Citalopram and the Curate's Egg in Geriatric Depression

TO THE EDITOR:

> Bishop: I see you have a bad egg.
>
> Curate: Oh, no, my lord, parts of it are excellent.

The report by Steven P. Roose, M.D., and colleagues on the treatment of old-old depressed patients with citalopram (1) concluded that medication was not more effective than placebo. In this multicenter study, there was a major effect of study site on response and remission rates to both placebo and active drug. Attempting to put the best face on the results, the authors suggested that more severely depressed patients tended to have a higher remission rate with medication. They also underscored the perspective that the placebo condition in such a trial "is not remotely close to a 'no-treatment' condition" (p. 2057).

Overall, the trial highlights the present sorry state of research into antidepressant efficacy. A more rigorous view of the data by site suggests that the trial lacked ecological validity. When rates of response and remission are higher for placebo than for active drug at six of nine sites (the authors' Figure 2), the pooled analysis becomes an exercise in futility. Moreover, the faintly encouraging secondary analyses lacked a sound base in any primary effect, and they were not corrected for multiple comparisons. These concerns are compounded by the multivariate statistical approach, which inflated the practical significance of the secondary analyses.

For instance, in a secondary analysis, the authors reported a significantly higher rate of response ($p=0.04$) to citalopram versus placebo in the high-severity group (defined by an initial Hamilton Depression Rating Scale score >24). Not only was this "significant" finding not subjected to Bonferroni correction, it did not hold up when the analysis was conducted on the primary outcome data ($\chi^2=3.07$, df=1, $p<0.08$).

Although inflating the trend for citalopram to be more effective in the high-severity group, the authors failed to point out that the low-severity group, in which there was absolutely no suggestion of a drug effect, constituted 61% of the sample. Their data comport with the recent recommendation from the National Institute for Clinical Excellence in Britain that "antidepressants should not be used for the initial treatment of mild depression because the risk-benefit ratio is poor" (2).

As to the authors' anodyne discussion of the perspective that placebo treatment in a clinical trial amounts to far more than no treatment, the point is so well known that it does not bear tedious repetition and elaboration. It is also irrelevant to the primary objective of the study, which was to determine whether the use of citalopram is associated with added therapeutic value beyond what can be achieved by the attentive clinical interest provided to all patients.

References

1. Roose SP, Sackeim HA, Krishnan KRR, Pollock BG, Alexopoulos G, Lavretsky H, Katz IR, Hakkarainen H (Old-Old Depression Study Group): Antidepressant pharmacotherapy in the treatment of depression in the very old: a randomized, placebo-controlled trial. Am J Psychiatry 2004; 161:2050–2059
2. National Collaborating Centre for Mental Health: Management of Depression in Primary and Secondary Care: Clinical Guideline 23. London, National Institute for Clinical Excellence, 2004, p 5. http://www.nice.org.uk/pdf/CG023NICEguideline.pdf

BERNARD J. CARROLL, M.B.B.S., PH.D., F.R.C.PSYCH.
Carmel, Calif.

ECT in Patients With Depression and Borderline Personality Disorder

TO THE EDITOR: Ulrike Feske, Ph.D., et al. were too negativistic in their article (1) when they stated, "our findings suggesting that borderline personality disorder patients may not respond adequately to ECT have potentially significant implications for the selection of candidates for ECT" (p. 2079). Although this is unarguable if taken literally, it sounds overly discouraging about the potential use of ECT in this situation.

First of all, there was an acute improvement in over 20% of depressed borderline personality disorder patients, most of whom had been nonresponsive to antidepressant medication. If this were generalizable, then it would amount to a large absolute number of potentially treatable individuals.

Second, in clinical practice, one often sees such patients having been managed with sequential medication trials and polypharmacy lasting over many years. ECT is not, of course, a substitute for the most important factor in treatment, which is a consistent, supportive, and skilled therapist. But if this most powerful biomedical treatment for depression fails, then the failure may help provide critical guidance to future therapy by discouraging the ongoing pursuit of an ultimate biological "magic bullet" that might yet make the patient feel better. To resolve such an issue, in selected cases, may give the therapist and patient more freedom to focus on other problems and may be well worth the effort and expense of ECT.

Reference

1. Feske U, Mulsant BH, Pilkonis PA, Soloff P, Dolata D, Sackeim HA, Haskett RF: Clinical outcome of ECT in patients with major depression and comorbid borderline personality disorder. Am J Psychiatry 2004; 161:2073–2080

DAVID E. NESS, M.D.
Pittsburgh, Pa.

Dr. Feske and Colleagues Reply

TO THE EDITOR: We agree with Dr. Ness that a course of ECT for patients with major depressive disorder and comorbid borderline personality disorder may be worthwhile for a fraction of such patients when other treatments have proved inadequate. Our major point still stands, however: with this group of patients, the prognosis of ECT was poor in the aggregate, and we had no valid basis for predicting which individual patient would benefit. In addition, previous studies have documented relapse rates as high as 84% 6 months after ECT without continuation therapy (1). Thus, even the longer-term prognosis of the patients who do respond with an acute remission of depressive symptoms remains guarded in the absence of an effective follow-up intervention. Adequately powered, randomized clinical trials with long-term follow-up evaluations (i.e., of at least 6-months' duration) and a comprehensive assessment of symptoms other than depression (i.e., anger, impulsivity, anxiety, substance use, and interpersonal adjustment) are needed to more fully evaluate the advantages and disadvantages of ECT for this subgroup of patients. In the absence of