Tamoxifen Relieves Symptoms of Mania in Bipolar Disorder Trial

**By Jane Salodof MacNeil**

**Southwest Bureau**

**Paris** — Tamoxifen, a drug that is widely used in the treatment of breast cancer, significantly reduced the manic symptoms of bipolar disorder in a randomized, placebo-controlled trial presented in a breaking news session at the annual congress of the European College of Neuropsychopharmacology.

Dr. Aysegul Yildiz-Yesiloglu reported that 14 of 29 acutely ill patients had had a 50% reduction in their scores on standard measures of mania with tamoxifen treatment. Only 1 of 21 patients improved on placebo during the 3-week trial. Depressive symptoms were not affected.

Although tamoxifen use in breast cancer is based on its antiestrogenic effects, the investigators were drawn to the drug’s activity as a protein kinase C (PKC) inhibitor, according to Dr. Yildiz-Yesiloglu, of Dokuz Eylul University in Izmir, Turkey, where the study was done.

She said the researchers hypothesized that inhibiting the PKC pathway could be important in bipolar disorder because lithium and valproate interfere with PKC signaling. For reasons not well understood, both mood stabilizers can reduce mania despite being structurally different.

Tamoxifen was chosen for the trial because it is the only direct PKC inhibitor approved for use in humans. It had been well tolerated in a pilot study that reported amelioration of manic symptoms in five of seven bipolar patients in the neuropsychiatric research unit at the Detroit Medical Center (Arch. Gen. Psychiatry 2000;57:95-7). Dr. Yildiz-Yesiloglu, currently at Harvard Medical School in Boston, and her colleagues randomized 67 manic patients in the double-blind study. All had provided written consent together with at least one first-degree relative. Six patients in the tamoxifen group and 11 patients in the placebo group dropped out because of severity of symptoms. This left 29 patients randomized to tamoxifen and 21 to placebo who completed the trial. To counteract any potential bias, Dr. Yildiz-Yesiloglu said the researchers performed secondary linear mixed-model analyses incorporating all patients and all observations up to the point a person dropped out the study.

Patients started on 20 mg of tamoxifen twice daily, and the dose was increased up to 40 mg twice daily. The only psychotropic agent they could use during the study was lorazepam as a rescue medication for anxiety. The number of tablets used declined significantly over the course of the study in patients treated with tamoxifen but not in those in the placebo group. Mania scores began dropping within 2 weeks of the start of tamoxifen treatment on both the Young Mania Rating Scale and the Positive and Negative Syndrome Scale. The improvements observed over 3 weeks with both scales were highly significant statistically, compared with placebo.

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