.09 ± 4.05, t = –2.728, p = .008).

Table 2. Symptom Profile of SRI Responders and Nonresponders With OCD

Variable	Responders (N = 67)	Nonresponders (N = 55)	χ^2/t Value	Significance
OCD subtypes, N (%)				
Obsessive	25 (37)	6 (11)	8.310	.004
Mixed	42 (63)	49 (89)	11.111	.001
Obsessions, N (%)				
Contamination	25 (37)	37 (67)	10.847	.001
Pathological doubts	25 (37)	30 (55)	3.623	.057
Aggressive	12 (18)	18 (33)	3.576	.060
Sexual	8 (12)	17 (31)	6.671	.010
Religious	14 (21)	13 (24)	0.132	.717
Symmetry/exactness	14 (21)	15 (27)	0.678	.410
Hoarding	5 (7)	8 (15)	1.592	.207
Miscellaneous	22 (33)	13 (24)	1.249	.264
Compulsions, N (%)				
Washing	19 (28)	36 (65)	16.789	< .001
Checking	22 (33)	26 (47)	2.638	.104
Repeating	7 (10)	24 (44)	17.554	< .001
Ordering	10 (15)	12 (22)	0.971	.324
Counting	1 (1)	1 (2)	…	1.000
Hoarding	5 (7)	8 (15)	1.522	.207
Miscellaneous (any)	14 (21)	35 (64)	22.960	< .001
Cognitive	7 (10)	21 (38)	13.138	< .001
Slowness	3 (4)	7 (13)	…	.077
Need to confess, ask	2 (3)	9 (16)	…	.022
Reassurance seeking	0	12 (22)	16.213	< .001
Superstitious behaviors	4 (6)	6 (11)	0.433	.511
Baseline YBOCS score, mean (SD)	18.96 (9.41)	25.30 (7.73)	–4.014	< .001
Current YBOCS score, mean (SD)	9.41 (7.66)	25.70 (8.36)	–11.210	< .001
Baseline CGI-S score, mean (SD)	4.04 (1.28)	5.07 (1.02)	–4.728	< .001
Current CGI-S score, mean (SD)	2.66 (0.88)	4.80 (1.17)	–11.206	< .001

Abbreviations: CGI-S = Clinical Global Impressions-Severity of Illness, OCD = obsessive-compulsive disorder, SRI = serotonin reuptake inhibitor, YBOCS = Yale-Brown Obsessive Compulsive Scale.
Symbol: … = not applicable.

Multiple logistic stepwise forward regression analysis was performed to identify potential predictors of response. The variables selected included those clinical variables that were significant in the univariate analysis. The 13 variables included current age; age at onset; contamination and sexual obsessions; washing, repeating, and miscellaneous compulsions; OCD subtypes (mixed and predominantly obsessional); baseline YBOCS score; and presence of "any comorbidity," tic disorders, major depressive disorder, and dysthymia. Considering the sample size, the number of predictor variables had to be limited. Therefore, the subcategories of miscellaneous compulsions were included as a single variable. Insight was not included in the regression analysis since the baseline insight scores were not available. The final model resulted in 6 variables with 78% overall correct prediction. The 5 variables that significantly predicted nonresponse were sexual obsessions ($\beta = 2.000$, SE = 0.643, $p = .002$), miscellaneous compulsions ($\beta = 0.296$, SE = 0.119, $p = .013$), washing compulsions ($\beta = 1.426$, SE = 0.534, $p = .008$), baseline YBOCS score ($\beta = 0.059$, SE = 0.030, $p = .049$), and major depressive disorder ($\beta = 2.552$, SE = 0.902, $p = .005$). The sixth variable was age at onset, which showed a trend toward prediction of nonresponse ($\beta = -0.065$, SE = 0.034, $p = .056$). Many variables that were significant in the univariate analysis did not enter the statistical model, suggesting confounding effects with the variables that entered the regression analysis.

The mean GAF score was higher in responders compared to nonresponders (72.89 ± 9.26 vs. 54.05 ± 11.83, $t = 9.862$, $p < .001$). Similarly, the mean Q-LES-Q score was significantly higher in responders than in nonresponders (56.91 ± 8.07 vs. 44.77 ± 9.49, $t = 7.661$, $p < .001$).

DISCUSSION

To our knowledge, this is the first study to systematically characterize SRI nonresponders in comparison with SRI responders by employing a fairly rigorous definition of nonresponse. Many previous studies have examined factors contributing to poor response to SRIs in OCD.[5,7–9,11,35] However, patients in these studies were not necessarily SRI nonresponders. Main strengths of our study include (1) rigorous definition of nonresponse to SRIs, (2) systematic and elaborate assessment of clinical profile using various instruments, and (3) assessments by qualified psychiatrists trained in assessing OCD subjects. On the basis of the regression analysis, we found sexual obsessions, miscellaneous and washing compulsions, increased baseline severity of illness, and comorbid major depressive disorder to be strong predictors of

Table 3. Comorbid Axis I and Axis II Disorders in SRI Responders and Nonresponders With OCD

Comorbid Diagnosis	Responders (N = 67)	Nonresponders (N = 55)	χ^2/t Value	Significance
Any Axis I comorbidity, N (%)	11 (16)	27 (49)	15.035	< .001
Mood disorders, N (%)				
Major depressive disorder	2 (3)	15 (27)	14.857	< .001
Bipolar I disorder	0	0	…	…
Bipolar II disorder	0	0	…	…
Dysthymia	3 (4)	10 (18)	5.958	.015
Anxiety disorders, N (%)	11 (16)	9 (16)	0.000	.994
Panic disorder without agoraphobia	2 (3)	2 (4)	…	1.000
Panic disorder with agoraphobia	0	1 (2)	…	.451
Agoraphobia	0	0	…	…
Generalized anxiety disorder	2 (3)	1 (2)	…	1.000
Social phobia	5 (7)	4 (7)	…	1.000
Specific phobias	0	0	…	…
Posttraumatic stress disorder	0	0	…	…
Somatoform disorders, N (%)	0	2 (4)	…	.201
Eating disorders, N (%)	0	0	…	…
Alcohol/substance dependence, N (%)	1 (1)	4 (7)	…	.174
Any psychotic disorder, N (%)	0	0	…	…
Tic disorders, N (%)	1 (1)	6 (11)	…	.045
Any personality disorder, N (%)	7 (10)	7 (13)		.694
Avoidant	3 (4)	2 (4)	…	1.000
Dependent	0	1 (2)	…	.451
Passive aggressive	0	2 (4)	…	.201
Obsessive-compulsive	4 (6)	3 (5)	…	1.000
Schizoid	0	0	…	…
Schizotypal	0	0	…	…
Paranoid	0	0	…	…
Borderline	0	0	…	…
Antisocial	0	0	…	…
Histrionic	0	0	…	…
Other personality disorders	0	0	…	…

Abbreviations: OCD = obsessive-compulsive disorder, SRI = serotonin reuptake inhibitor.
Symbol: … = not applicable.

nonresponse to treatment. Nonresponders had significantly earlier onset of illness compared to responders in the univariate analysis. In the regression analysis, early age at onset showed a trend toward prediction of nonresponse to SRIs.

Our study suggests that SRI nonresponders have an earlier age at onset of OCD. The published data on the relationship between age at onset and treatment response are conflicting. Some studies found no relationship between age at onset and SRI nonresponse,[18,22,35,36] whereas few other studies have reported poor response to treatment in those with early age at onset of OCD.[5,7,8] Our finding that those with earlier age at onset have poor response to treatment is in agreement with the long-term follow-up study of Skoog and Skoog,[37] who reported poor outcome in those with early onset OCD. In the study by Ravizza et al.,[8] nonresponders also had a longer duration of illness, whereas in our study and in the study by Ackerman et al.,[5] length of illness was similar in responders and nonresponders. This suggests that adults with early age at onset have poorer response to SRIs independent of the length of the illness.

Certain obsessions and compulsions and mixed OCD (those with prominent obsessions and compulsions) were associated with nonresponse. In the published data, relationship between treatment response and symptom profile is somewhat unclear. For example, mixed OCD was associated with poor treatment response in 2 previous studies,[8,10] but other studies found no association between OCD subtypes and outcome.[18,22] That mixed OCD is associated with poor outcome is also in accordance with some of the longitudinal studies of OCD.[37] Our finding that cleaning and washing compulsions are predictive of treatment nonresponse is shared by other researchers also.[8,9] However, no previous study has found miscellaneous compulsions and sexual obsessions to be related to treatment nonresponse. On the other hand, somatic obsessions and hoarding have been reported to be associated with SRI nonresponse.[7] In the univariate analysis, it is clear that cognitive compulsions and reassurance seeking are significantly associated with nonresponse. It is well known that those with cognitive compulsions (also called ruminators) respond poorly to behavior therapy,[38] but our finding also suggests that they tend to respond poorly to even pharmacologic interventions. That certain obsessions and compulsions predict SRI nonresponse needs further investigation because of the conflicting findings.

Treatment nonresponders also had more severe OCD and higher rates of "any comorbidity," major depressive disorder, and tic disorders. Our observation that severity

predicts treatment response is supported by the findings of previous studies that reported more severe OCD in nonresponders compared to less severe OCD in responders.[22,39,40] Our results demonstrate that Axis I comorbidity, particularly comorbid major depressive disorder, predicts treatment nonresponse. Although tic disorders were overrepresented in nonresponders, the overall rate of tic disorders was low in our sample. Major depression is a common comorbid condition in OCD, found in about one third of the patients.[11,41,42] Initial studies mention that levels of depression play an important role in the outcome.[43] A few earlier studies indicated that those with comorbid major depression had the best response,[15,16] but subsequent studies did not consistently identify depression as a response predictor.[18–21] However, our finding that major depressive disorder predicts SRI nonresponse is consistent with that of some previous reports. Depression has been reported to interfere with the response to both pharmacologic and behavioral treatments of OCD.[44,45] Some of the recent studies have also found an association between comorbid major depression and SRI nonresponse.[5,11,17,46] In view of the fact that major depression is a common comorbid condition in OCD and that it could potentially influence the treatment response, carefully designed treatment studies involving OCD patients with and without depression need to be conducted. It is also important to identify in future studies the nature of the relationship between the severity of depression and the treatment response, since there is some suggestion that the relationship is nonlinear[5]; that is, a U-shaped relationship possibly exists between severity of depression and response.

Previous studies have shown Axis II comorbidity, particularly schizotypal personality disorder, to predict treatment nonresponse,[13,14] but the overall rate of personality disorders in itself was low in our sample. A recent study from this center also found low rates of personality disorders.[47] It is possible that the questions in the SCID-II are not entirely culturally appropriate, resulting in underdiagnosis of personality disorders. Recent studies have shown that poor insight is associated with treatment nonresponse.[7,11,22] In our study also, poor insight patients were significantly overrepresented in nonresponders. Poor insight OCD could be a distinct subtype of OCD with underlying biological differences involving dopaminergic dysregulation[48] and poor treatment response to SRIs. The relationship between insight and treatment response requires further systematic exploration, since a large study did not find an association between insight and response to sertraline.[34]

In conclusion, our study has identified certain clinical predictors of SRI nonresponse. It appears that severe OCD and certain clinical characteristics are predictors of nonresponse to SRIs. Early age at onset showed a trend toward prediction of nonresponse. While age at onset, washing compulsions, major depressive disorder, and tics have been previously identified to predict poor response, our study has for the first time identified the presence of miscellaneous compulsions and sexual obsessions to predict SRI nonresponse. From the univariate analysis, there is also a suggestion that mixed OCD and poor insight are associated with treatment nonresponse.

Certain limitations of our study need to be kept in mind. Firstly, the subjects were recruited from a specialty OCD clinic. Therefore, the sample is less likely to be representative of the general population of OCD subjects. Secondly, treatment was not controlled. The choice of SRIs was decided by the treating clinician. Because of this limitation, the findings cannot be attributed to any particular SRI. Thirdly, no formal reliability exercises were carried out for the instruments used. Lastly, we employed only CGI-I to determine treatment response because CGI-I has certain advantages over YBOCS, as mentioned earlier. However, the International Refractory OCD Consortium advocates use of both the YBOCS and the CGI-I.[23] Because of this, our results may not be directly comparable to the results of future studies in this area that may use both scales to determine treatment response.

The study of treatment nonresponders has important clinical implications. Nonresponse is associated with serious impairment in functioning and lowered quality of life as seen in this study. It is important to identify treatment modalities that are effective in this subgroup of patients. For example, it may be necessary to examine whether a combination of behavior therapy with drugs works better in nonresponders. Alternatively, the role of atypical antipsychotic augmentation in SRI nonresponders may be an important area of investigation, since there is some suggestion from the present study and a previous study[11] that this group may be overrepresented by poor insight patients. It is possible that nonresponders are neurobiologically different from responders. The study of predictors of treatment nonresponse, however, is intricately linked to the concept of nonresponse. Therefore, there is an urgent need to operationalize the definition of nonresponse and use the definition uniformly across the studies for the findings to be more meaningful.

Drug names: citalopram (Celexa and others), clomipramine (Anafranil and others), escitalopram (Lexapro), fluoxetine (Prozac and others), paroxetine (Paxil, Pexeva, and others), sertraline (Zoloft).

REFERENCES

1. Abramowitz J. Effectiveness of psychological and pharmacological treatments for obsessive-compulsive disorder: a quantitative review. J Consult Clin Psychol 1997;65:44–52
2. Greist JH, Jefferson JW, Kobak KA, et al. Efficacy and tolerability of serotonin transport inhibitors in obsessive-compulsive disorder: a meta-analysis. Arch Gen Psychiatry 1995;52:53–60
3. Piccinelli M, Pini S, Bellantuono C, et al. Efficacy of drug treatment in obsessive-compulsive disorder: a meta-analytic review. Br J Psychiatry 1995;166:424–443

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4. Pigott TA, Seay SM. A review of the efficacy of selective serotonin reuptake inhibitors in obsessive-compulsive disorder. J Clin Psychiatry 1999;60:101–106
5. Ackerman DL, Greenland S, Bystritsky A, et al. Predictors of treatment response in obsessive-compulsive disorder: multivariate analyses from a multicenter trial of clomipramine. J Clin Psychopharmacol 1994;14: 247–254
6. Stein DJ, Spadaccini E, Hollander E. Meta-analysis of pharmacotherapy trials for obsessive-compulsive disorder. Int Clin Psychopharmacol 1995; 10:11–18
7. Erzegovesi S, Cavallini MC, Cavadeni P, et al. Clinical predictors of drug response in obsessive-compulsive disorder. J Clin Psychopharmacol 2001;21:488–492
8. Ravizza L, Barzega G, Bellino S, et al. Predictors of drug treatment response in obsessive-compulsive disorder. J Clin Psychiatry 1995;56: 368–373
9. Alarcon RD, Libb JW, Spitler D. A predictive study of obsessive-compulsive disorder response to clomipramine. J Clin Psychopharmacol 1993;13:210–213
10. Jenike MA. Management of patients with treatment-resistant obsessive-compulsive disorder. In: Pato MT, Zohar J, eds. Current Treatments of Obsessive-Compulsive Disorder. Washington, DC: American Psychiatric Press; 1991:135–155
11. Ravi Kishore V, Samar R, Janardhan Reddy YC, et al. Clinical characteristics and treatment response in poor and good insight obsessive-compulsive disorder. Eur Psychiatry 2004;19:202–208
12. Leonard HL, Swedo SE, Lenane MC, et al. A 2- to 7-year follow-up study of 54 obsessive-compulsive children and adolescents. Arch Gen Psychiatry 1993;50:429–439
13. Jenike MA, Baer L, Minichiello WE, et al. Concomitant obsessive-compulsive disorder and schizotypal personality disorder. Am J Psychiatry 1986;143:530–532
14. Baer L, Jenike MA, Black DW, et al. Effect of Axis II diagnoses on treatment outcome with clomipramine in 55 patients with obsessive-compulsive disorder. Arch Gen Psychiatry 1992;49:862–866
15. Capstick N, Seldrup J. Phenomenological aspects of obsessional patients treated with clomipramine. Br J Psychiatry 1973;122:719–720
16. Marks IM, Stern RS, Mawson D, et al. Clomipramine and exposure for obsessive-compulsive rituals, 1. Br J Psychiatry 1980;136:1–25
17. Overbeek T, Schruers K, Vermetten E, et al. Comorbidity of obsessive-compulsive disorder and depression: prevalence, symptom severity, and treatment effect. J Clin Psychiatry 2002;63:1106–1112
18. DeVeaugh-Geiss J, Katz R, Landau P, et al. Clinical predictors of treatment response in obsessive-compulsive disorder: exploratory analyses from multicenter trials of clomipramine. Psychopharmacol Bull 1990;26: 54–59
19. Goodman WK, Kozak MJ, Liebowitz M, et al. Treatment of obsessive-compulsive disorder with fluvoxamine: a multicentre, double-blind, and placebo-controlled trial. Int Clin Psychopharmacol 1996;11:21–29
20. Katz RJ, DeVeaugh-Geiss J. The antiobsessional effects of clomipramine do not require concomitant affective disorder. Psychiatry Res 1990;26: 54–59
21. Tollefson GD, Rampey AH, Potvin JH, et al. A multicenter investigation of fixed-dose fluoxetine in the treatment of obsessive-compulsive disorder. Arch Gen Psychiatry 1994;51:559–567
22. Hollander E, Bienstock CA, Koran LM, et al. Refractory obsessive-compulsive disorder: state of the art treatment. J Clin Psychiatry 2002; 63(suppl 6):20–29
23. Pallanti S, Hollander E, Bienstock C, et al. Treatment nonresponse in OCD: methodological issues and operational definitions. Int J Neuropsychopharmacol 2002;5:181–191
24. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition. Washington, DC: American Psychiatric Association; 1994
25. Goodman WK, Price LH, Rasmussen SA, et al. The Yale-Brown Obsessive Compulsive Scale (YBOCS), 1: development, use and reliability. Arch Gen Psychiatry 1989;46:1006–1011
26. Goodman WK, Price LH, Rasmussen SA, et al. The Yale-Brown Obsessive Compulsive Scale (YBOCS), 2: validity. Arch Gen Psychiatry 1989;46:1012–1016
27. The ICD-10 Classification of Mental and Behavioural Disorders: Clinical Descriptions and Diagnostic Guidelines. Geneva, Switzerland: World Health Organization; 1992
28. First MB, Spitzer RL, Gibbon M, et al. Structured Clinical Interview for DSM-IV Axis I Disorders, Patient Edition (SCID-I/P, version 2.0). New York, NY: Biometrics Research Department, New York State Psychiatric Institute; 1995
29. First MB, Spitzer RL, Gibbon M, et al. Structured Clinical Interview for DSM-IV Axis II Personality Disorders (SCID-II). New York, NY: Biometrics Research Department, New York State Psychiatric Institute; 1997
30. Paul DL, Hurst CR. Schedule for Tourette and Other Behavioral Syndromes: Adult version A3. Yale Family Genetic Study of Tourette Syndrome. New Haven, Conn: Yale Child Study Center; 1996
31. Eisen JL, Phillips KA, Baer L, et al. The Brown Assessment of Beliefs Scale: reliability and validity. Am J Psychiatry 1998;155:102–108
32. Endicott J, Nee J, Harrison W, et al. Quality of Life Enjoyment and Satisfaction Questionnaire: a new measure. Psychopharmacol Bull 1993;29:321–326
33. Guy W. ECDEU Assessment Manual for Psychopharmacology. US Dept Health, Education, and Welfare publication (ADM) 76-338. Rockville, Md: National Institute of Mental Health; 1976:218–222
34. Eisen JL, Rasmussen SA, Phillips KA, et al. Insight and treatment outcome in obsessive-compulsive disorder. Compr Psychiatry 2001; 42:494–497
35. Ackerman DL, Greenland S. Multivariate meta-analysis of controlled drug studies for obsessive-compulsive disorder. J Clin Psychopharmacol 2002;22:309–317
36. Thoren P, Asberg M, Cronholm B, et al. Clomipramine treatment of obsessive-compulsive disorder, 1: a controlled clinical trial. Arch Gen Psychiatry 1980;37:1281–1285
37. Skoog G, Skoog I. A 40 year follow-up of patients with obsessive-compulsive disorder. Arch Gen Psychiatry 1999;56:121–127
38. Buchanan AW, Meng KS, Marks IM. What predicts improvement and compliance during the behavioral treatment of obsessive-compulsive disorder? Anxiety 1996;2:22–27
39. Goodman WK, Price LH, Rasmussen SA, et al. Efficacy of fluvoxamine in obsessive-compulsive disorder: a double-blind comparison with placebo. Arch Gen Psychiatry 1989;46:36–44
40. Greist J, Chouinard G, DuBoff E, et al. Double-blind parallel comparison of three doses of sertraline and placebo in outpatients with obsessive-compulsive disorder. Arch Gen Psychiatry 1995;52:289–295
41. Rasmussen SA, Eisen JL. The epidemiology and differential diagnosis of obsessive-compulsive disorder. J Clin Psychiatry 1992;53(suppl 4):4–10
42. Jaisoorya TS, Janardhan Reddy YC, Srinath S. Is juvenile obsessive-compulsive disorder a developmental subtype of the disorder? findings from an Indian study. Eur Child Adolesc Psychiatry 2003;12:290–297
43. Marks I. Are there anticompulsive or antiphobic drugs? review of the evidence. Psychopharmacol Bull 1982;18:78–84
44. Hollander E, Mullen L, DeCaria CM, et al. Obsessive-compulsive disorder, depression, and fluoxetine. J Clin Psychiatry 1991;52:418–422
45. Foa EB. Failure in treating obsessive-compulsives. Behav Res Ther 1979;17:169–176
46. Goodman WK, Price LH, Delgado PL, et al. Specificity of serotonin reuptake inhibitors in the treatment of obsessive-compulsive disorder: comparison of fluvoxamine and desipramine. Arch Gen Psychiatry 1990;47:577–585
47. Reddy YCJ, D'Souza SM, Shetti C, et al. An 11- to 13-year follow-up of 75 subjects with obsessive-compulsive disorder. J Clin Psychiatry 2005;66:744–749
48. Sobin C, Blundell ML, Weiller F, et al. Evidence of a schizotypy subtype in OCD. J Psychiatr Res 2000;34:15–24

