# Treatment of Borderline Personality Disorder With Risperidone

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***Background:*** Of the various Axis II disorders, borderline personality disorder (BPD) is among the more critical to treat. There are at present few results in terms of clinical outcome with the psychotropic agents available. Possible targets for pharmacotherapy are affective symptoms, cognitive disturbances, and impulsive, self-injurious behaviors. In previous studies, atypical antipsychotics at low-to-moderate doses provided symptom reduction with good tolerability. Our purpose was to assess the efficacy of risperidone in BPD, focusing on its effects on impulsive-aggressive behavior.

***Method:*** Fifteen BPD outpatients (DSM-IV diagnosis) with prominent histories of aggressive behavior were included in an 8-week open-label study with risperidone at low-to-moderate doses. Axis II codiagnoses included antisocial personality disorder (N = 4). Exclusion criteria included current Axis I diagnosis or any major medical or neurologic illness. Efficacy measures were the 21-item Hamilton Rating Scale for Depression, the Brief Psychiatric Rating Scale, the DSM-IV Global Assessment of Functioning, and the self-rated Aggression Questionnaire. Evaluations were carried out at baseline and at the end of the treatment.

***Results:*** Thirteen patients completed the trial; 2 patients dropped out because of lack of compliance. Final mean dose of risperidone was 3.27 mg/day. There was a significant (p = .0057) reduction in aggression based on Aggression Questionnaire scores. This amelioration was coupled with an overall improvement, including a reduction in depressive symptoms and an increase in energy and global functioning.

***Conclusion:*** Risperidone at low-to-moderate doses can improve BPD symptomatology. Further studies are needed to explore the efficacy of risperidone versus placebo as well as in comparison to other potential treatments for BPD.

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Of the various Axis II disorders, borderline personality disorder (BPD) has historically been among the more difficult for clinicians to identify and treat. There are at the moment only few studies regarding pharmacologic management of BPD and few clear results in terms of clinical outcome for treatment with the various psychotropic agents available. The lack of data is mainly due to the clinical heterogeneity of BPD. Evidence suggests that selective symptoms or psychopathologic dimensions are linked to specific alterations of central neurotransmission systems and to response to different psychopharmacologic agents. In BPD patients, possible targets for pharmacotherapy are affective dysregulation, impulsive-behavioral dyscontrol, and cognitive-perceptual symptoms.[1,2]

The impulsive-behavior symptom domain consists of recurrent suicidal threats, parasuicidal behaviors, impulsive-aggression, assaultiveness, property destruction, binge behaviors (on drugs, alcohol, sex, or food), and cognitive impulsivity with low frustration tolerance. These symptoms appear to be dimensions of personality characterizing BPD, both transmitted in families and correlated with reduced serotonergic neurotransmission.[3–5] Serotonin selective reuptake inhibitors (SSRIs) have been proposed as the first-line treatments for dysregulation of impulsive behavior. Improvement in impulsive aggression appeared to be independent of effects on depression and anxiety[6] and also independent of comorbid major depressive disorder.[7]

Failure to respond to SSRIs should prompt consideration of low-dose neuroleptics, which have a well-defined, but nonspecific, efficacy against impulsive behavior.[2] Early observations with neuroleptics at low doses reported a short-term efficacy on BPD hostility and aggression,[8–12] but more recent studies[13,14] have questioned the efficacy of these drugs in this symptomatologic domain. Furthermore, the persistent and recurrent nature of symptoms in BPD often requires a continuation of pharmacotherapy. Long-term neuroleptic administration to borderline patients, even if at low doses, can lead to important neurologic side effects like akathisia, which has been linked to increased violence in psychiatric subjects.[15]

Lithium carbonate[16,17] and the anticonvulsant mood stabilizers[8,18–20] may also be helpful in the context of impulsive aggression.

The advent of a new class of medication termed *atypical antipsychotics*, combining serotonergic and dopaminergic properties, seems to offer wide opportunities for the treatment of BPD. In recent open-label studies, the new antipsychotics clozapine[21–25] and olanzapine,[26] at low-to-moderate doses, have been usefully employed for the management of BPD impulsive-aggressive behavior. Substantial improvements have also been reported for affective symptoms and cognitive-perceptive disturbances, with fewer side effects in comparison with neuroleptics.

To our knowledge, only 2 case reports[27,28] have tested risperidone as a potential treatment for BPD. The purpose of this study was to assess whether risperidone would reduce symptoms of BPD, focusing mainly on its effects on impulsive-aggressive behavior.

## METHOD

Fifteen consecutive patients (9 men and 6 women) at the Department of Neuroscience, Psychiatric Section, University of Turin, who met DSM-IV criteria for BPD on the Structured Clinical Interview for the Diagnosis of Axis II disorders (SCID-II)[29] entered the study. Axis II codiagnoses included antisocial personality disorder (N = 4).

Patients were screened for the presence of exclusionary comorbid Axis I diagnoses by using the Structured Clinical Interview for DSM-IV (SCID).[30] Patients were excluded from the trial if they suffered from any major medical or neurologic illness. Patients under the age of 18 years or older than 55 were excluded from the study. All subjects, after a complete description of the study and full explanation of possible side effects of the treatment, provided their informed consent. All patients were required to be free of any psychotropic drug for at least 2 weeks before entering the study. During the medication trial, patients were receiving no specific psychotherapeutic approach and were subjected only to clinical management (a 15-minute medication visit once a week).

Demographic and clinical characteristics of the study population are shown in Table 1. Subjects had classic histories of the chaotic life style of this personality disorder and were characterized by prominent profiles of aggression expressed with self-injurious behaviors, suicidal gestures, aggression against property, hostile outbursts, and assaultiveness. Previous psychiatric history of the patients was characterized by repeated hospitalization periods, repeated unsuccessful drug treatments, and marked functional impairment (9 patients stopped working or studying at least 6 months before). Previous pharmacologic treatments, identified from clinical charts and interviews with psychiatrists previously in charge of the patients, included neuroleptics, SSRIs, mood stabilizers, and benzodiazepines.

All patients in the study were treated and examined weekly in the outpatient setting of our research clinic.

**Table 1. Demographic and Clinical Characteristics of 15 Patients With Borderline Personality Disorder[a]**

| Variable | Value |
|---|---|
| Sex, N (male/female) | 9/6 |
| Age, mean ± SD, y | 31.9 ± 5.58 |
| DSM-IV codiagnoses, N (%) | |
| Antisocial personality disorder | 4 (27) |
| Previous diagnosis, N (%) | |
| Major depression | 5 (33) |
| Dysthymia | 3 (20) |
| Panic disorder | 2 (13) |
| Social phobia | 2 (13) |
| Psychosis not otherwise specified | 2 (13) |
| Alcoholism | 4 (27) |
| Drug abuse or dependence | 3 (20) |
| Hospitalization days in previous 12 mo, mean ± SD | 84.9 ± 41.3 |
| Previous treatments, N (%) | |
| Neuroleptics | 12 (80) |
| SSRIs | 4 (27) |
| Mood stabilizers | 8 (53) |
| Benzodiazepines | 15 (100) |

[a]Abbreviation: SSRI = selective serotonin reuptake inhibitor.

Subjects were treated with open-label risperidone orally for 8 weeks. Risperidone was started at 1 mg/day to be taken each evening and then individually increased by 1-mg increments, as needed or tolerated, in weekly meetings, to a maximum of 4 mg by week 4. The dose established by week 4 was held constant to the end of the study. No concurrent psychotropic medication was allowed.

All patients were assessed by the same research psychiatrist at baseline and at the end of the 8-week treatment utilizing both clinician and self-rating tools. Principal efficacy measures were the Brief Psychiatric Rating Scale (BPRS)[31] together with its factors, the DSM-IV Global Assessment of Functioning (GAF),[32] and, as a specific outcome measure of aggression, the self-rated Aggression Questionnaire (AQ).[33] Moreover, we employed the 21-item Hamilton Rating Scale for Depression (HAM-D-21)[34] to assess risperidone's effects on borderline patients' mood, even though this scale is not refined to assess depressive experiences peculiar to these subjects, such as chronic emptiness and boredom.

An intent-to-treat, last-observation-carried-forward (LOCF) analysis was used. Data gathered from this study were compared using Student paired 2-tailed *t* tests.

## RESULTS

Thirteen patients completed the entire 8 weeks of the study; 2 patients dropped out because of lack of compliance. The final mean ± SD risperidone dose for patients was 3.27 ± 0.458 mg/day.

Changes in outcome measures within the study period are displayed in Table 2. Mean score analysis for both clinician-rated and self-rated scales revealed a significant improvement during the period of risperidone administration. At the end of the study, BPRS total scores showed a

Table 2. Changes in Outcome Measures Within the Study Period for 15 Patients With Borderline Personality Disorder[a]

| Measure | Mean Baseline[b] | Mean Last Observation[b] | % Change | t | p Value (2-tail) |
|---|---|---|---|---|---|
| BPRS total | 45.9 ± 3.31 | 36.3 ± 8.17 | 21 | 4.19 | .0003 |
| BPRS anxiety and depression | 3.03 ± 0.63 | 2.62 ± 0.60 | 14 | 1.87 | .0725 |
| BPRS anergia | 2.85 ± 0.30 | 2.43 ± 0.41 | 15 | 3.21 | .0033 |
| BPRS thought disturbance | 1.43 ± 0.24 | 1.33 ± 0.24 | 7 | 1.13 | .2676 |
| BPRS hostility and suspicion | 3.35 ± 0.85 | 2.33 ± 1.26 | 30 | 2.61 | .0144 |
| HAM-D-21 | 16.5 ± 2.07 | 13.5 ± 2.83 | 18 | 3.32 | .0025 |
| GAF | 44.7 ± 5.63 | 57.7 ± 12.08 | 29 | –3.78 | .0008 |
| AQ | 85.1 ± 9.64 | 70.1 ± 16.96 | 18 | 2.99 | .0057 |

[a]Abbreviations: AQ = Aggression Questionnaire, BPRS = Brief Psychiatric Rating Scale, GAF = Global Assessment of Functioning, HAM-D-21 = 21-item Hamilton Rating Scale for Depression.
[b]Values are mean ± SD.

statistically significant reduction of 21% of baseline score. The broad general trend toward amelioration also included a decrease in depressive symptomatology: HAM-D scores were statistically significantly better at the last rating, with a mean decrease of 18% of baseline evaluation. Focusing on symptoms of aggression, we observed a significant improvement on the self-rated AQ total score between the start and the end of the trial, with an 18% change of baseline levels. In addition to improvement in symptomatology, substantial changes in global assessment of function were observed, with a 13-point increase in the mean GAF score.

The analysis of specific BPRS subscales revealed significantly lower scores in "hostility and suspicion" and "anergy" factors and a trend toward amelioration in "anxiety-depression" factor; other BPRS factors failed to reach statistical significance.

Side effects noted included insomnia (4 patients); agitation (3 patients); somnolence, anxiety, and headache (2 patients each); and dizziness, nausea, and tiredness (1 patient each). Side effects were, however, mild and well tolerated so that none of the patients dropped out owing to medication intolerance.

## DISCUSSION

Under our experimental conditions, risperidone administration to a small sample of BPD patients was followed by a rapid decrease in impulsive-aggressive behavior and by an amelioration in all symptomatologic areas.

Our open-label study, conducted with standardized tools assessing several dimensions of BPD, confirms and extends data of previous open-label studies with atypical antipsychotics, clozapine and olanzapine, at low-to-moderate doses in BPD, showing significant reduction in self-mutilation, aggression, and violence.[21,22,25,26] Our results are similar to those of previous case reports assessing risperidone efficacy in BPD,[27,28] reporting improvement in aggression, mood, and anergy. Indices of central serotonergic deficits and dopaminergic hyperactivity have been linked to impulsive aggression, whether self or other directed.[4,5] The capability of risperidone to affect serotonergic and dopaminergic systems could provide explanations regarding its antiaggressive efficacy for such patients. The therapeutic benefits of risperidone in aggression have previously been observed; for instance, reductions of seclusion and restraint, hostility, and self-mutilation in psychiatric patients have been reported.[28,35–37]

The improvement achieved in aggression following treatment with atypical antipsychotics seems not necessarily to be linked to or completely explained by amelioration in psychosis.[21,38] In our study, we failed to reach statistical significance in evaluation of "psychotic-like" symptoms, which can probably be ascribed to the weak magnitude of this dimension in our sample, as shown by low "thought disturbance" BPRS factor scores at baseline assessment.

Treatment with risperidone was followed by substantial improvements in clinician-rated scale scores assessing affective dysregulation. Affective symptoms of BPD may be biologically and psychopathologically distinguished from those of mood disorders.[39–41] Traditional neuroleptics have been shown to acutely improve depression that occurs with personality disorders.[42,43] Other authors observed an increase in depressive scores after continuation therapy with haloperidol.[14] Possible mood-stabilizing properties attributed to atypical antipsychotics[44–46] could be responsible for the improvements we observed in affective symptoms.

In addition to a decrease in BPD symptomatology, a substantial improvement in global assessment of function during the course of this trial was observed. Therefore, this study offers encouraging evidence for the role of risperidone in the management of this common and severe psychiatric disorder.

This study must be interpreted with caution due to the small number of subjects and the open nature of treatment. Data need to be confirmed in a larger number of subjects. Moreover, long-term studies are required to assess persistence of positive effects and tolerability of risperidone after prolonged administration and its capability to prevent worsening of symptomatology even after its withdrawal.

Double-blind placebo-controlled studies are needed to fully clarify the amount of improvement in different BPD dimensions attributed to specific risperidone effect. Comparisons to other atypical antipsychotics or different classes of medication that seem to offer benefits for the treatment of BPD should be undertaken, in order to definitely assess the risk-to-benefit ratio for each drug employed for the treatment of this psychiatric disorder.

*Drug names:* clozapine (Clozaril and others), haloperidol (Haldol and others), olanzapine (Zyprexa), risperidone (Risperdal).

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