

Fluoxetine decreased depressive symptoms in children and adolescents with non-psychotic major depressive disorder

Emslie GJ, Rush AJ, Weinberg WA, et al. A double-blind, randomized, placebo-controlled trial of fluoxetine in children and adolescents with depression. *Arch Gen Psychiatry* 1997 Nov;54:1031-7.

Objective

To evaluate the efficacy and safety of fluoxetine in treating children and adolescents who have non-psychotic major depressive disorder (MDD).

Design

Randomised, double blind, placebo controlled trial with 8 weeks of follow up.

Setting

Outpatient mood disorders programme in Dallas, USA.

Patients

96 patients (mean age 12 y, 54% boys) who met the *Diagnostic and Statistical Manual of Mental Disorders, 3rd edition, revised* criteria for MDD. Exclusion criteria were bipolar disorder; psychotic depression; independent sleep wake disorder; substance abuse; anorexia nervosa; bulimia; previous treatment with fluoxetine, 20 mg/day, for ≥ 3 weeks; or a first degree relative with bipolar I disorder.

Intervention

48 patients received fluoxetine, 20 mg/day, and 48 patients received a matching placebo.

Main outcome measures

Primary outcomes were response (Clinical Global Impressions [CGI] scale improvement rating) and depressive symptoms (Children's Depression Rating Scale-Revised [CDRS-R]) which were measured weekly by clinicians. Secondary outcomes were global functioning (Children's Global Assessment Scale) and general psychopathology (Brief Psychiatric Rating Scale-Children) which were also assessed weekly by clinicians. Patient self reports of depressive symptoms at the beginning and the end of treatment were also used (Beck Depression Inventory or the Children's Depression Inventory and the Weinberg Screening Affective Scale).

Main results

Analysis was by intention to treat. Patients who received fluoxetine were more likely to be much or very much improved according to the CGI scale improvement rating than patients who received placebo ($p=0.02$) (table). Compared with placebo, fluoxetine led to lower CDRS-R scores at week 5 ($p<0.03$), week 6 ($p<0.04$), week 7 ($p<0.04$), and week 8 ($p<0.008$). Treatment was stopped due to lack of efficacy in 7 and 19 patients receiving fluoxetine and placebo, respectively ($p=0.006$)*, and due to side effects in 4 and 1 patients receiving fluoxetine and placebo, respectively ($p=0.36$)*. Improvement in general psychiatric symptoms, global functioning, and self reported depressive symptoms did not differ between treatments.

Conclusion

Compared with placebo, fluoxetine was effective and safe in the treatment of children and adolescents who had non-psychotic major depressive disorder.

* p values calculated from data in article.

Fluoxetine v placebo in children with non-psychotic major depressive disorder†

Outcome at 8 weeks	Fluoxetine EER	Placebo CER	RBI (95% CI)	ABI EER - CER	NNT (CI)
Much or very much improved	56%	33%	69% (7 to 174)	23%	5 (3 to 33)

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

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Commentary

This study by Emslie *et al* is a landmark study for child and adolescent psychiatry. It is the largest randomised controlled trial (RCT) to date of an antidepressant medication in a child and adolescent population, the first such study to report a superior drug response compared with placebo for adolescents, the second to do so for children,¹ and the first to use an intent to treat analysis.

The finding of fluoxetine and placebo response rates comparable to those from RCTs of fluoxetine and other antidepressants in adults,² and the finding of no age group by treatment interaction suggest that depressed individuals of all ages may be similar in their response to antidepressant medication. Until now, RCTs of

depressed children and adolescents have been plagued by small samples.³ Although this is the largest study to date, it is worth noting that it took almost 4 years to complete. Multicentre trials are essential if important research findings from populations of depressed children and adolescents are to be relayed to clinicians in a timely fashion. In the meantime, the use of antidepressants in depressed children and adolescents is widespread despite lack of evidence for their efficacy from RCTs.^{4,5} Clinicians now have this exemplary study to support their current use of fluoxetine, but it is unlikely that its publication will lead to major changes in clinical practice.

Finally, it is important to note that less than one third of patients treated with

fluoxetine achieved complete remission of their symptoms. This suggests that either a longer duration of treatment with fluoxetine or the use of adjunctive treatments in this population is required, or both.

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