# Comparison of Risperidone and Olanzapine in Bipolar and Schizoaffective Disorders

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***Objective:*** To compare risperidone and olanzapine for efficacy, tolerability, need for concomitant mood stabilizers, and cost of treatment in bipolar and schizoaffective disorders.

***Method:*** We conducted a retrospective chart review of 36 consecutive outpatients with DSM-IV bipolar or schizoaffective disorder seen in 3 settings who received risperidone or olanzapine for at least 1 month between May and August 1997.

***Results:*** The mean ± SD doses were 3.7 ± 3.5 mg/day of risperidone and 12.0 ± 5.4 mg/day of olanzapine. Between-treatment differences in patient characteristics, psychiatric history, Clinical Global Impressions scale ratings, and duration of treatment were not significant. Similar proportions of patients in the 2 groups reported side effects, including extrapyramidal symptoms, akathisia, tardive dyskinesia, and precipitation of mania by the respective drug. Patients in the olanzapine group received a significantly higher dose of concomitant lithium than those receiving risperidone (mean daily lithium doses: risperidone group, 750 ± 150 mg; olanzapine group, 1211 ± 186 mg; p = .006). The total daily acquisition cost per patient was $11.84 for olanzapine versus $5.81 for risperidone.

***Conclusion:*** Olanzapine and risperidone were equally efficacious and safe in the treatment of patients with bipolar or schizoaffective disorder, but treatment costs and dose of concomitant lithium were lower in risperidone-treated patients.

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Primary care physicians are being increasingly called upon to treat psychiatric disorders, including mood and anxiety disorders. The atypical antipsychotics, by virtue of their superior side effect profile, are being increasingly embraced by primary care physicians in the treatment of a wide variety of psychiatric disorders including mood and anxiety disorders, behavioral disturbances in dementia, conduct disorders in children, attention-deficit/hyperactivity disorder, and psychotic disorders among others.

Conventional neuroleptics have been the mainstay of treatment in patients with bipolar or schizoaffective disorder who need antipsychotic treatment. Atypical antipsychotics, however, offer several advantages to conventional neuroleptics, including superior efficacy for negative and mood symptoms and a lower risk of extrapyramidal symptoms (EPS) and tardive dyskinesia. Several preliminary studies have now demonstrated that atypical antipsychotics, including risperidone,[1] olanzapine,[2] clozapine,[3] quetiapine,[4] and ziprasidone,[5] are efficacious in patients with bipolar and schizoaffective disorder.

In the present retrospective study, we compared the efficacy and tolerability of antipsychotic medication, concomitant mood stabilizer use, and daily costs of treatment in patients receiving risperidone and olanzapine for bipolar disorder or schizoaffective disorder.

  

**Table 1. Demographic Data of Patients With Bipolar or Schizoaffective Disorder**

| Variable[a] | Risperidone (N = 18) | Olanzapine (N = 18) | p Value |
|---|---|---|---|
| Age, mean ± SD, y | 47.9 ± 15.3 | 47.2 ± 11.6 | .878 |
| Sex | | | |
| Male | 14 (78) | 11 (61) | .278 |
| Female | 4 (22) | 7 (39) | |
| Ethnicity | | | |
| White | 15 (83) | 17 (94) | .603 |
| African American | 2 (11) | 1 (6) | |
| Other | 1 (6) | 0 (0) | |
| Past psychiatric history | | | |
| Yes | 16 (89) | 14 (78) | .658 |
| No | 2 (11) | 4 (22) | |

[a]Values shown as N (%) unless otherwise noted.

**Table 2. Relative Prevalence of DSM-IV Axis I Diagnoses[a]**

| | Risperidone (N = 18) | | Olanzapine (N = 18) | | |
|---|---|---|---|---|---|
| Diagnosis | N | % | N | % | p Value |
| Bipolar disorder, type I | | | | | |
| With manic features | 2 | 11 | 2 | 11 | 1.000 |
| With depressive features | 2 | 11 | 1 | 6 | 1.000 |
| With mixed features | 4 | 22 | 3 | 17 | 1.000 |
| Bipolar disorder, type II | | | | | |
| With hypomanic features | 0 | 0 | 0 | 0 | NA |
| With depressive features | 0 | 0 | 1 | 6 | 1.000 |
| Bipolar disorder NOS | 1 | 6 | 1 | 6 | 1.000 |
| Schizoaffective disorder | | | | | |
| Bipolar type | | | | | |
| With manic features | 1 | 6 | 2 | 11 | 1.000 |
| With depressive features | 2 | 11 | 3 | 17 | 1.000 |
| With mixed features | 2 | 11 | 2 | 11 | 1.000 |
| Depressed type | 4 | 22 | 3 | 17 | 1.000 |

[a]Abbreviations: NA = not applicable, NOS = not otherwise specified.

## METHOD

We conducted a retrospective chart review of 36 consecutive outpatients with DSM-IV schizoaffective or bipolar disorder treated with risperidone or olanzapine for at least 1 month between May and August 1997 at a state psychiatric institution (Hutchings Psychiatric Center, Syracuse, N.Y.), a Veterans Administration hospital (Syracuse VA Medical Center, Syracuse, N.Y.), and a day-treatment program (Guidepost Continuing Day Treatment, Olean, N.Y.). Most of the patients were receiving concomitant treatment with mood stabilizers. The primary hypothesis was that the efficacy and tolerability of risperidone and olanzapine would be similar, but that the difference in the treatment costs would be substantial.

The primary measure of outcome was daily cost of treatment based on dose of risperidone and olanzapine. Secondary outcomes included duration of treatment, side effects (type and severity), precipitation of mania by the respective antipsychotic drug, use of concomitant mood stabilizers, symptom improvement as measured by the Clinical Global Impressions scale (CGI; baseline values were obtained at start of risperidone or olanzapine treatment, and follow-up values were assigned at the time of chart review),[6] and improvement of the most recent mood episode.

**Table 3. Measures of Efficacy Using the Clinical Global Impressions Scale (CGI)[a]**

| Measure[b] | Risperidone (N = 18) | Olanzapine (N = 18) | p Value |
|---|---|---|---|
| Positive symptoms | 2.4 ± 0.9 | 2.7 ± 0.8 | .345 |
| Negative symptoms | 3.1 ± 0.9 | 2.9 ± 0.8 | .448 |
| Cognitive symptoms | 3.4 ± 0.7 | 3.1 ± 0.8 | .261 |
| Work functioning | 3.6 ± 0.7 | 3.8 ± 0.6 | .481 |
| Social functioning | 3.0 ± 0.7 | 3.2 ± 0.8 | .490 |
| Most recent mood episode | 2.4 ± 1.0 | 2.7 ± 1.1 | .398 |

[a]CGI scored as follows: 1 = marked improvement, 2 = moderate improvement, 3 = minimal improvement, 4 = no improvement, 5 = worsening.
[b]Values shown as mean ± SD change in CGI score from baseline.

### Statistical Analysis

Categorical baseline characteristics, diagnoses, and tardive dyskinesia were analyzed using the Pearson chi-square test. Continuous baseline variables, CGI scores, side effects (EPS and akathisia), and dose and duration of treatment were assessed using the Student t test. The Fisher exact test was utilized for contingency table analyses that had at least 1 expected cell count less than 5. Since 5 correlated outcome variables (CGI scores) were analyzed, a Bonferroni adjustment to the type I error rate was employed to preserve the overall error rate of .05.

All p values $\leq .05$ but $\geq .01$ imply marginal significance, whereas those $< .01$ indicate a clinically significant difference in the mean values between the risperidone and olanzapine groups. All tests of significance were 2-tailed.

## RESULTS

Background characteristics of patients in the 2 groups were similar, including sex, age, ethnicity, psychiatric history, and diagnosis (Tables 1 and 2).

### Efficacy and Safety

CGI ratings on 5 measures of symptom improvement are shown in Table 3 and Figure 1. Between-group differences in change from baseline values were not significant. Severity of adverse events in the 2 groups is shown in Table 4; between-group differences were not significant. One patient from each group experienced precipitation of mania when risperidone or olanzapine therapy was initiated.

### Medication Doses and Costs

Mean daily doses were 3.5 ± 3.6 mg of risperidone and 11.9 ± 5.9 mg of olanzapine. According to average wholesale prices,[7] the daily cost per patient in 1998 was $5.81 for risperidone and $11.84 for olanzapine (Table 5). Use

**Figure 1. Changes in Clinical Global Impressions Scale (CGI) Scores From Baseline to End of Treatment**

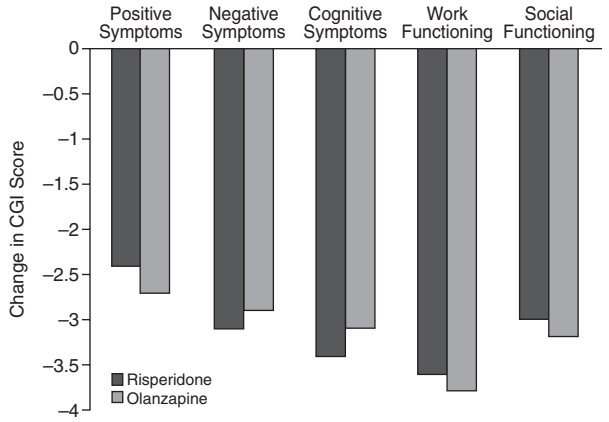


**Table 5. Daily Doses, Duration of Treatment, and Costs of Treatment**

| Variable | Risperidone (N = 18) | Olanzapine (N = 18) | p Value |
|---|---|---|---|
| Dose, mean ± SD, mg/d | 3.5 ± 3.6 | 11.9 ± 5.9 | < .001 |
| Duration of treatment, mean ± SD, mo | 14.8 ± 10.7 | 10.5 ± 8.6 | .200 |
| Daily cost, mean, $ | 5.81 | 11.84 | < .001 |

**Table 6. Concomitant Mood Stabilizers**

| | Risperidone (N = 18) | | Olanzapine (N = 18) | | |
|---|---|---|---|---|---|
| Mood Stabilizer | N | % | N | % | p Value |
| Lithium carbonate | 3 | 17 | 7 | 39 | .137 |
| Carbamazepine | 2 | 11 | 0 | 0 | .486 |
| Clonazepam | 1 | 6 | 4 | 22 | .338 |
| Divalproex | 11 | 61 | 9 | 50 | .502 |
| Valproic acid | 0 | 0 | 0 | 0 | NA |

**Table 4. Presence and Severity of Side Effects[a]**

| Side Effect | Risperidone (N = 18) | Olanzapine (N = 18) | p Value |
|---|---|---|---|
| EPS, mean ± SD[b] | 0.2 ± 0.5 | 0.2 ± 0.5 | .756 |
| Akathisia, mean ± SD[b] | 0.1 ± 0.2 | 0.1 ± 0.3 | .560 |
| Tardive dyskinesia, N (%) | | | |
| Yes | 2 (11) | 1 (6) | .446 |
| No | 9 (50) | 13 (72) | |
| Unable to determine | 7 (39) | 4 (22) | |

[a]Abbreviation: EPS = extrapyramidal symptoms.
[b]EPS and akathisia ratings: 0 = none, 1 = mild, 2 = moderate, 3 = severe.

**Table 7. Daily Doses (mean ± SD mg/day) of Concomitant Mood Stabilizers[a]**

| Mood Stabilizer | Risperidone | Olanzapine | p Value |
|---|---|---|---|
| Lithium carbonate | 750 ± 150 (N = 3) | 1211 ± 186 (N = 7) | .006 |
| Carbamazepine | 950 ± 919 (N = 2) | NA (N = 0) | NA |
| Clonazepam | 1.5 (N = 1) | 2.1 ± 1.9 (N = 4) | NA |
| Divalproex | 1534 ± 548 (N = 11) | 1639 ± 486 (N = 9) | .660 |

[a]Abbreviation: NA = not applicable.

of concomitant mood stabilizers, including lithium, carbamazepine, divalproex sodium, and clonazepam, was similar in the 2 groups (Table 6). Patients in the olanzapine group received a significantly higher daily dose of concomitant lithium (1211 ± 186 mg) compared with patients in the risperidone group (750 ± 150 mg; p = .006) (Table 7).

## DISCUSSION

Ghaemi et al.[1] have reported that risperidone may be more effective and better tolerated than conventional antipsychotics in the treatment of bipolar disorder. In their survey, 64% of risperidone-treated patients showed large improvements on the CGI, and Global Assessment of Functioning scores improved from 48.2 ± 4.9 to 58.0 ± 7.3 (p < .001). Treatment was well tolerated, and no patient experienced worsening of mood symptoms while receiving risperidone. In 1999, Ghaemi et al.[8] concluded that risperidone has bidirectional mood-stabilizing properties. They reported that the mean response rate in 6 studies[1,9–13] of patients with schizoaffective or bipolar disorder, both with and without psychosis, was 51%. In 4 of these studies,[1,9–11] in which risperidone was an adjunct to mood stabilizers, there were no reports of induction of mania.

Sachs et al.[14] conducted a 3-week, double-blind, multicenter, randomized trial comparing risperidone (1–6 mg/day) with placebo as add-on therapy to lithium or divalproex in the acute management of bipolar mania. Significantly greater improvement in Young Mania Rating Scale (YMRS) scores was seen in patients receiving risperidone and a mood stabilizer than in those receiving placebo and a mood stabilizer (p = .009), with 57% of risperidone patients showing at least a 50% reduction in YMRS score. Most patients (76.5%) receiving risperidone and a mood stabilizer were rated as much or very much improved on the CGI, compared with 57.4% of patients receiving placebo and a mood stabilizer. The benefit of risperidone was apparent among patients with and without associated psychotic features.

Only 3 other controlled trials[15–17] assessing the effects of atypical antipsychotics in bipolar patients have been published. Risperidone, haloperidol, and lithium were equivalent in efficacy in a 28-day double-blind study involving 45 inpatients with mania.[15] In a double-blind 3-week study, olanzapine was superior to placebo for symptoms of acute mania in 139 patients who had failed treatment with mood stabilizers.[16] A 4-week replication study again found olanzapine monotherapy superior to placebo in 115 patients hospitalized for acute mania.[17]

Olanzapine has also demonstrated efficacy similar to that of divalproex sodium in the treatment of acute mania, although weight gain was significantly greater with olanzapine than with divalproex (3.4 kg vs. 1.7 kg, p = .045).[18] In a recent study, Tohen et al.[19] looked at patients who had achieved symptomatic remission of bipolar disorder at the end of acute therapy with olanzapine combined with lithium or valproate and found that 55.3% of placebo-treated patients versus 36.7% of olanzapine-treated patients relapsed into either mania or bipolar depression during an 18-month trial (p = .149). Time to bipolar relapse was significantly earlier in placebo- versus olanzapine-treated patients.

Our study found olanzapine and risperidone to be equally efficacious in the treatment of patients with bipolar or schizoaffective disorder. This finding is consistent with previous studies[15–19] showing that all atypical antipsychotics have similar efficacy but different side effect profiles in the treatment of bipolar and schizoaffective disorders.

The limitations of our study include those inherent to a retrospective chart review as well as lack of a structured diagnostic interview to diagnose psychiatric disorders, small sample size, short duration of follow-up, and a lack of systematic investigation of side effects using clinician-elicited adverse event scales.

Future areas of research should include the comparative efficacy of atypicals in populations seen in primary care practice since there is evidence to indicate that this group of patients may have a different phenomenology, longitudinal course, response to treatment, dosage requirement, and, possibly, a different prognosis as compared with patients seen in tertiary care psychiatric clinics.

## CONCLUSIONS

The results of the present survey of patients with bipolar or schizoaffective disorder indicate that risperidone and olanzapine were equally efficacious and safe, but the costs of treatment were lower with risperidone, and olanzapine-treated patients required a higher dose of concomitant lithium than risperidone-treated patients. These results confirm those of previous studies of risperidone and olanzapine in bipolar patients.

*Drug names:* carbamazepine (Tegretol and others), clonazepam (Klonopin and others), clozapine (Clozaril and others), divalproex sodium (Depakote), haloperidol (Haldol and others), lithium (Eskalith and others), olanzapine (Zyprexa), quetiapine (Seroquel), risperidone (Risperdal), valproic acid (Depakene and others), ziprasidone (Geodon).

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