

Prophylactic citalopram reduced recurrences of unipolar major depression

Klysner R, Bent-Hansen J, Hansen HL, et al. Efficacy of citalopram in the prevention of recurrent depression in elderly patients: placebo-controlled study of maintenance therapy. *Br J Psychiatry*. 2002;181:29-35.

QUESTION

In elderly outpatients with unipolar major depression who have responded to acute and continuation treatment with citalopram, is prophylactic treatment with citalopram more effective than placebo for recurrence prevention?

DESIGN

Randomized {allocation concealed*}†, blinded (clinicians, patients, {data collectors, outcome assessors, and data safety and monitoring committee}†),* placebo-controlled trial with ≥ 48 -week follow-up.

SETTING

A psychiatric research clinic in Denmark.

PATIENTS

121 outpatients ≥ 65 years of age (mean age 75 y, 77% women) with unipolar major depression (*Diagnostic and Statistical Manual of Mental Disorders, 4th edition [DSM-IV]*, 296.2x or 296.3x and Montgomery Åsberg Depression Rating Scale [MADRS] score ≥ 22) who responded to acute and continuation treatment with citalopram (20 to 40 mg) for 8 and 16 weeks, respectively. Response to both phases of treatment was defined by a MADRS score ≤ 11 . Exclusion

criteria included an index episode that lasted > 12 months; a history of schizophrenia, mania, hypomania, epilepsy, or drug or alcohol misuse; and a score of ≥ 5 on MADRS item 10 (suicidality). Follow-up was 100%.

INTERVENTION

Patients were allocated to prophylactic treatment with citalopram (20, 30 or 40 mg/d; $n = 60$) or placebo ($n = 61$) for ≥ 48 weeks.

MAIN OUTCOME MEASURES

Time from randomization to recurrence of a depressive episode (defined by a MADRS score ≥ 22 confirmed after 3 to 7 d).

MAIN RESULTS

Analysis was by intention to treat. Time from randomization to recurrence of a depressive episode was greater in the citalopram group than in the placebo group ($P < 0.001$). The

corresponding rate of recurrences was lower in the citalopram group than the placebo group (Table). Fewer patients in the citalopram group than the placebo group discontinued the allocated medication (Table).

CONCLUSION

In elderly outpatients with unipolar major depression who have responded to acute and continuation treatment with citalopram, prophylactic treatment with citalopram was more effective than placebo for recurrence prevention.

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*See Glossary.

†Information provided by author.

Citalopram vs placebo for prophylactic prevention of recurrences in unipolar major depression for ≥ 48 weeks†

Outcomes	Citalopram	Placebo	RRR (95% CI)	NNT (CI)
Recurrence	32%	67%	53% (30 to 69)	3 (2 to 6)
Discontinuation of allocated medication	62%	90%	32% (16 to 46)	4 (3 to 8)

†Abbreviations defined in Glossary; RRR, NNT, and CI calculated from data in article.

COMMENTARY

Depression is particularly disabling in elderly patients, and the question of when to discontinue antidepressants following remission is under-researched, with much of our current practice based on a less-than-solid evidence base. The trial by Klysner and colleagues provides good evidence for the beneficial effects of continuing citalopram for ≥ 48 weeks after remission from a depressive episode.

Should all elderly patients who respond to antidepressants have continuation therapy based on the results of this study? It would be premature to make such a recommendation from a single trial; clearly, we need more trials supported by systematic reviews. Such a review is currently being done under the aegis of the Cochrane Collaboration (1).

Klysner and colleagues showed in a post hoc analysis that patients receiving 20 mg did as well as (or better than) those receiving higher doses. Does this mean that clinicians can safely lower doses in the continuation phase? Probably not—those on higher doses may have had more severe depression, which probably took longer to treat. Only trials that compare different dosing regimens for patients randomized to continuation treatment will be able to answer this question.

Does this study suggest a specific benefit for continuation on citalopram? There is no theoretical reason why one antidepressant should be

better than any other in this context. Another study in elderly patients found a benefit for continuation therapy with tricyclic dothiepin (2). Tolerability profiles may be the most important feature of an antidepressant in this context. Continuation means asking patients to take medication for more than a year to prevent symptoms that have already been treated. In this situation, differences in side effect profiles, which did not matter much in short-term acute treatment (3), may have a more important effect on compliance in the longer maintenance phase.

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