Treatment With Low Doses of Tranylcypromine Resulted in a Disappointing Remission Rate

TO THE EDITOR: The article by Patrick J. McGrath, M.D., et al. from the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) Study team (1) reported that treatment with the monoamine oxidase inhibitor (MAOI) tranylcypromine resulted in a 6.9% remission and 12.1% response rate for patients who had not achieved remission in three prior medication trials. These rates are not in accordance with most previous controlled studies on tranylcypromine in refractory depression (some also with patients who failed three prior medication trials), in which response rates up to 50% were found (1–3).

As acknowledged by the authors, tranylcypromine treatment was probably not optimal, since patients received rather low daily doses of tranylcypromine (mean=36.9 mg, maximum: 60 mg). In most other trials in refractory depression, dosages up to 100 mg (or even higher) were used.

One of the first randomized placebo-controlled trials in depression, by the Medical Research Council (MRC), evaluated the effect of another MAOI: phenelzine (4). In this study, both electroconvulsive therapy and imipramine (maximum: 150 mg/day) were more effective than both phenelzine (maximum: 45 mg/day) and placebo. Together with the risks associated with the use of MAOIs (e.g., tyramine effect) this led to almost complete disappearance of the MAOIs from the therapeutic arsenal. Nevertheless, phenelzine in doses up to 90 mg/day was found to be an effective treatment for patients who had not responded to previous antidepressants (3).

One of the conclusions by the authors is that the combination of venlafaxine and mirtazapine "may be preferred over tranylcypromine for patients with highly treatment-resistant depression who have not benefited adequately from several prior treatments" (1, pp. 1538–1539). In order to prevent that something may now happen with tranylcypromine as the result of the STAR*D trial similar to what occurred with phenelzine after the MRC trial, we would like to add that this only appears true for low doses of tranylcypromine, but that tranylcypromine (and phenelzine) at higher doses are still valid treatment options for refractory depression.

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Drs. van den Broek and Birkenhäger report no competing interests.

Dr. McGrath and Colleagues Reply

TO THE EDITOR: We agree with the important point raised by Drs. Nolen et al. Their landmark studies, cited in our paper, clearly suggest that doses of tranylcypromine higher than those approved by the Food and Drug Administration (FDA) in the United States show substantial efficacy in treatment-resistant depression. Because STAR*D decided to use dosages only up to the FDA recommended maximum, STAR*D was unable to test the effectiveness of the doses Nolen et al. and others have used for treatment-resistant depression. As indicated in our article, even the maximum allowable dose was infrequently used. The low likelihood of remission in STAR*D patients treated with tranylcypromine, together with its low dosing and poor tolerance, support our conclusion that tranylcypromine is not a treatment clinicians in most practice settings are likely to use optimally or successfully. Nevertheless, we fully agree with Nolen et al. that a vigorous trial of an MAOI should be considered for depressed patients not responsive to multiple other antidepressant trials. However, the experience of STAR*D suggests that tranylcypromine and other MAOI treatment may be better handled by a psychopharmacology specialist who is knowledgeable about these agents, and who is aware that higher than recommended doses of tranylcypromine may be very effective for select patients.

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