

# Review: clomipramine is more effective than SSRIs for paediatric obsessive compulsive disorder

Geller DA, Biederman J, Stewart SE, *et al.* Which SSRI? A meta-analysis of pharmacotherapy trials in pediatric obsessive-compulsive disorder. *Am J Psychiatry* 2003;160:1919–28.

## Q Which serotonergic drug is most effective in paediatric obsessive compulsive disorder?

### METHODS

 **Design:** Systematic review with meta-analysis.

 **Data sources:** MEDLINE and PsycINFO; hand search of reference lists and conference abstracts.

 **Study selection and analysis:** Included studies were prospective, randomised, and double blind, had placebo or active comparator controls, and were in children aged  $\leq 19$  years who met full DSM criteria for obsessive compulsive disorder (OCD). Parallel, withdrawal, substitution, and crossover randomised controlled trials (RCTs) were included. Meta-analysis used a random effects model and multiple regression. Sensitivity analyses and tests for heterogeneity were conducted.

 **Outcomes:** Effect sizes calculated from dependent outcome measures (Children's Yale-Brown Obsessive Compulsive Scale, NIMH Global OCD scale, Clinical Global Impression of severity, Leyton Obsessional Inventory-Child Version).

### MAIN RESULTS

Twelve RCTs, with 1044 participants, met the inclusion criteria. Clomipramine and four SSRIs (paroxetine, fluoxetine, fluvoxamine, and sertraline) were investigated. Drug treatment was significantly more effective than placebo (pooled standardised mean difference (SMD) 0.46, 95% CI 0.37 to 0.55;  $p < 0.001$ ; no significant heterogeneity of SMDs,  $p = 0.39$ ). Each individual drug was more effective than placebo (pooled effects comparison;  $p < 0.001$  for all comparisons *v* placebo). Clomipramine was significantly more effective than each of the SSRIs (pooled effects comparison; clomipramine *v* paroxetine  $p = 0.003$ ; *v* fluoxetine  $p < 0.03$ ; *v* fluvoxamine  $p = 0.001$ ; *v* sertraline  $p < 0.001$ ). There was no significant difference between any of the individual SSRIs.

### CONCLUSIONS

All of the drugs considered were significantly better than placebo for paediatric OCD, but the effect size was not large. Although clomipramine was shown to be more effective than the SSRIs for

paediatric OCD it may not be the best first line treatment, as it is associated with frequent adverse effects.

### Commentary

A decade ago, little was known regarding the evidence-based treatment of paediatric obsessive compulsive disorder (OCD). Thus, the meta-analysis reported by Geller and colleagues is remarkable in part because it illustrates the progress made in the psychopharmacology of OCD in youth. It is worth noting here that the authors included a trial (March 1990<sup>1</sup>) which is a subset of a trial already included (DeVeugh-Geiss, 1992<sup>2</sup>). Although this might affect the results of the meta-analysis, it is unlikely to invalidate the overall conclusions. One striking finding is that the benefits of medication with an SSRI in this patient population are modest at best. Fewer than 20% of patients remit; the great majority are partial responders. As a result, many patients cycle from one drug to another or end up taking multiple augmenting medications. One third of paediatric patients with OCD taking an SSRI are also taking a neuroleptic, with only exacerbations and side effects to show. The evidenced-based key to the treatment of OCD is cognitive behavioural psychotherapy alone or in combination with an SSRI. We have shown (AACAP annual meeting, October, 2003, Miami, FL, USA) that the ordering of effect sizes relative to placebo for sertraline (moderate), CBT (large), and combined treatment (larger) tracks the probability of remission, with over 50% of patients remitting after 12 weeks of combined treatment. The implications of the meta-analysis and our NIMH funded comparative treatment trial<sup>3</sup> are clear. Patients should start treatment with CBT or the combination of CBT with an SSRI. Medication monotherapy, although helpful, is not satisfactory as initial treatment of OCD in children and adolescents.<sup>4 5</sup> As CBT is not widely available, the key to improving the public health of youth with OCD is the wider dissemination of expert cognitive behavioural psychotherapy.

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- 4 March J, Frances A, Kahn D, *et al.* Expert consensus guidelines: Treatment of obsessive-compulsive disorder. *J Clin Psychiatry* 1997;58:1–72.
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