Risperidone Versus Pimozide in Tourette's Disorder: A Comparative Double-Blind Parallel-Group Study

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Background: The treatment of Tourette's disorder with classical neuroleptics is limited by their side effects. Risperidone is a new efficacious antipsychotic with a low propensity for extrapyramidal side effects. To establish risperidone's therapeutic potential in Tourette's disorder, we studied the safety and efficacy of risperidone in comparison with pimozide in patients with Tourette's disorder diagnosed according to DSM-III-R.

Method: In a 12-week, multicenter, double-blind, parallel-group study, 26 patients were treated with risperidone (mean daily dose = 3.8 mg), and 24 patients were treated with pimozide (mean daily dose = 2.9 mg).

Results: There was significant improvement of tics with respect to the Tourette's Symptom Severity Scale (TSSS) for both groups. Forty-one patients completed the study. At endpoint, 54% (14/26) of the risperidone patients and 38% (9/24) of the pimozide patients had only very mild or no symptoms on the global severity rating of the TSSS. Both treatment groups had improved significantly at endpoint in regard to Global Assessment of Functioning and Clinical Global Impressions scale outcomes. Symptoms of anxiety and depressive mood improved significantly from baseline in both groups. Obsessive-compulsive behavior improvement reached significance only in the risperidone group. Although the severity of extrapyramidal side effects was low in both groups, fewer patients in the risperidone group reported extrapyramidal side effects (N = 4) compared with the pimozide group (N = 8). Depression, fatigue, and somnolence were reported as the most prominent side effects in both treatment groups.

Conclusion: Both drugs were efficacious and well tolerated in patients with Tourette's disorder. Risperidone may become the first-line drug in the treatment of Tourette's disorder owing to a more favorable efficacy and tolerability profile.

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Tourette's disorder is a neuropsychiatric disorder characterized by multiple motor and vocal tics with onset before the age of 18 years.[1] Tics are often associated with obsessive-compulsive symptoms, symptoms of attention-deficit/hyperactivity disorder (ADHD), and emotional features such as anxiety and mood disturbances.[2] Tic suppression is most readily achieved with neuroleptics, with haloperidol and pimozide being the 2 most widely used compounds. The use of these drugs is restricted by their acute side effects such as sedation, cognitive impairment, and extrapyramidal symptoms (EPS).[3] Moreover, long-term treatment with conventional neuroleptics can lead to the serious complication of tardive dyskinesia.[4] Although the tics may be the most striking feature of Tourette's disorder, patients often experience the psychiatric comorbidity as even more disabling. When concurrent ADHD is prominent, clonidine or methylphenidate can be the initial treatment.[5] The often-encountered obsessive-compulsive behavior in Tourette's disorder patients, such as repetitive counting, ordering, and touching, may require serotonin reuptake inhibitors.[2] Antidepressants can be prescribed for concurrent anxiety and depression. Thus, depending on the target symptoms, patients may sometimes require a combination treatment of various drugs.

The new, atypical antipsychotics have different pharmacologic profiles compared with conventional neuroleptics, are efficacious in positive and negative symptoms and in cognitive dysfunction in schizophrenia, and, most importantly, induce fewer EPS.[6] Theoretically, they could

therefore offer new possibilities in the treatment of Tourette's disorder. Recently, several atypical antipsychotics have been introduced.

One such antipsychotic, the benzisoxazole derivative risperidone, has potent serotonin 5-HT_{2A} and dopamine D_2 receptor antagonistic properties. It also binds less potently to α_1- and α_2-adrenergic receptors and the histamine H_1 receptor.[7] The drug has been shown to be an effective antipsychotic, with reported alleviation of negative symptoms and fewer EPS compared with conventional neuroleptics in the treatment of patients with schizophrenia.[8,9] In addition, preliminary studies suggest risperidone's efficacy in affective illness and obsessive-compulsive disorders.[10,11]

In a previous, open-label study,[12] we examined the possibilities for risperidone in the treatment of 11 Tourette's disorder patients. The drug was efficacious and well tolerated, and no EPS were reported. Since then, several studies have reported favorable findings for risperidone in Tourette's disorder patients, although EPS were reported in some.[13–15] These studies comprised case reports and open-label studies that did not compare risperidone to a known anti-Tourette's medication. We, therefore, undertook a study to compare the efficacy and safety of risperidone with the commonly used first-line drug pimozide in a double-blind, randomized, parallel-group study for 12 weeks in 50 patients aged 10 years or older. Pimozide was used for comparison since this drug may be superior to haloperidol for controlling Tourette's disorder symptoms and it induces fewer EPS than haloperidol.[16] We hypothesized that risperidone would be as effective as the dopamine antagonist pimozide for the treatment of tics in Tourette's disorder. Preference for either one of the 2 compounds could then be based on the differences in side effect profile, with risperidone likely to have fewer EPS in comparison with pimozide. We further evaluated the effect of risperidone and pimozide on associated obsessive-compulsive symptoms and on anxiety and mood disturbances.

METHOD

The study included patients 10 to 65 years of age with a primary diagnosis of Tourette's disorder according to DSM-III-R.[17] Subjects were recruited at 12 neurologic and psychiatric outpatient clinics in Belgium, the Netherlands, and South Africa. Each patient or his or her legal guardian gave written informed consent. The trial was approved by the local ethical committees and was performed in accordance with the Declaration of Helsinki. The study was designed as a multicenter, double-blind, randomized, parallel-group study.

Patients were screened with regard to their demographic characteristics and their medical and psychiatric history. Electrocardiograms (ECGs) and blood and urine samples were collected for safety screens. Motor and vocal tics were assessed using the Tourette's Syndrome Severity Scale (TSSS),[18] and the Clinical Global Impressions (CGI) and Patient Global Impressions (PGI) scales.[19] The TSSS rates the frequency and disruption of tic behavior on 5 factors, yielding a total score from 0 to 9 and a global severity rating from 0 to 6. The inclusion criteria were a minimum severity of moderate on the TSSS (3 on a 6-point scale) and a score of at least moderately ill on the CGI-Severity of Illness scale (3 on a 6-point scale). After a washout period of 1 to 5 weeks, a baseline assessment on the efficacy parameters was performed. The minimum washout period for depot medication was 1 treatment cycle, and the washout period was 2 weeks for oral antipsychotics and antidepressants, with the exception of fluoxetine, which was to be discontinued at least 5 weeks prior to randomization.

To evaluate the safety of both risperidone and pimozide and to compare the effectiveness of both treatments, patients were evaluated at baseline (i.e., after washout period); at 1, 2, 4, and 8 weeks after baseline; and at trial termination. At the beginning of the study and during follow-up visits, motor and vocal tics were evaluated on the TSSS, and during each visit, a CGI and PGI were scored. EPS were assessed at each visit using the Extrapyramidal Symptom Rating Scale (ESRS).[20] This scale consists of a questionnaire and a behavioral scale (including a parkinsonism factor, a dystonia factor, and a dyskinesia factor) and a clinical global impression scale of overall severity of parkinsonism and dyskinesia. The obsessive-compulsive symptoms were assessed at baseline and at termination, using the Yale-Brown Obsessive Compulsive Scale (Y-BOCS),[21] a clinician-rated 10-item scale (from 0 to 40). The Y-BOCS measures the presence and severity of obsessions and compulsions along the dimensions of time, interference, distress, resistance, and control. Anxiety and depressed mood symptoms were determined on the Hamilton Rating Scale for Anxiety (HAM-A)[22] at baseline and at endpoint. The Global Assessment of Functioning (GAF)[17] was used to evaluate changes in social and occupational functioning. Physical and neurologic examinations were performed at baseline and at termination. Vital signs, body weight, ECGs, and blood and urine samples were taken at selection and at termination. Adverse events and any concomitant medications were recorded throughout the study.

Patients eligible for the trial were assigned to either risperidone or pimozide according to a computer-generated randomization code. A fixed-dose titration regimen for the first week of treatment (risperidone from 0.5 to 2 mg/day and pimozide from 1 to 2 mg/day) was followed by a flexible dosing period of 7 weeks. When necessary, a maximum dose of 6 mg/day was allowed for both drugs at the end of the 7-week period, with maximum increments of 1 mg/week. The dose preferably remained constant for the last 4 weeks of the trial. However, it was permissible to reduce the dose at any time to a minimum of 1 mg/day.

Table 1. Demographic Data and Clinical Characteristics of 50 Patients With Tourette's Disorder

Variable	Risperidone (N = 26)	Pimozide (N = 24)
Sex		
Male	23	21
Female	3	3
Age, y		
Median	20.0	23.5
Range	11–50	11–45
Age at onset, y		
Median	8.0	8.5
Range	5–16	3–13
Psychiatric comorbidity		
Obsessive-compulsive behavior	9	14
Generalized anxiety disorder	1	2
Attention-deficit/hyperactivity disorder	1	1

Risperidone and pimozide were presented in identical capsules containing 0.5 or 1 mg risperidone, or 1 mg pimozide. Capsules were administered once daily in the evening. No other psychotropic medications, including antipsychotics and antidepressants, were permitted within 2 weeks prior to and during the study. Antiparkinsonian medication and benzodiazepines were discontinued during the washout period and when possible were limited during the treatment period.

For statistical analysis, an intention-to-treat analysis was performed. All statistical tests were interpreted at the 5% significance level (2-tailed). Baseline characteristics were compared using the Mann-Whitney U test for ordinal data and the Fisher exact test for nominal data. Between-treatment differences were compared at endpoint (carrying forward the last observation when needed) and at other timepoints when appropriate. For all efficacy parameters, within-group comparisons were performed using the Wilcoxon matched pairs signed rank test and the Friedman test. Between-group comparisons were performed using van Elteren and analysis of covariance (ANCOVA) tests. ESRS items were compared at each timepoint using the van Elteren test to examine the difference between the treatment groups. In addition, the analysis was stratified by age (17 years or younger vs. 18 years or older) to investigate the possible effect of age on efficacy and safety parameters.

RESULTS

Fifty patients, 11 to 50 years of age, met the study criteria. Of these, 26 patients received risperidone, 24 patients pimozide. The median age at onset was 8.0 years in the risperidone group and 8.5 years in the pimozide group. Obsessive-compulsive symptoms were present in 9 patients in the risperidone-treated group and in 14 in the pimozide-treated group. One patient in the risperidone group and 2 in the pimozide group had generalized anxiety disorder. Two subjects, 1 in each group, had ADHD. In general, the 2 groups were comparable at baseline, although it was noted that the pimozide group had more patients with obsessive-compulsive symptoms. Demographic data are summarized in Table 1. Forty-one patients completed the study. Five patients in the risperidone group (4 owing to adverse events, 1 owing to insufficient response) and 4 in the pimozide group (2 owing to adverse events, 1 owing to noncompliance, and 1 lost to follow-up) discontinued before completion. At endpoint, the mean dose of risperidone was 3.8 mg/day (range, 0.5–6 mg/day), and the mean dose of pimozide was 2.9 mg/day (range, 1–6 mg/day).

The outcome measurements for the tics, anxiety, and obsessive-compulsive symptoms are displayed in Table 2. Both treatments were associated with significant improvement of tics on the TSSS ($p < .001$). Moreover, scores on the Global Severity Rating Scale of the TSSS showed substantial improvement with only very mild or no symptoms in 54% (14/26) of the risperidone patients and 38% (9/24) of the pimozide patients (at baseline, patients with no or only mild symptoms had been excluded). No significant differences were found between the 2 treatment groups in regard to improvement on the TSSS. Similarly, improvement on the CGI was significant in both groups ($p < .05$), with no significant difference between the 2 treatments. At endpoint 65% (N = 32) of patients in both groups were much or very much improved as compared with baseline. One patient in the risperidone group, who withdrew after 2 weeks because of inefficacy and adverse events, had a worsening of his tics. The PGI findings were in agreement with the CGI findings, showing 15 patients in each group being much or very much improved from baseline, without significant difference between risperidone and pimozide treatment.

At baseline, the risperidone group had a smaller number of patients with obsessive-compulsive symptoms (N = 9, 35%, for risperidone vs. N = 14, 58%, for pimozide) and a lower mean score on the Y-BOCS (8.8 for risperidone vs. 13.5 for pimozide) as compared with the pimozide group. These differences, however, were not statistically significant. At endpoint, the mean change from baseline in Y-BOCS scores reached statistical significance for the risperidone group (–3.1, $p < .05$), but did not for the pimozide group (–5.2, $p < .10$), and the global severity score of the Y-BOCS had improved significantly for both treatment groups. No significant differences were detected between the treatment groups for the total change in Y-BOCS scores from baseline to endpoint.

The HAM-A total score decreased significantly within each treatment group, but no significant difference was detected between the groups. Social and occupational functioning, as assessed by the GAF, showed a significant improvement from baseline to endpoint for both treatment groups and no significant difference between the 2 treatment groups at endpoint.

Table 2. Efficacy of Risperidone and Pimozide in 50 Patients With Tourette's Disorder[a]

Scale	Risperidone (N = 26) Baseline	Shift From Baseline to Endpoint	Pimozide (N = 24) Baseline	Shift From Baseline to Endpoint	Difference in Mean Shifts [95% CI]
TSSS					
Global impression score	3.7	–1.8[b]***	3.8	–1.7[b]***	–0.1 [–0.9, 0.7]
Total score	4.3	–2.4[b]***	4.3	–2.3[b]***	–0.2 [–1.1, 0.8]
Patients with no or only mild symptoms (%)	0	14 (54)	0	9 (38)	...
CGI					
Mean score	3.5	–1.6[b]***	3.7	–1.8[b]***	0.1 [–0.5, 0.8]
Patients much or very much improved (%)	...	17 (65)	…	15 (63)	...
PGI					
Patients much or very much improved (%)	...	15 (58)	…	15 (63)	...
HAM-A					
Total anxiety mean score	0.6	–0.2[b]***	0.6	–0.2[b]*	–0.1 [–0.3, 0.2]
Somatic anxiety factor mean score	0.3	–0.2[b]*	0.3	–0.1	–0.1 [–0.3, 0.1]
Psychic anxiety factor mean score	0.8	–0.3[b]***	1.0	–0.3[b]*	0.0 [–0.3, 0.3]
Y-BOCS					
Obsession mean score	3.8	–1.6	5.9	–3.0	1.4 [–2.0, 4.8]
Compulsion mean score	4.7	–1.5[b]*	7.5	–2.2[b]*	0.7 [–1.7, 3.1]
Total score	8.8	–3.1[b]*	13.5	–5.2	2.1 [–3.3, 7.4]
GAF					
Mean score	71.5	+6.1[b]*	65.6	+9.2[b]*	–3.1 [–13.3, 7.0]

[a]Abbreviations: CGI = Clinical Global Impressions scale, CI = confidence interval, GAF = Global Assessment of Functioning, HAM-A = Hamilton Rating Scale for Anxiety, PGI = Patient Global Impressions scale, TSSS = Tourette Symptom Severity Scale, Y-BOCS = Yale-Brown Obsessive Compulsive Scale.
[b]Represents a significant change from baseline. For TSSS and CGI, Friedman test was used; for HAM-A, Y-BOCS, and GAF, Wilcoxon test was used.
*p < .05. ** p < .01. ***p < .001.

When stratified by age, the 2 treatment groups younger than 18 years of age had consistently better scores at baseline and at endpoint for efficacy parameters. However, with respect to efficacy, these scores were not statistically significantly lower than those for the adult groups. Within the age groups, no significant differences were seen between the pimozide and the risperidone groups. In addition, the shifts at endpoint versus baseline were comparable between the age groups, as well as between the risperidone and pimozide group.

The number of patients reporting EPS spontaneously as an adverse event was lower in the risperidone group (N = 4) than in the pimozide group (N = 8). No statistically significant differences in ESRS scores were found between treatment groups. For both the risperidone- and pimozide-treated groups, ESRS scores were low at baseline (3.5 and 4.0, respectively) and showed no significant changes at endpoint (3.5 and 3.9, respectively). Of the other adverse events, only insomnia and injuries differed significantly between the 2 groups, both being more frequent in the pimozide group. None of the injuries (eye trauma, muscle injury, fall, bite, lymph node biopsy, and an accident) was considered to be related to the trial medication. In both treatment groups, the most frequent adverse events were somnolence, fatigue, and depression (Table 3). The increase in mean body weight was statistically significant in both groups, but did not differ between the 2 treatment groups, with a mean weight gain of 3.9 kg (range, 3.0–4.9 kg) in the risperidone group (N = 22) and 2.9 kg (range, 1.8–4.1 kg) in the pimozide group (N = 20). However, when stratified by age, the risperidone group under 18 years of age had more weight gain than the group 18 years of age and older (4.5 kg vs. 3.5 kg, respectively), whereas the weight gain in the pimozide group was comparable in patients under 18 years of age (2.7 kg) and 18 years of age and older (3.1 kg). The differences between risperidone and pimozide were not statistically significant in either age group. In regard to ECG and laboratory parameters, no clinically relevant differences were detected. There were no clinically significant changes in blood pressure or heart rate. Thus, except for weight gain, the safety profiles for the younger and older treatment groups were comparable.

DISCUSSION

The major finding of this study is that risperidone is at least as effective as pimozide in the treatment of Tourette's disorder. In addition, we found that both treatments had a similar effect on comorbid symptoms. The incidence of EPS was low in both groups. Akathisia, bothersome especially in hyperkinetic Tourette's disorder patients, was reported less often in the risperidone group. The side effect profiles were similar, with a low incidence

Table 3. Safety and Tolerability of Risperidone and Pimozide in 50 Patients With Tourette's Disorder[a]

	Risperidone (N = 26)		Pimozide (N = 24)	
Variable	N	Mean Increase, kg	N	Mean Increase, kg
Anti-EPS medication	1[b]		2[c]	
Patients with EPS-like adverse events	4		8	
Adverse events				
Somnolence	12		10	
Fatigue	10		9	
Depression	8		6	
Insomnia	1		7*	
Injuries	1		6*	
Headache	5		2	
Hyperkinesia	2		5	
Vital signs	NS		NS	
ECG	NS		NS	
Body weight				
All patients	22	3.9***	20	2.9***
< 18 years	10	4.5**	7	2.7
≥ 18 years	12	3.5***	13	3.1***

[a]Abbreviations: ECG = electrocardiogram, EPS = extrapyramidal symptoms, NS = not significant.
[b]Patient stopped medication during trial.
[c]One patient started medication during trial.
*p < .05. **p < .01. ***p < .001 (Wilcoxon matched pairs signed rank test).

in both groups and with sedation and depression as the main adverse events. The findings for efficacy and safety were comparable for children and adults.

Our results confirm earlier uncontrolled reports on the beneficial use of risperidone in children, adolescents, and adults with tics. Lombroso et al.[14] reported a statistically significant reduction in tic scores in children and adolescents, ranging from a 26% to 66% reduction as compared with baseline. The most common side effects were somnolence and fatigue. During the 11 weeks of treatment, 1 patient developed an acute dystonic reaction after the risperidone dosage had been rapidly increased. Bruun and Budman[13] treated 38 patients with Tourette's disorder aged 8 to 53 years with risperidone in an open-label study for 4 weeks. Twenty-two patients improved while taking risperidone. Eight patients dropped out because of side effects such as light-headedness and sedation. Despite the conservative titration scheme in that study, 6 subjects experienced EPS, including akathisia and severe dystonia. These findings underline the need to start low and increase the dosing slowly.

In the present study, the response of the comorbid psychiatric disorder was evaluated. Both groups displayed a significant improvement of anxiety and mood disturbances as well as social and occupational functioning. In addition, the 23 patients with obsessive-compulsive symptoms showed improvement in both treatment regimens according to the Y-BOCS. However, the change from baseline was only significant for the risperidone group. Three other studies[13–15] have reported a favorable response to risperidone in Tourette's disorder patients with obsessive-compulsive symptoms; however, none of them evaluated these alterations systematically. Thus, risperidone appears to have a positive effect on obsessive-compulsive symptoms in patients with Tourette's disorder. Whether this improvement can be sustained requires further study.

The average dosing of risperidone in our study (3.8 mg/day) seems high since, in our experience, 1 to 2 mg/day of risperidone often suffices for long-term treatment. This higher dosing may have influenced the rate of reported EPS. In addition, the first-week dose titration schedule for risperidone may have been too rapid. The slight decrease in standing blood pressure and concomitant increase in heart rate in some patients using risperidone were not clinically relevant, but they suggest that a more cautious dosing strategy for risperidone is warranted. No ECG changes were found in either the risperidone or the pimozide treatment group. Weight gain warrants special clinical attention whenever treatment with antipsychotics is initiated, especially in young patients and when atypical antipsychotics are involved.[23] In our study, weight gain was seen predominantly in the risperidone group of patients younger than 18 years. The low incidence of insomnia in the risperidone group compared with that in the pimozide group and the elimination half-life of 20 hours of the active fraction of risperidone (i.e., risperidone plus the active metabolite, 9-OH-risperidone) suggest that risperidone can be given in once-a-day dosing, preferably at night. We evaluated neither subjective nor cognitive changes induced by the neuroleptics and may therefore have missed some differentiating effects, both positive and negative, between risperidone and pimozide. Given many patients' lifelong need for medication, longitudinal studies are warranted to evaluate risperidone's optimal dosing, efficacy, and tolerability in long-term treatment of Tourette's disorder.

The improvement of tics in the patients treated with the reference drug pimozide is in accordance with other pharmacologic studies of classical neuroleptics.[24,25] The beneficial effect of pimozide in this study further supports the purported role of the D_2 receptor in the pathophysiology of Tourette's disorder and in the tic suppression mechanism of antipsychotic drugs. In this respect, hypersensitivity of dopamine receptors, as well as dysregulation in presynaptic dopamine function in the striatum, has been proposed as an underlying mechanism for tic disorders.[26] However, dopaminergic activity is modulated by other neurotransmitter systems, e.g., the serotonergic projections from the raphe nuclei[27] and the noradrenergic projections from the locus ceruleus.[28] This modulation may be reflected clinically by the fact that SSRIs can worsen tics[29] and that clonidine, a presynaptic α_2 receptor agonist, reduces tics.[4]

The interaction with other neurotransmitter systems is of special interest when one looks at the response of Tourette's disorder to the atypical antipsychotics with their different receptor binding profiles. For example, cloza-

pine, which has a very broad receptor binding profile with only low D_2 affinity, was not effective in the treatment of tics in 7 patients in a double-blind crossover study.[30] Interestingly, with low doses of clozapine, tic symptoms even worsened. On the other hand, the substituted benzamides sulpiride and remoxipride have been shown to be effective tic suppressors.[31,32] However, these agents exert their action through selective D_2/D_3 antagonism. Risperidone is characterized by a high affinity for 5-HT_{2A} receptors, a moderately high affinity for D_2 receptors, and considerable affinity for α_1- and α_2-adrenoceptors.[33] The high affinity for 5-HT_2 receptors relative to D_2 receptors has been hypothesized to be an essential feature for the therapeutic response of negative symptoms and the low EPS liability of risperidone and other atypical antipsychotics.[34–36] Therefore, the potent 5-HT_{2A} antagonistic action of risperidone may also have contributed to the favorable EPS profile found for risperidone in this study. Modulation of serotonergic neurotransmission may take place not only through blockade of postsynaptic 5-HT_{2A} receptors, since in preclinical studies risperidone also enhanced 5-HT availability in the frontal cortex.[37,38] Therefore, in addition to the 5-HT_2 receptor blockade, an increased cortical output of 5-HT acting on other postsynaptic 5-HT receptors may have supported the drug's effects on psychiatric symptoms in this study, given the involvement of the serotonergic system in obsessive-compulsive disorder, anxiety, and depression. New selective 5-HT agents now provide the means to further study these interesting issues in Tourette's disorder. Tic suppression of atypical antipsychotics, at least for risperidone, could be, in part, attributed to the drug's noradrenergic affinity; consider, for example, clonidine's efficacy in Tourette's disorder. However, it should also be noted that the doses of risperidone in the range used in this study (0.5–6 mg/day) are expected to yield both a high 5-HT_{2A} receptor occupancy and a moderate-to-high D_2 receptor occupancy.[39] Hence, a plausible conclusion is that, whereas combined 5-HT_2/D_2 antagonism underlies risperidone's atypical action profile, dopamine D_2 receptor blockade per se accounts for the observed efficacy of risperidone in tic suppression.

The low EPS liability of risperidone may enable the clinician to better titrate risperidone to achieve beneficial effects on the Tourette's disorder symptoms without inadvertently creating undesirable motor side effects. As in long-term treatment for schizophrenic patients,[40] fewer acute EPS may very well mean less tardive dyskinesia in Tourette's disorder patients. This possibility further prompts the preference for risperidone over classical neuroleptics in the long-term treatment of Tourette's disorder.

In conclusion, the atypical antipsychotic risperidone was as efficacious and as well tolerated as the conventional antipsychotic pimozide in the treatment of both young and adult patients with Tourette's disorder, and risperidone and pimozide had an equal effect on comorbid symptoms. The reported incidence of akathisia was lower in the risperidone group. Risperidone may soon become a first-line drug in the treatment of Tourette's disorder.

Drug names: clonidine (Catapres and others), clozapine (Clozaril and others), fluoxetine (Prozac), haloperidol (Haldol and others), methylphenidate (Ritalin and others), pimozide (Orap), risperidone (Risperdal).

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