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Tamoxifen May Help Treat Mania in Patients With Bipolar Disorder

CHICAGO – A small, three-week trial of tamoxifen, a drug typically used to treat breast cancer, indicates that it also may decrease symptoms of mania in patients with bipolar disorder, according to a report in the March issue of *Archives of General Psychiatry*, one of the *JAMA/Archives* journals.

Tamoxifen interferes with the effects of the hormone estrogen, which accounts for its effects against breast cancer, according to background information in the article. However, tamoxifen also inhibits the actions of a family of enzymes known as protein kinase C. Abnormal levels of activity by these enzymes have been associated with bipolar disorder and related dysfunctions, such as distractibility, impaired judgments and disorganized thoughts.

Animal studies and human pilot trials have suggested that tamoxifen may be effective in treating mania—an abnormally elevated mood that features impulsive behavior, higher energy and activity levels, and disconnected thoughts—in patients with bipolar disorder. Ayşegül Yildiz, M.D., of the Dokuz Eylül University Medical School, Izmir, Turkey, and colleagues conducted a clinical trial with 66 patients age 18 to 60, all of whom were diagnosed with bipolar disorder and were currently in a manic state or a mixed state that included mania. Participants were randomly assigned to take tamoxifen (40 milligrams to 80 milligrams per day) or identical placebo tablets twice daily for up to three weeks. Participants in both groups also were given up to 5 milligrams per day of the sedative lorazepam as needed to control their symptoms.

A total of 50 patients—29 assigned to take tamoxifen and 21 assigned to take placebo—completed the 21-day trial. Patients in the tamoxifen group had significantly lower scores on tests used to measure the severity of mania at the end of the three-week period, while those in the placebo group had scores that

slightly increased. Almost half (48 percent) of patients taking tamoxifen responded to the drug—defined as a reduction of at least half in mania scores—compared with 5 percent of those taking placebo, and 28 percent vs. zero achieved cutoff scores for mania remission.

Patients taking tamoxifen also used less lorazepam during the study—an average of 25.2 milligrams compared with 41.8 milligrams for patients in the placebo group. “Moreover, all subjects used less lorazepam as the trial progressed, and the rate of decrease was 2.5 times greater with tamoxifen,” the authors write. Both tamoxifen and placebo were well tolerated.

“The findings encourage further clarification of the role of protein kinase C in the pathophysiologic mechanism of bipolar 1 disorder and development of novel anti-protein kinase C agents as potential antimanic or mood-stabilizing agents,” the authors conclude.

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