Risperidone was as effective as pimozide for Tourette's disorder

Bruggeman R, van der Linden C, Buitelaar JK, et al. ***Risperidone versus pimozide in Tourette's disorder: a comparative double-blind parallel-group study****. J Clin Psychiatry 2001 Jan;****62****:50–6.*

Source of funding: Janssen Research Foundation, Beerse, Belgium.

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QUESTION: In patients with Tourette's disorder, is risperidone as effective and safe as pimozide?

Design
12 week randomised (allocation concealed*), blinded (unclear)*, controlled trial.

Setting
12 neurological and psychiatric outpatient clinics in Belgium, the Netherlands, and South Africa.

Patients
50 patients who were 11–65 years of age (mean age range 20.0–23.5 y, 88% men) and had a primary diagnosis of Tourette's disorder according to *DSM-III-R*. Inclusion criteria were at least moderate severity on the Tourette's Syndrome Severity Scale (TSSS) and at least moderately ill on the Clinical Global Impression (CGI) Severity of Illness scale. 41 patients (82%) completed the study.

Intervention
Patients underwent a washout period of 1–5 weeks and were allocated to 0.5–2.0 mg/day of risperidone (n = 26) or 1–2 mg/day of pimozide (n = 24) for the first week. A flexible dosing period ensued for 7 weeks during which a maximum of 6 mg/day was allowed for both drugs by the end of the treatment period.

Main outcome measures
Tic severity (TSSS, CGI scale, Patient Global Impressions [PGI] scale); obsessive compulsive symptoms (Yale-Brown Obsessive Compulsive Scale [Y-BOCS]); anxiety and depressed mood symptoms (Hamilton Rating Scale for Anxiety [HAM-A]); and social and occupational functioning (Global Assessment of Functioning [GAF]). Extrapyramidal symptoms (EPS) were measured using the Extrapyramidal Symptom Rating Scale (ESRS).

Main results
Analysis was by intention to treat. Global impression and total scores on the TSSS improved significantly from baseline ($p < 0.001$) in both risperidone and pimozide groups. The groups did not differ at 8 weeks, nor did the groups differ for the proportion of patients with mild or no symptoms on the Global Severity Rating Scale of the TSSS or for the proportion of patients much or very much improved on the CGI or PGI (table). The groups also did not differ for total change in Y-BOCS, HAM-A, or GAF scores at 8 weeks. ESRS scores were low in both groups. The results were not affected by patient age. Sedation and weight gain were common side effects of both treatments.

Conclusion
In children and adults with Tourette's disorder, risperidone was as effective and safe as pimozide.

*See glossary.

COMMENTARY

Pharmacotherapy in Tourette's syndrome should be reserved for problems that are functionally disabling and not remediable by non-drug interventions. For most clinicians, initial treatment for tics includes the use of such α-adrenergic receptor agonists as clonidine or guanfacine.[1] If a patient fails these first line medications or presents with severe tics, one generally considers medications in the classical neuroleptic or atypical neuroleptic category.

In the study by Bruggeman *et al*, supported by manufacturers of risperidone (Janssen), a parallel study design was used to compare pimozide, a typical neuroleptic, with risperidone, an atypical neuroleptic. Both medications improved results on the TSSS, a scale which unfortunately provides non-specific information. Defining more precisely what improves in treatment studies is essential. For example, as has been noted in a recent study of baclofen in Tourette's syndrome,[2] improvement on global scores may be related to beneficial effects on factors other than tics. Hence, could improvements in non-tic symptoms after treatment with pimozide or risperidone account in part for improvement on global tic scales? Although the sample size exceeds that of other studies, the fact that 12 centres participated raises unanswered questions of inter rater reliability. Given the frequent co-occurrence of attention deficit hyperactivity disorder in Tourette's syndrome, it is surprising that only 2 of 50 patients had this problem. Other methodological concerns include groupings not matched for obsessive compulsive behaviour, lack of a placebo group, short drug washout period, rapid titration schedules, and the concurrent use of other medications.

5 of 26 patients started on risperidone dropped out of the study (4 because of adverse events and 1 because of insufficient response). Depression, fatigue, and somnolence were common in both groups and EPS can occur with either medication. Weight gain was greater with risperidone in patients < 18 years. Further studies are also required to establish the long term optimal dosing, efficacy, and tolerability of risperidone.

Bruggeman *et al* suggest that risperidone should be considered first line treatment. Based on our interpretation of existing data, we advocate that the question has yet to be resolved, and that typical and atypical neuroleptics remain second line treatments for most patients with tic disorders.

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1 Kurlan R. New treatments for tics? *Neurology* 2001;**56**:580–1.
2 Singer HS, Wendlandt J, Krieger M, *et al.* Baclofen treatment in Tourette syndrome: a double-blind, placebo-controlled, crossover trial. *Neurology* 2001;**56**:599–604.

Risperidone v pimozide in children and adults with Tourette's disorder at 8 weeks†

Outcomes	Risperidone	Pimozide	RBI (95% CI)	NNT
Mild or no symptoms on TSSS Global Severity Rating Scale	54%	38%	44% (–22 to 175)	Not significant
Much or very much improved on CGI scale	65%	63%	4.6% (–32 to 63)	Not significant
			RBR (CI)	NNT
Much or very much improved on PGI scale	58%	63%	7.7% (–47 to 42)	Not significant

†TSSS=Tourette's Syndrome Severity Scale; CGI=Clinical Global Impressions; PGI=Patient Global Impressions; RBR=relative benefit reduction. Other abbreviations defined in glossary; RBI, RBR, NNT, and CI calculated from data in article.