Continuing fluoxetine treatment may delay relapse in children and adolescents with major depressive disorder


Q Does fluoxetine prevent relapse of major depressive disorder in children and adolescents?

METHODS

Design: Randomised controlled trial.
Allocation: Unclear.
Blinding: Double blinded.
Follow up period: 32 weeks.
Setting: USA; time frame not reported.

Patients: Forty children and adolescents in remission (Children’s Depression Rating Scale, Revised (CDRS-R) score <28) from major depressive disorder (DSM-IV) after 19 weeks treatment with fluoxetine (20–60 mg daily) or switching to placebo.

Intervention: Continuing fluoxetine treatment (20–60 mg daily) or switching to placebo.

Outcomes: Primary outcome: relapse (CDRS-R score >40 plus clinical deterioration over 2 weeks, or clinician’s diagnosis of relapse); adverse events. Secondary outcomes: change in depression scores.

Patient follow up: 100%.

MAIN RESULTS

Continuing fluoxetine increased time to relapse compared with switching to placebo (180.7 days with fluoxetine v 71.2 days with placebo; p = 0.046). Fewer people in the fluoxetine group experienced relapse than in the placebo group (estimated at 34% with placebo; p = 0.046). Fewer people in the fluoxetine group discontinued treatment because of agitation.

CONCLUSIONS

In children and adolescents who achieve remission from major depression with fluoxetine (20–60 mg daily), continuing fluoxetine treatment can delay relapse compared with switching to placebo.

The observed effect may not be entirely due to continued treatment with fluoxetine. Randomisation is less effective at balancing confounding factors in studies with small sample sizes. In this study the fluoxetine group was significantly older than the placebo group at baseline (mean 13.45 years v 11.65 years; p = 0.025). The placebo group contained more participants who had needed higher doses of fluoxetine to achieve remission than the continuing fluoxetine group (60 mg/day fluoxetine: 10% of placebo group v 0% of fluoxetine group; 40 mg/day: 15% of placebo group v 5% of placebo group).

Notes

Three randomised controlled trials have demonstrated that fluoxetine has greater short term efficacy than placebo in children and adolescents with depression. Until now, there have been no studies looking at longer term efficacy in this age group. Clinicians and guideline writers trying to decide on how long to prescribe fluoxetine once remission has been attained have therefore relied on data from adult studies. It has generally been recommended that fluoxetine should be continued for at least 6 months after clinical recovery.

The study by Emslie et al clearly supports this current practice. As well as being statistically significant, the results were highly clinically significant: participants were twice as likely to relapse if they discontinued fluoxetine. These results are likely to help us in discussions with our patients who may be reluctant to continue to take their medication once they see themselves as better.

A duration of 32 weeks was chosen for the relapse-prevention phase. A larger study would be needed to define the optimum length of time more precisely. However, it clearly shows that the duration of maintenance treatment needs to be of a significant time period and our current practice of 6 months is reasonable.

This study also shows us that even if people with depression continue fluoxetine, a third may relapse. This shows the importance of continued close monitoring of our patients once in remission and of educating them and their families to watch for early warning signs of relapse.

It is common practice now for antidepressants to be gradually withdrawn. In this study, there appeared to be no increase in rates of physical symptoms if there was sudden withdrawal. However, the authors conceded that in view of the small sample size, conclusions that tapered withdrawal of fluoxetine is not necessary can only be tentative.

Dr Paul Wilkinson, MB BChir, MRCPsych
Research Psychiatrist, Section of Developmental Psychiatry, University of Cambridge, Cambridge, UK.

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_Evid Based Mental Health_ 2005 8: 37
doi: 10.1136/ebmh.8.2.37

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