

Risperidone was safe and effective for short term treatment of children with autism and serious behavioural disturbances

McCracken JT, McGough J, Shah B, et al. *Risperidone in children with autism and serious behavioral problems*. *N Engl J Med* 2002;347:314–21.

QUESTION: In children with autism and serious behavioural disturbances, is risperidone safer and more effective than placebo?

Sources of funding: National Institutes of Health; Korczak Foundation; Janssen Pharmaceutica.

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Design

Randomised (unclear allocation concealment*), blinded (clinicians, patients, and outcome assessors)*, placebo controlled trial with 8 weeks of follow up.

Setting

5 university centres in the US.

Risperidone v placebo for children with autism at 8 weeks‡

Outcome	Risperidone	Placebo	RBI (95% CI)	NNT (CI)
Positive response§	69%	12%	501% (193 to 1210)	2 (2 to 3)

‡Abbreviations defined in glossary; RBI, NNT, and CI calculated from data in article.

§Positive response was ≥25% reduction in score on the Irritability subscale of the Aberrant Behavior Checklist and a rating of much or very much improved on the Clinical Global Impressions – Improvement scale.

COMMENTARY

Treatment of children with autism has not typically been based on anything so mundane as randomised clinical trials. This is true for conventional medications as well as controversial treatments. Indeed, the treatment that has been examined most rigorously is secretin.¹

The trial by McCracken *et al* is a focused attempt to examine conventional medication for ameliorating specific behavioural symptoms common in autism. 2 previous blinded trials examined behavioural response to risperidone in people with autism; 1 included 31 adults and another studied 20 people with developmental disabilities including autism.^{2–3} Over 50% of patients in these studies improved with risperidone. Consistent with the trial by McCracken *et al*, the most common side effects were weight gain and sedation. No permanent or serious side effects were reported.

The trial by McCracken *et al* monitored follow up over a 6 month period. The study carefully addressed the complex issues regarding behavioural assessment and outcome measurement.⁴ The data cannot be generalised to all children with autism spectrum disorders since the patients were selected from a larger group for severe behaviour that did not respond to another treatment. It may be that risperidone is more effective for children with less severe behaviours, although the frequency of weight gain and sedation needs to be considered in treatment selection. The role of behavioural or educational interventions used in concert with risperidone was not addressed but will be in future studies by this group. However, this study validates the clinical impression that risperidone is effective in decreasing serious behavioural problems but not core symptoms in children with autism.

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Patients

101 children who were 5–17 years of age (mean age 8.8 y, 81% boys), met the *DSM-IV* criteria for autistic disorder, and presented with tantrums, aggression, or self injurious behaviour. Other inclusion criteria were weight of ≥15 kg, mental age ≥18 months, and no serious medical disorders or other psychiatric disorders requiring medication. Children receiving a psychotropic drug that was effective for aggression, tantrums, or self injurious behaviour were excluded. Follow up was complete.

Intervention

Patients were allocated to risperidone (n=49) or placebo (n=52). For children who weighed <20 kg, the initial dose of risperidone was 0.25 mg/day; for children who weighed 20–45 kg, the initial dose was 0.5 mg at bedtime, increased to 0.5 mg twice/day on day 4, and increased to a maximum of 2.5 mg/day by day 29; for children who weighed >45 kg, the maximal dose was 1.5 mg in the morning and 2.0 mg at bedtime.

Main outcome measures

The primary outcomes were scores on the Irritability subscale of the Aberrant Behavior Checklist and the Clinical Global Impressions–Improvement (CGI–I) scale. Children who had ≥25% reduction on the Irritability score and a rating of much or very much improved on the CGI–I were considered to have a positive response.

Main results

Analysis was by intention to treat. Withdrawal occurred in 6% of the risperidone group and 35% of the placebo group. At 8 weeks, patients who received risperidone had a greater mean decrease from baseline on the Irritability score than did patients who received placebo (14.9 v 3.6, $p < 0.001$). More children who received risperidone had a positive response than did children who received placebo (table). Patients in the risperidone group had a greater increase in weight than patients in the placebo group (2.7 v 0.8 kg, {95% CI for the 1.9 kg difference, 0.88 to 2.9}†). No serious adverse events occurred in the risperidone group.

Conclusion

In children with autism and serious behavioural disturbances, risperidone was safe and effective for the short term treatment of tantrums, aggression, and self injurious behaviour.

*See glossary.

†CI calculated from data in article.