Citalopram not effective for repetitive behaviour in autistic spectrum disorders

**QUESTION**

**Question:** How effective and safe is citalopram treatment for reducing repetitive behaviour in children and adolescents with autistic spectrum disorders?

**Patients:** 149 participants aged 5–17 years who met DSM-IV-TR criteria for autistic disorder, Asperger disorder, or pervasive developmental disorder not otherwise specified, as determined by an experienced clinician (median age 9 years, 73% male, 49% with non-verbal IQ above 70). Eligible participants had to have an illness severity rating of at least moderate on the Clinical Global Impressions (CGI) Severity of Illness scale and at least a moderate score (≥28) on the Children’s Yale–Brown Obsessive Compulsive Scale for Pervasive Developmental Disorders (CYBOCS-PDD).

**Intervention:** Citalopram (10 mg/5 ml, in liquid form) or placebo for 12 weeks. All participants started with 2.5 mg/day citalopram which was increased daily, biweekly or weekly depending on weight, to a possible maximum dose of 20 mg/day. These doses were continued until the CGI improvement (CGI-I) scale was rated as improved or above, but reduced if a dose limiting adverse effect was suspected.

**Outcomes:** Primary outcomes: illness severity (CGI-I rated by the treating clinician, scored from 1 (very much improved) to 7 (very much worse); global response (CGI-I score of 1 or 2). Secondary outcomes: compulsive behaviours (CYBOCS-PDD); composite response (score of 1 or 2 on the CGI-I and ≥25% reduction on the CYBOCS-PDD); compulsive, restrictive, ritualistic, sameness, self-injurious and stereotyped behaviours (subscalaes of the Repetitive Behaviour Scale Revised, RBS-R); the Aherent Behaviour Checklist Community version (ABC-CV, which measures irritability, social withdrawal, hyperactivity, stereotype and inappropriate speech); and adverse events. Outcomes were assessed at baseline and every 2 weeks for 12 weeks.

**Patient follow-up:** 82.6% completed; 100% included in last observation carried forward analyses. All patients were included in the intention to treat analyses.

In this well designed, large, double blind, placebo controlled randomised clinical trial, King and colleagues found that citalopram was not superior to placebo for reduction of repetitive behaviour in children and adolescents with ASDs but was associated with significantly more adverse behavioural effects and medical symptoms. The high placebo response rate of 34%, which has also been found in some other studies involving this population, illustrates the importance of double blind, placebo controlled trials. Although the reduction in irritability associated with citalopram relative to placebo (p = 0.03) was not clinically meaningful, the children who participated in this study were much less irritable at baseline than those who participated in previous risperidone trials, so the possibility that citalopram is effective for irritability in this population cannot be excluded.

Currently, the weight of evidence clearly does not support the use of SSRIs for the treatment of repetitive behaviours in children with ASDs. However, further investigation is necessary to determine whether SSRIs are effective for other target symptoms such as irritability or anxiety in this population.

**METHODS**

**Design:** Randomised controlled trial.

**Allocation:** Unclear.

**Blinding:** Double blinded.

**Follow-up period:** 12 weeks (treatment period only).

**MAIN RESULTS**

There was no significant difference between the citalopram and placebo groups in responders based on the CGI-I at 12 weeks (32.9% with citalopram vs 34.2% with placebo; relative risk 0.96; 95% CI 0.61 to 1.51). Both groups improved over time on the CGI-I but there was no difference between them (p=0.94). There was also no difference on the combined response criteria (CGI-I and CYBOCS-PDD; 20.6% with citalopram vs 13.2% with placebo; p=0.28). Compulsive and repetitive behaviours, as assessed by the CYBOCS-PDD and the six subscales of the RBS-R, also showed no differences between the groups. There was a small but statistically significant difference between the citalopram and placebo groups for the change between baseline and 12 weeks in the irritability component of the ABC-CV but not in other components (mean difference irritability: −2.27, 95% CI −4.3 to −0.2; p=0.03). Adherence to treatment was high in both groups (96.1% for citalopram vs 98.6% for placebo; p=0.08). More adverse events occurred in the citalopram group than in the placebo group (absolute risk for at least one treatment related event: 97.3% with citalopram vs 86.8% with placebo; p=0.03). More participants receiving citalopram withdrew because of an adverse event (12.5% with citalopram vs 9.2% with placebo; significance not reported).

**CONCLUSIONS**

Citalopram is not an effective treatment for children with autistic spectrum disorders with moderate or severe repetitive behaviour. More placebo controlled trials of medications used in these children are needed to assess whether the risks outweigh the benefits.

**ABSTRACTED FROM**


**Correspondence to:** Bryan H King, Seattle Children’s Hospital, University of Washington, 4800 Sand Point Way NE, Seattle, WA 98105, USA; bhking@u.washington.edu

**Sources of funding:** National Institutes of Health.

---

**COMMENTARY**

Psychotropic medications, including selective serotonin reuptake inhibitors (SSRIs), are commonly prescribed for children and adolescents with autism spectrum disorders (ASDs) to target associated maladaptive behaviours, comorbid psychiatric conditions or even core symptoms of the disorder.¹

Previous small, double blind, placebo controlled randomised clinical trials of fluoxetine in adults (n=30) and fluoxetine in children (n=39) have suggested that these SSRIs are superior to placebo for reducing repetitive behaviours associated with autism.¹ However, the majority of the published evidence supporting the use of SSRIs is from open label trials that are subject to publication bias, placebo effects and other shortcomings of uncontrolled trials.¹ In addition, although the details have not yet been published, Autism Speaks announced in 2009 that an industry sponsored controlled trial (n=158) demonstrated that fluoxetine was not superior to placebo for reducing repetitive behaviours in children and adolescents with autistic disorder.²

In this well designed, large, double blind, placebo controlled randomised clinical trial, King and colleagues found that citalopram was not superior to placebo for reduction of repetitive behaviour in children and adolescents with ASDs but was associated with significantly more adverse behavioural effects and medical symptoms. The high placebo response rate of 34%, which has also been found in some other studies involving this population, illustrates the importance of double blind, placebo controlled trials. Although the reduction in irritability associated with citalopram relative to placebo (p = 0.03) was not clinically meaningful, the children who participated in this study were much less irritable at baseline than those who participated in previous risperidone trials, so the possibility that citalopram is effective for irritability in this population cannot be excluded.

Currently, the weight of evidence clearly does not support the use of SSRIs for the treatment of repetitive behaviours in children with ASDs. However, further investigation is necessary to determine whether SSRIs are effective for other target symptoms such as irritability or anxiety in this population.

Scott M Myers, MD

Geisinger Health System, Danville, PA, USA

**Competing interests:** None


Citalopram not effective for repetitive behaviour in autistic spectrum disorders

_Evid Based Mental Health_ 2010 13: 22
doi: 10.1136/ebmh.13.1.22

Updated information and services can be found at:
http://ebmh.bmj.com/content/13/1/22

**References**

This article cites 3 articles, 0 of which you can access for free at:
http://ebmh.bmj.com/content/13/1/22#BIBL

**Email alerting service**

Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

**Topic Collections**

Articles on similar topics can be found in the following collections

Autism (88)
Pervasive developmental disorder (88)
Neurology (1070)
Clinical trials (epidemiology) (989)
Epidemiology (1570)

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/