Brief Reports

Recurrence of First-Episode Geriatric Depression After Discontinuation of Maintenance Antidepressants

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Objective: Later age at onset of depression appears to be a risk factor for early recurrence. Therefore, the authors examined the 2-year outcomes of elderly patients with first-episode major depression following discontinuation of their maintenance antidepressant medication. **Method:** The study group consisted of 21 elderly patients who had recovered from a first lifetime episode of major depression. They had taken maintenance antidepressant medication for 2 years and had not had a relapse or recurrence during that time. The antidepressant was then withdrawn, and patients were followed for another 2 years or until recurrence, whichever occurred first. **Results:** The cumulative probability of suffering a recurrence of major depression was 61%. Eleven of the 12 patients who suffered a recurrence restarted the antidepressant, and 10 responded. **Conclusions:** Elderly patients with first-episode major depression were at high risk of recurrence following discontinuation of maintenance antidepressant medication. However, the vast majority of patients who experienced a recurrence responded to reinstated treatment.

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Several naturalistic studies have found that later age at onset of depression is associated with a high risk of early recurrence (1–3). For example, Zis et al. (2) reported that 70% of patients aged 60 years or older had a relapse or recurrence of depression within 2 years of their first depressive episode compared with 30% of patients aged 20 to 30 years. These findings have prompted some psychiatrists to suggest that long-term treatment should be considered for all elderly patients with major depression, regardless of whether they are experiencing a first lifetime episode or a recurrent episode (4). However, this point of view is controversial.

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When deciding on the length of antidepressant treatment for a patient, it is necessary to consider the likelihood of a recurrence of depression following discontinuation of treatment. To date, this issue has not been examined in elderly patients with first-episode depression. Therefore, the purpose of this exploratory study was to determine the probability of recurrence of major depression following the discontinuation of maintenance antidepressant medication in elderly patients who had recovered from a first lifetime episode of the disorder. A second objective was to determine the frequency and speed of response to reinstated treatment in those patients who suffered a recurrence.

METHOD

The study group consisted of 21 patients, aged 60 years or older (mean age=74.4 years, SD=6.6), who had been treated for a first lifetime episode of DSM-III-R unipolar nonpsychotic major depression. The absence of a past history of major depression was determined by patients' responses to questions in the Structured Clinical Interview for DSM-III-R (5) and by collateral history obtained from reliable informants. At index assessment, none of these patients had another concurrent axis I diagnosis; a lifetime history of schizophrenia, schizoaffective disorder, paranoid disorder, or dementia; any neuro-

logical disorder affecting the central nervous system; or acute uncontrolled medical illness. All subjects had given written informed consent. Before treatment, patients had a 17-item Hamilton Depression Rating Scale (6) score of 16 or above. The episode of depression had responded (Hamilton depression scale score of 10 or below) to either nortriptyline (with or without adjunctive lithium) as a first line of treatment (N=19) or phenelzine as a second line of treatment (N=2). The patients had been on maintenance regimens of the medications that they had responded to, and they had remained free of relapse or recurrence of major depression for 2 years from the time of response.

Following the 2 years of maintenance treatment, patients had their antidepressant medication and, when applicable, adjunctive lithium withdrawn over a period of 8 weeks. These patients were then followed for 2 years from the start of discontinuation or until recurrence, whichever occurred first. Recurrence was diagnosed if a patient met symptomatic criteria for DSM-III-R major depression for at least 1 week and had a Hamilton depression scale score of 16 or above.

The following measures were used to explore the relationship between clinical variables and time to recurrence: Hamilton depression scale, anxiety subscale of the Hospital Anxiety and Depression Scale (7), Mini-Mental State (8), Life Events and Difficulties Schedule modified for the elderly (9), and the physical illness rating scale of Burvill et al. (10).

If a patient had a recurrence, he or she restarted the discontinued antidepressant. Patients were treated with the same dose of antidepressant that they had previously responded to. This dose was usually achieved within 1 week of reinstatement of the medication. If a patient had previously been given adjunctive lithium, this medication was only restarted if he or she failed to respond (Hamilton depression scale score of 10 or below) to a 6-week trial of antidepressant monotherapy.

The Kaplan-Meier product limit method was used to estimate the cumulative probability of having a recurrence during the 2-year follow-up phase. A Cox regression analysis examined the effect of demographic and clinical variables on time to recurrence. For patients who suffered a recurrence, paired t tests were used to compare time to response of the recurrent episode with that of the index episode. The binomial test was used to assess the probability of response to reinstated treatment. For all tests, statistical significance was set at $p \leq 0.05$ (two-tailed).

RESULTS

The cumulative probability of a recurrence of major depression was 60.6%. Fifty-eight percent of new episodes occurred within 6 months and 92% within 12 months from the start of discontinuation of medication. None of the following variables was a statistically significant predictor of recurrence: age; sex; duration of the index episode; time to respond to treatment of the index episode; Hamilton depression scale score at index assessment; Hamilton depression scale, Hospital Anxiety and Depression Scale anxiety subscale, and Mini-Mental State scores at the start of follow-up; and chronic physical illness, life event, and life difficulty scores for the 6 months before the start of follow-up.

Eleven (91.7%) of the 12 patients who had a recurrence agreed to restart antidepressant medication. Nine (81.8%) of the 11 patients responded to reintroduction of the antidepressant alone, and one (9.1%) of the 11 patients responded to the antidepressant and adjunctive lithium. The result of the binomial test ($p=0.02$) suggested that 10 responses out of 11 treatment trials was unlikely to be due to chance. The mean time for response to treatment was 4.5 weeks (SD=1.8), which was not significantly different from the 4.6 weeks (SD=2.3) needed to respond to treatment of the index episode ($t=-0.12$, $df=9$, $p=0.91$).

DISCUSSION

Elderly patients with first lifetime episodes of major depression were at high risk of recurrence following discontinuation of their maintenance antidepressant medication. However, the vast majority of patients who experienced a recurrence responded to reinstated treatment. These preliminary findings from an open study need to be replicated in a randomized, placebo-controlled discontinuation study.

What are the implications of our findings for management? In the absence of specific predictors of recurrence, one approach is to consider long-term treatment for all elderly patients with major depression. Obviously, this approach requires careful consideration of the risk-benefit ratio of using antidepressant medication on a long-term basis in elderly patients. However, our experience, and that of others, is that long-term treatment with appropriately selected antidepressant medication is safe and well tolerated in most elderly patients (4, 11).

In the light of our finding of favorable response to reinstated treatment, an alternative strategy is to treat first-episode patients for a shorter period of time and to then treat recurrences when they arise. This approach is based on the assumption that each patient would be followed on a regular basis and that adequate treatment would be reinstated in a timely manner in case of a recurrence. However, there is considerable evidence that in primary care, many cases of depression are not detected, and even when depression is recognized, it is often inadequately or inappropriately treated (12). Therefore, this approach may falter in routine clinical practice.

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