Open-Label Trial of Acamprosate as a Treatment for Anxiety

To the Editor: Acamprosate calcium, employed in Europe for more than a decade as a treatment in alcoholism,[1,2] has recently been licensed in the United States as an agent for the maintenance of alcohol abstinence. Acamprosate acts on the γ-aminobutyric acid (GABA) receptor site in the central nervous system (CNS)[3] and appears to be well tolerated by neither inducing tolerance/dependence nor altering seizure threshold.

Method. In this small, open-label trial of acamprosate, we treated 21 patients with a clinical DSM-IV diagnosis of an anxiety disorder, including panic disorder, generalized anxiety disorder, and anxiety not otherwise specified; patients with these disorders were enrolled prospectively from approximately February to September 2007. Psychotic disorders and attention-deficit/hyperactivity disorder were exclusionary. Most patients were also concomitantly being treated with psychotherapy and taking other medications (including medications for anxiety), which were continued without modification when acamprosate was introduced. Patients were seen monthly. Dosage began at 300 mg qd, and was raised by 300 mg qd each month.

Results. Eighteen of the 21 patients (86%) completed at least 1 month of treatment. Of those who discontinued treatment, the most common reasons were nausea (13% [n = 21] in present trial; 4% reported in US Food and Drug Administration [FDA]-approved licensing information) and CNS effects (slurred speech and cognitive slowing, 13% [n = 21] in present trial; 30% reported in FDA-approved licensing information).

Statistical analyses included all patients who completed at least 1 month of treatment. Most patients (n = 8, 44%) attended 4 or more sessions; 6 patients (33%) attended 2 sessions; and 4 patients (22%) attended 3 sessions (mean ± SD = 3.5 ± 1.4; range, 2–6). Fifty-six percent (n = 10) were women. Mean ± SD age was 36 ± 11.5 years, and the range was 21–54 years. The median dose required was 714 mg/d.

Three outcome measures were examined: the Clinical Global Impressions-Severity of Illness scale (CGI-S),[4] the Hamilton Anxiety Rating Scale (HARS),[5] and the Zung Anxiety Status Inventory.[6] Because there were varying numbers of sessions, all analyses were conducted on the baseline and last observation carried forward. Data were collected at monthly intervals for 4 months. Both the CGI-S and HARS showed significant changes between baseline and endpoint (CGI-S: $t_{17} = 4.61$, $P < .001$, Cohen $d = 1.62$; HARS $t_{16} = 3.29$, $P < .01$, Cohen $d = 0.85$). The Zung Anxiety Status Inventory showed a strong trend toward significance ($t_{16} = 2.03$, $P = .06$, Cohen $d = 0.60$). As for 2 measures examining side effects, the patient-evaluated assessment of side effects (Patient Global Impressions scale[4]) trended toward significance ($t_{12} = 1.85$, $P = .09$, Cohen $d = 0.45$), and the clinician-evaluated assessment of side effects (CGI-Improvement scale[4]) showed a significant drop over time ($t_{12} = 2.21$, $P < .05$, Cohen $d = 0.80$).

In this open-label study, acamprosate demonstrated a significant positive effect in decreasing anxiety for most patients. The side effect profile was substantially similar to that reported in the clinical trials. However, these data must be interpreted with caution as preliminary. Limitations to this study include the fact that only 1 clinician was involved in all aspects of the treatment. Although the clinician and the patients rated anxiety separately, the clinician based ratings on interviews with the patients. Thus, there were no truly "blind" raters. In addition, the sample size was modest; however, the effect sizes were substantial.

Acamprosate is a nonaddicting medication. It is not clear that its antianxiety effects are as immediate or obvious as those of the benzodiazepines. These effects are most likely cumulative over time and require taking the medication regularly. Present preliminary results are sufficiently promising to justify larger, more rigorously conducted trials.

REFERENCES

1. Kiefer F, Helwig H, Tarnaske T, et al. Pharmacological relapse prevention of alcoholism: clinical predictors of outcome. *Eur Addict Res.* 2005;11(2):83–91.
2. Verheul R, Lehert P, Geerlings PJ, et al. Predictors of acamprosate efficacy: results from a pooled analysis of seven European trials including 1485 alcohol-dependent patients. *Psychopharmacology (Berl).* 2005;178(2-3):167–173.
3. Cammack J, Ghasemzadee B, Adams R. The pharmacological profile of glutamate-evoked ascorbic acid efflux measured by in vivo electrochemistry. *Brain Res.* 1991;565(1):17–22.
4. Guy W. ECDEU Assessment Manual for Psychopharmacology. US Dept Health, Education, and Welfare publication (ADM) 76-338. Rockville, Md: National Institute of Mental Health; 1976:218–222.
5. Hamilton M. The assessment of anxiety states by rating. *Br J Med Psychol.* 1959;32:50–55.
6. Zung WWK. A rating instrument for anxiety disorders. *Psychosomatics.* 1971;12:371–379.

Marc Hertzman, MD
mhertzman@hotmail.com
Ivy S. Patt, PhD
Lisa A. Spielman, PhD

Author affiliations: Private practice, Rockville, Maryland (all authors).

Financial disclosure: **Drs Hertzman**, **Patt**, and **Spielman** report no financial affiliations or other relationships relevant to the subject of this letter. ***Funding/support:*** None.
doi:10.4088/PCC.08l00714