Ziprasidone in the Treatment of Borderline Personality Disorder: A Double-Blind, Placebo-Controlled, Randomized Study

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Objective: The aim of this double-blind, placebo-controlled study was to evaluate the efficacy and tolerability of ziprasidone in the treatment of adult patients with borderline personality disorder.

Method: Sixty DSM-IV borderline personality disorder patients were included from March 2004 to April 2006 in a 12-week, single-center, double-blind, placebo-controlled study. The subjects were randomly assigned to ziprasidone or placebo in a 1:1 ratio following a 2-week baseline period. The Clinical Global Impressions scale for use in borderline personality disorder patients (CGI-BPD) was the primary outcome measure, and other scales and self-reports related to affect, behavior, psychosis, general psychopathology domains, and clinical safety were included.

Results: Analysis of variance indicated no statistically significant differences between ziprasidone and placebo in the CGI-BPD. Nor were significant differences observed between groups in depressive, anxiety, psychotic, or impulsive symptoms. The mean daily dose of ziprasidone was 84.1 mg/day (SD = 54.8; range, 40–200). The drug was seen to be safe, and no serious adverse effects were observed.

Conclusion: This trial failed to show a significant effect of ziprasidone in patients with borderline personality disorder.

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Borderline personality disorder affects approximately 2% of the general population, 10% of all patients seen at psychiatric outpatient clinics, and 20% of psychiatric inpatients.[1] These patients consume high levels of health care resources and constitute a significant social and economic burden. The 2001 American Psychiatric Association (APA) Practice Guideline for the Treatment of Patients With Borderline Personality Disorder[1] and the recently updated 2005 APA Guideline Watch[2] recommend that pharmacologic treatment for borderline personality disorder have an important adjunctive role, especially for diminution of symptoms such as affective instability, impulsivity, psychotic-like symptoms, and self-destructive behavior. Studies conducted with low doses of conventional antipsychotics have shown significant improvements in specific symptoms such as hostility and impulsiveness and mood and psychotic symptoms. However, the use of these drugs is limited due to poor tolerability and noncompliance.[1,3,4]

The introduction of atypical antipsychotics, which have a more favorable tolerance profile, has increased clinicians' options for treating borderline personality disorder. Olanzapine has proven its efficacy in 4 double-blind, placebo-controlled clinical trials in patients with borderline personality disorder.[5–8] In our previous trial,[7] olanzapine was associated with improvement in depressive, anxiety, and impulsivity/aggressive behaviors. Recently, aripiprazole has also proven its efficacy in the treatment of patients with borderline personality disorder in a double-blind, placebo-controlled study.[9]

Ziprasidone is an atypical antipsychotic with a pharmacologic action on serotonergic, dopaminergic, and adrenergic receptors. It has proven to be effective for schizophrenia, schizoaffective, and acute mania disorders, and the incidence of side effects is low.[10,11] In addition, its strong antagonism for the 5-HT_{1A} receptor and its moderate inhibition of 5-HT and norepinephrine reuptake, similar to tricyclic antidepressants, confer possible anxiolytic and antidepressant properties.[12] A previous open-label, uncontrolled study suggested that ziprasidone was useful for improving anxious, depressive, and psy-

chotic symptoms and a safe treatment for adult borderline personality disorder patients in acute exacerbations.[13] Similarly, a naturalistic study performed in psychiatric emergency units[14] suggested that intramuscular atypical antipsychotics (ziprasidone and olanzapine) may be effective, fast, and safe in the management of agitated borderline personality disorder patients.

Although clinical findings and the pharmacologic activity of ziprasidone suggest the drug may have therapeutic benefits in borderline personality disorder patients, no controlled studies have yet been conducted in these patients. We carried out a randomized, double-blind, placebo-controlled study to evaluate efficacy and tolerability of ziprasidone in the management of borderline personality disorder patients with moderate-high clinical severity.

MATERIALS AND METHOD

Subjects

From March 2004 to April 2006, a total of 127 patients were referred from clinical services (outpatients and psychiatric emergency services). Inclusion criteria consisted of (1) meeting the DSM-IV diagnostic criteria for borderline personality disorder as assessed by 2 semistructured diagnostic interviews: the Structured Clinical Interview for DSM-IV Axis II Disorders[15] and the Revised Diagnostic Interview for Borderlines[16]; (2) age between 18 and 45 years; (3) no comorbidity with schizophrenia, drug-induced psychosis, organic brain syndrome, alcohol or other substance dependence, bipolar disorder, mental retardation, or major depressive episode in course; (4) Clinical Global Impressions (CGI)-Severity of Illness[17] scores ≥ 4; and (5) current use of medically accepted contraception in the case of female patients.

Patients were allowed to continue treatment with benzodiazepines, antidepressants, and mood stabilizers if they had been initiated prior to inclusion, but doses could not be modified during the study. The maximum benzodiazepine dose allowed was 40 mg/day (diazepam equivalent). No antipsychotics other than the study drug were allowed. A physical examination, complete laboratory tests, a pregnancy test, and an electrocardiogram (EKG) were performed for all patients admitted to the study.

The study followed the main principles outlined in the Declaration of Helsinki and was approved by the Sta. Creu i St. Pau Hospital Clinical Research Ethics Review Board, by the Spanish Drug Agency, and by the Ministry of Health, Spain. After giving a full description of the study, written informed consent was obtained from all participating patients.

Design

This was a single-center, randomized, double-blind, placebo-controlled clinical trial consisting of 2 phases: the selection phase (2-week baseline period) and the experimental phase (12 weeks). During the selection phase, subjects had 2 evaluation visits (weeks 0, 2) to establish a preintervention baseline but underwent no therapeutic intervention. Given the characteristic fluctuations of symptoms in this disorder, 2 measurements were made during this phase. Patients were then randomly assigned to ziprasidone or placebo (1:1 ratio). Randomization was performed by blocks of 4 generated using the SPSS software package (SPSS Inc., Chicago, Ill.). Participants were evaluated every 2 weeks by an experienced psychiatrist and participated in weekly, 2-hour, nonspecific group psychotherapy sessions.

Medication was dispensed by the investigator at each follow-up visit, and participants were given enough capsules for the between-visit interval. All unused medication was returned to the investigators. Compliance was assessed by direct questioning of patients and by counting the capsules returned at follow-up visits. Treatment doses were flexible; the drug was started at 40 mg/day for the first 2 weeks and ranged from 40 to 200 mg/day of ziprasidone or placebo during the course of the trial, depending on symptoms, patient response, and the presence of secondary effects.

Material

The main measure used to evaluate efficacy was the CGI scale for use in borderline personality disorder patients (CGI-BPD).[18] The following secondary efficacy variables were also evaluated at each visit: affective symptoms with the 17-item Hamilton Rating Scale for Depression (HAM-D-17)[19]; anxiety symptoms with the Hamilton Rating Scale for Anxiety (HAM-A)[20]; psychotic symptoms with the Brief Psychiatric Rating Scale (BPRS)[21]; psychiatric symptoms with the Symptom Checklist-90-Revised (SCL-90-R)[22]; impulsiveness with the Barratt Impulsiveness Scale[23]; and hostility/irritability with the Buss-Durkee Inventory.[24] Safety was evaluated by assessing treatment-emergent adverse events, EKG, and laboratory assessment. The presence of extrapyramidal side effects was measured using the modified Udvalg for Kliniske Undersogelser (UKU) Side Effect Rating Scale.[25]

Data were also obtained using pragmatic variables regarding the most dysfunctional behaviors observed in borderline personality disorder by biweekly behavioral reports: episodes of impulsiveness, aggressiveness, parasuicide/self-injuring behaviors, suicide attempts, and visits to psychiatric emergency services.

Statistical Analyses

Data were analyzed using the SPSS 14.0 software package (SPSS Inc., Chicago, Ill.). All analyses were conducted on an intent-to-treat basis. Given the instability of symptoms over time, the pretreatment baseline values

were determined based on the mean value at the 2 visits that took place during the selection phase. Patients were included in the analyses only if they had a baseline measure and at least 1 postbaseline measure.

The χ^2 test and Student t test were used to assess between-group differences in demographic data and baseline value. Student t test was also used for the pre- and postintervention variables. The analysis of variance (ANOVA) and covariance (ANCOVA) models were used to compare intergroup differences with respect to the different efficacy and safety measurement outcomes. The end point was based on a last-observation-carried-forward (LOCF) strategy. All tests of hypotheses were performed with a 2-sided significance level of .05.

RESULTS

Patient Demographics and Baseline Clinical Characteristics

Of a total of 127 subjects evaluated, 65 met the inclusion criteria, 5 of whom dropped out of the study during the selection phase. Finally, 60 subjects (49 females and 11 males) were randomly assigned and initiated the experimental phase: 30 in the ziprasidone group and 30 in the placebo group (Figure 1).

As shown in Table 1, there were no significant differences between the 2 groups in terms of demographic variables or concomitant treatments observed at baseline. Table 2 presents data regarding severity of the sample. Patients in the placebo group presented more severe symptoms prior to treatment in most scales compared to the ziprasidone group. There were significant pretreatment differences between the 2 groups in HAM-D-17 scale scores (ziprasidone: mean = 17.14, SD = 4.5 vs. placebo: mean = 19.9, SD = 4.2; p = .019) and in the Global Severity Index of the SCL-90 scores (ziprasidone: mean = 2.20, SD = 0.8 vs. placebo: mean = 2.71, SD = 0.5; p = .016).

Efficacy

Table 2 summarizes the mean pre- and postintervention measurements. During the study, both groups showed a significant improvement in most of the psychopathology scales according to the t test analysis. Global score on the CGI-BPD improved in patients in the ziprasidone group (Figure 2). In the t test analysis, improvements were also observed in impulsivity, suicide, affect instability, anger, and paranoid items. There were no pre- and posttreatment differences in abandonment, unstable relations, identity, or emptiness items. In the placebo group, there were no differences in the global score but differences were found in the unstable relations, impulsivity, suicide, affect instability, and anger items.

No significant differences were found between groups in any scale in the ANOVA analysis of differences. Ziprasidone-treated patients did not show a greater decrease in clinical anxiety (HAM-A scale), clinical psychotic symptoms (BPRS scale), or impulsivity symptoms, as compared to placebo-treated patients. Given the between-group differences on the pretreatment HAM-D-17 scale, the ANCOVA was performed by entering the baseline depressive scores as covariants. No significant intergroup differences in depressive scale scores were observed.

In the behavioral reports, no differences were observed with regard to the frequency of impulsive/aggressive behaviors, self-injuring/suicidal behavior, or number of visits to emergency psychiatric services.

Figure 1. Flow Diagram of Patient Progress Throughout Phases of the Study

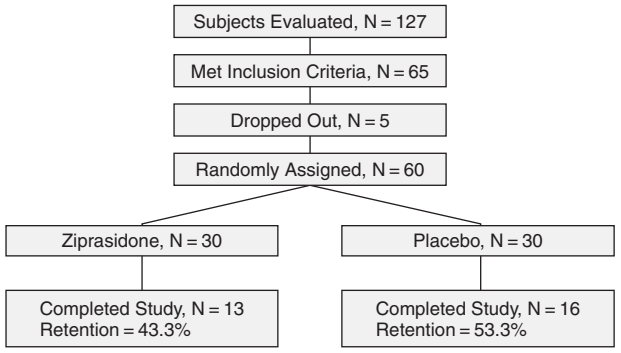


Table 1. Demographic Variables and Concomitant Pharmacologic Treatments at Baseline for 60 Patients With Borderline Personality Disorder in a Randomized, Controlled Trial

Variable	Ziprasidone (N = 30)	Placebo (N = 30)	p
Age, mean (SD)	29.10 (5.96)	29.33 (6.33)	NS[a]
Gender, female, N (%)	24 (80.0)	25 (83.3)	NS[b]
Completed study, N (%)	13 (43.3)	16 (53.3)	NS[b]
Pharmacologic treatment, N (%)			
Benzodiazepines	23 (76.7)	25 (83.3)	NS[b]
Antidepressants	21 (70.0)	22 (73.3)	NS[b]
Mood stabilizers	12 (40.0)	12 (40.0)	NS[b]

[a]t test.
[b]χ^2 test.
Abbreviation: NS = not significant.

Safety

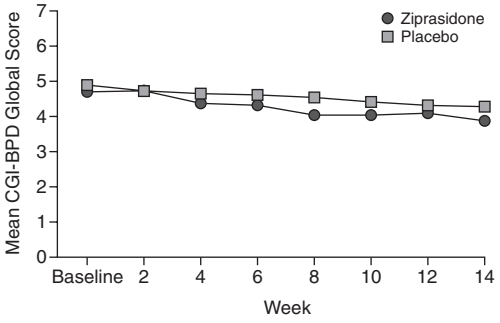
The mean daily dose of ziprasidone during the experimental phase was 84.1 mg/day (SD = 54.8; range, 40–200). No significant differences were detected between the 2 groups in dropout rates; 56.7% (17/30) in the ziprasidone group and 46.7% (14/30) in the placebo group did not complete the study. The reasons for withdrawal in the ziprasidone group were need of psychiatric hospitalization (N = 4), adverse events/patient decision (N = 9), clinician decision/insufficient treatment effect (N = 3),

Table 2. Rating Scale Scores Before Versus After Treatment

	Ziprasidone				Placebo			
	Pretreatment		Posttreatment		Pretreatment		Posttreatment	
Rating Scale	Mean	SD	Mean	SD	Mean	SD	Mean	SD
CGI-BPD								
Global	4.78	0.6	3.88	0.6**	4.90	0.8	4.3	1.1
Abandonment	4.59	1.2	4.44	1.2	4.83	1.0	4.53	1.1
Unstable relations	4.70	1.3	4.37	1.1	4.90	1.3	4.50	1.0*
Identity	4.78	1.0	4.62	1.1	4.97	1.1	5.03	1.0
Impulsivity	4.74	1.3	4.00	1.4*	4.63	1.6	3.96	1.5*
Suicide	3.33	1.5	2.70	1.6*	3.57	1.4	3.13	1.5*
Affect instability	5.41	0.7	4.44	0.6*	5.20	1.0	4.53	1.1*
Emptiness	4.81	1.5	4.70	1.5	4.63	1.8	4.40	1.7
Anger	4.19	1.4	3.66	1.4*	4.13	1.2	3.56	1.2*
Paranoid ideation	2.41	1.2	1.96	1.2*	2.40	1.4	2.23	1.1
HAM-D-17[a]	17.14	4.5	14.24	6.5*	19.90	4.2	16.07	5.5*
HAM-A	19.037	5.0	15.79	6.9*	20.33	4.9	16.53	5.3*
BPRS	13.76	5.1	10.52	5.7**	15.43	6.1	12.33	7.2**
BIS	71.47	18.9	67.73	22.7	77.18	10.7	69.13	21.2
BDI	46.00	12.9	43.42	13.18	49.00	10.46	47.75	13.5
SCL-90-R: GSI[a]	2.20	0.8	2.06	0.8	2.71	0.5	2.39	0.8*

[a]Pretreatment differences between ziprasidone and placebo.
*p < .05, t test.
**p < .001, t test.
Abbreviations: BDI = Buss-Durkee Inventory, BIS = Barratt Impulsiveness Scale, BPRS = Brief Psychiatric Rating Scale, CGI-BPD = Clinical Global Impressions scale for use in borderline personality disorder patients, GSI = Global Severity Index of the SCL-90-R, HAM-A = Hamilton Rating Scale for Anxiety, HAM-D-17 = 17-item Hamilton Rating Scale for Depression, SCL-90-R = Symptom Checklist-90-Revised.

Figure 2. Mean Change in CGI-BPD Global Score From Baseline During the Study[a,b]



[a]In the ANOVA analysis of differences between ziprasidone and placebo groups, there were no significant differences (F = 1.11, df = 2.88,158.38; p = .344).
[b]Last observation carried forward.
Abbreviations: ANOVA = analysis of variance, CGI-BPD = Clinical Global Impressions scale for use in borderline personality disorder patients.

and other reasons (N = 1). In the placebo group, the reasons for withdrawal were need of psychiatric hospitalization (N = 3), patient decision (N = 4), and clinician decision/lack of efficacy (N = 7).

Significant differences were detected between groups with respect to the presence of secondary effects as spontaneously reported by patients. Treatment-emergent adverse events were experienced by 11 of the 30 ziprasidone-treated patients and by 4 of the 30 placebo-treated patients. No serious treatment-related adverse events occurred in either group, but 4 patients treated with ziprasidone dropped out because of these effects. There were significant differences between groups in some secondary effects. In the ziprasidone group, 6 patients reported minor sedation (p = .039), 4 had dizziness (p = .035), and 3 reported an "uneasy feeling" (p = .071). In the placebo-treated group, 1 patient reported minor sedation, 1 complained of headache, and 2 patients had gastrointestinal symptoms.

Patients did not spontaneously report any movement disorders, and we did not observe dystonia, akathisia, rigidity, or hyperkinesia in any patients. The modified-UKU scores indicated no significant differences between the 2 groups in the evaluation of movement disorders.

In laboratory parameters, no statistically significant differences were detected between groups. Two patients in the ziprasidone-treated group presented hyperprolactinemia but it was not clinically relevant. No significant changes in weight or blood pressure were seen with either treatment. No EKG changes in the QTc interval were found in the ziprasidone group.

DISCUSSION

To our knowledge, this is the first randomized, double-blind study to compare ziprasidone and placebo in patients with borderline personality disorder. The pharmacologic profile of ziprasidone, its efficacy in psychotic symptoms, and its possible anxiolytic and antidepressant effect sug-

gest a priori that this drug may have therapeutic benefits in borderline personality disorder patients.[10–12] Moreover, previous open-label trials with borderline personality disorder patients in acute exacerbations observed that it was a useful and safe treatment.[13,14] Nevertheless, our study did not find significant differences between ziprasidone and placebo; efficacy of both agents was similar in improving mood and anxiety symptoms and impulsivity in borderline personality disorder patients.

There are several possible explanations for the differences between our results in this trial and those from a previous study conducted with ziprasidone in borderline personality disorder patients. First, the dose of ziprasidone used here (84.1 mg/day) was lower than that used in the previous study (102.7 mg/day).[13] Second, in the ziprasidone group, the majority of patients discontinued the study during the first 2 weeks, and, with the LOCF strategy, this could have masked the differences between ziprasidone and placebo. Our previous study showed that including specific and active psychotherapy reduces the dropout rate in a pharmacologic trial.[7] Third, in the present study, treatment was initiated with a low dose of ziprasidone (40 mg/day) during the first 2 weeks. In the previous open-label study, treatment was administered at flexible doses ranging from 40 to 160 mg/day according to the clinician's decision, and patients initiated treatment with a high dose.[13] Other studies conducted with ziprasidone report that patients initiating ziprasidone therapy with an initial dose of at least 120 mg/day had better medication adherence than those initiating at a lower dose.[26] Lastly, previous studies with other drugs in borderline personality disorder patients have also demonstrated significant short-term improvements that disappeared over the mid- and long term.[27] Ziprasidone may perhaps be more appropriate for a short duration in patients in crisis.

Several clinical trials have shown the efficacy of atypical antipsychotics in borderline personality disorder patients, but no studies with negative findings have been published to date. One clinical trial with risperidone, however, found negative results but has not been published.[1] Olanzapine has proven its efficacy in 4 double-blind, placebo-controlled clinical trials in patients with borderline personality disorder.[5–8] A global improvement was observed in depressive, anxiety, and impulsivity/aggressive symptoms.[7] Aripiprazole has also proven efficacious in another clinical trial.[9] It is important to note that these studies also used a lower dose than recommended. One explanation for these different results is the marked pharmacokinetic and pharmacodynamic differences between these drugs. For example, the sedative action of ziprasidone may be lower than that of other antipsychotics such as olanzapine.

Ziprasidone proved to be safe and no severe adverse effects were reported. Although 2 patients treated with ziprasidone presented with hyperprolactinemia, this was not clinically significant. Ziprasidone was not associated with weight gain, extrapyramidal symptoms, or clinically significant EKG changes. Several patients complained of mild somnolence, an uneasy feeling, or dizziness.

Another important point must be considered. In our primary outcome measure, the CGI-BPD, we observed changes in the t test analysis only in impulsivity, affect instability, suicide, and anger. We observed no modifications in feelings of emptiness, abandonment, or identity. These characteristic symptoms of borderline personality disorder should perhaps not be evaluated in short clinical trials, as improvement is unlikely in only 3 months.

Study Limitations

This study has several limitations. First, due to the characteristics of our sample, the results cannot be extrapolated to inpatients, to patients with less clinically severe disorders, or to subjects with active comorbid Axis I disorders. Second, the majority of patients included in our sample were receiving concomitant treatment with benzodiazepines and/or antidepressants. Despite the fact that stable doses were maintained, we cannot rule out possible drug-drug interactions. Selecting only "drug-free individuals" or those who did not use toxic substances would have resulted in a less representative sample. Third, in spite of randomization, the placebo group showed greater severity. Nevertheless, the pretreatment differences between groups were only significant in depressive symptoms and in the Global Severity Index of the SCL-90, and the ANCOVA analyses were performed by entering the baseline depressive scores as covariants. Another limitation that should be pointed out is the high dropout rate in the study. However, high dropout rates are common in pharmacologic trials of borderline personality disorder patients, ranging from 30% to 87.5%.[1,7] By including a psychosocial intervention, we pretended to improve compliance and lower dropout rates but were unsuccessful. Finally, the psychosocial intervention may have masked the differences between ziprasidone and placebo.

Summary

This double-blind, placebo-controlled study failed to demonstrate that ziprasidone was more effective than placebo in improving symptoms of borderline personality disorder. Future clinical trials using higher doses in larger samples are needed to replicate these findings.

Drug names: aripiprazole (Abilify), diazepam (Valium and others), olanzapine (Zyprexa), ziprasidone (Geodon).

REFERENCES

1. American Psychiatric Association. Practice Guideline for the Treatment of Patients With Borderline Personality Disorder. Am J Psychiatry 2001;158(suppl 10):1–52

2. Oldham JM. Guideline Watch: Practice Guideline for the Treatment of Patients With Borderline Personality Disorder. Arlington, Va: American Psychiatric Association; 2005
3. Cowdry RW, Gardner DL. Pharmacotherapy of borderline personality disorder: alprazolam, carbamazepine, trifluoperazine and tranylcypromine. Arch Gen Psychiatry 1988;45:111–119
4. Soloff PH, Cornelius J, George A, et al. Efficacy of phenelzine and haloperidol in borderline personality disorder. Arch Gen Psychiatry 1993;50:377–385
5. Zanarini MC, Frankenburg FR. Olanzapine treatment of female borderline personality disorder patients: a double-blind, placebo-controlled pilot study. J Clin Psychiatry 2001;62:849–854
6. Bogenschutz MP, Nurnberg HG. Olanzapine versus placebo in the treatment of borderline personality disorder. J Clin Psychiatry 2004; 65:104–109
7. Soler J, Pascual JC, Campins J, et al. A double-blind, placebo-controlled study of borderline personality disorder: olanzapine plus dialectical behavior therapy. Am J Psychiatry 2005;162:1221–1224
8. Zanarini MC, Frankenburg FR, Parachini EA. A preliminary, randomized trial of fluoxetine, olanzapine, and the olanzapine-fluoxetine combination in women with borderline personality disorder. J Clin Psychiatry 2004;65:903–907
9. Nickel MK, Muehlbacher M, Nickel C, et al. Aripiprazole in the treatment of patients with borderline personality disorder: a double-blind, placebo-controlled study. Am J Psychiatry 2006;163:833–838
10. Tandon R. Introduction: ziprasidone appears to offer important therapeutic and tolerability advantages over conventional, and some novel, antipsychotics. Br J Clin Pharmacol 2000;49(suppl 1):1S–3S
11. Keck P Jr, Buffenstein A, Ferguson J, et al. Ziprasidone 40 and 120 mg/day in the acute exacerbation of schizophrenia and schizoaffective disorder: a 4-week placebo-controlled trial. Psychopharmacology 1998;140:173–184
12. Wilner KD, Anziano RJ, Johnson AC, et al. The anxiolytic effect of the novel antipsychotic ziprasidone compared with diazepam in subjects anxious before dental surgery. J Clin Psychopharmacol 2002;22: 206–210
13. Pascual JC, Oller S, Soler J, et al. Ziprasidone in the acute treatment of borderline personality disorder in psychiatric emergency services [letter]. J Clin Psychiatry 2004;65:1281–1283
14. Pascual JC, Madre M, Soler J, et al. Injectable atypical antipsychotics for agitation in borderline personality disorder. Pharmacopsychiatry 2006;39:117–118
15. First MB, Spitzer RL, Gibbon M, et al. The Structured Clinical Interview for DSM-III-R Personality Disorders (SCID-II), 1: description. J Personal Disord 1995;9:83–91
16. Barrachina J, Soler J, Campins MJ, et al. Validation of a Spanish version of the Diagnostic Interview for Borderlines-Revised (DIB-R) [in Spanish]. Actas Esp Psiquiatr 2004;32:293–298
17. 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
18. Pérez V, Barrachina J, Soler J, et al. Modification of the Clinical Global Impression (CGI) scale for use in borderline personality disorder patients (CGI-BPD). Actas Esp Psiquiatr 2007;35:229–235
19. Hamilton M. A rating scale for depression. J Neurol Neurosurg Psychiatry 1960;23:56–62
20. Hamilton M. The assessment of anxiety states by rating. Br J Med Psychol 1959;32:50–55
21. Overall JE, Gorham DR. The Brief Psychiatric Rating Scale. Psychol Rep 1962;10:799–812
22. Derogatis LR. SCL-90-R: Administration, Scoring and Procedures Manual for the Revised Version. Baltimore, Md: Johns Hopkins University School of Medicine; 1977
23. Barrat ES. Impulsiveness and aggression. In: Monahan J, Steadman HJ, eds. Violence and Mental Disorder: Developments in Risk Assessment. Chicago, Ill: The University of Chicago Press; 1995:61–79
24. Buss AH, Durkee A. An inventory for assessing different kinds of hostility. J Consult Psychol 1957;21:343–349
25. Lingiaerde O, Ahlfors UG, Bech P, et al. The UKU Side Effect Rating Scale: a new comprehensive rating scale for psychotropic drugs and a cross-sectional study of side effects in neuroleptic-treated patients. Acta Psychiatr Scand Suppl 1987;334:1–100
26. Mullins CD, Shaya FT, Zito JM, et al. Effect of initial ziprasidone dose on treatment persistence in schizophrenia. Schizophr Res 2006; 83:277–284
27. Cornelius JR, Soloff PH, Perel JM, et al. Continuation pharmacotherapy of borderline personality disorder with haloperidol and phenelzine. Am J Psychiatry 1993;150:1843–1848

