Correspondence

EDITED BY STANLEY ZAMMIT

Prophylaxis of depression in older people

I read with interest the recent article by Wilson *et al* (2003). On the basis of a randomised, double-blind placebo-controlled trial, they conclude that sertraline is not effective in preventing recurrent episodes of depression. However, I would like to make certain observations.

First, looking at Table 2 (p. 494), we find that the number of patients remaining in the study at 100-week follow-up is 15 in the sertraline group and 12 in the placebo group. These numbers are too small to draw any major conclusions. Also, looking at the same table, we find that at 4-week follow-up there were six recurrences of depression in the placebo group compared with only two in the sertraline group; that is, the sertraline group had significantly fewer recurrences of depression in the first 4 weeks of prophylactic therapy.

Second, I would like to make an observation about statistical *v.* clinical significance. Again looking at Table 2, we find that the number of cumulative recurrences were fewer in the sertraline group than in the placebo group at all points of the maintenance phase over 2 years. Even though these numbers did not reach statistical significance, they are clinically significant. This opinion is based on two reasons: first, for a physician, prevention of even one case of recurrence is important and satisfying; second, from a community and financial perspective, sertraline prophylaxis has been found to be more cost-effective than treating each new episode of depression with dothiepin (Hatziandreu *et al*, 1994). If Wilson *et al* had included an analysis of treatment costs (including the cost of treating episodes of recurrent depression) in both the groups, it might have made interesting reading.

Third, as Wilson *et al* pointed out, failure to increase the dose of sertraline at the earliest signs of recurrence contributed to the greater number of recurrences observed in their study. There should have been provision to increase the dose of sertraline as and when the clinical situation demanded it. After all, a significant number of patients do require a daily dose in excess of 50 mg sertraline (Suri *et al*, 2000), a dose that was used to treat almost three-quarters of the patients in this study.

In conclusion, the data presented by Wilson *et al* are insufficient to suggest making any changes in the current practice of prescribing sertraline for treatment and prophylaxis of depression in older people.

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Author's reply: In response to Dr Kumar's comments there are some important issues that need addressing. First, Dr Kumar introduces his letter in saying that we conclude that sertraline is not effective in preventing recurrent episodes of depression. This is not the case. We only stated that there is no evidence that sertraline has a prophylactic efficacy when used at the dose that achieved remission.

Second, we agree that if we had conducted an end-point analysis on the 27 subjects who completed the 100-week follow-up, then the study would have been relatively meaningless. We conducted a survival analysis on 113 subjects. This is a well-founded and recognised method of analysis of this type of study.

Third, we concur with Dr Kumar in that the prophylactic management of recurrent depression is critical. We do not advocate treating each episode as a new episode when prophylactic management is indicated. However, we do make the point that preventive techniques should be based on evidence of efficacy and effectiveness.

Dr Kumar suggests that we should have adopted a protocol that enabled increase in dose 'when the clinical situation demanded it'; presumably when we thought a patient was experiencing the early stages of a recurrence. This misses the point of the paper. Our study (which is of a power similar to or greater than equivalent studies in this field) shows that the dose of sertraline required to achieve remission does not have prophylactic efficacy. This is important, as what evidence there is suggests that therapeutic doses of dothiepin (Old Age Depression Interest Group, 1993), nortriptyline (Reynolds *et al*, 1999) and citalopram (Klysner *et al*, 2002) do have prophylactic efficacy. The implications for guidelines concerning the long-term management of older people with depression are self-evident.

Dr Kumar has failed to present arguments that undermine our conclusions. There is no evidence that the dose of sertraline required to achieve remission has prophylactic efficacy. The 8.4% reduction in risk of recurrence (over 100 weeks) that it offers is unlikely to instil clinical confidence in prophylactic efficacy when evidence indicates that other drugs for which the dose does not need to be changed are available.

Declaration of interest

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Old Age Depression Interest Group (1993) How long should the elderly take antidepressants? A double-blind placebo-controlled study of continuation/prophylaxis therapy with dothiepin. *British Journal of Psychiatry*, **162**, 175–182.

Reynolds, C. F., III, Frank, E., Perel, J. M., *et al* (1999) Nortriptyline and interpersonal psychotherapy as maintenance therapies for recurrent major depression. A randomized controlled trial in patients older than 59 years. *JAMA*, **281**, 39–45.

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