ADHD Drug Eases Anxiety, Not Depression

BY KERRI WACHTER Senior Writer

WASHINGTON — The attention-deficit hyperactivity drug atomoxetine does not appear to improve comorbid depression in adolescents, but it does appear to reduce comorbid anxiety in children and adolescents, according to data from two studies presented at the annual meeting of the Pediatric Academic Societies.

Both trials were sponsored by Eli Lilly & Co., maker of atomoxetine (Strattera).

In the first study, patients aged 8-17 years, who met the DSM-IV diagnostic criteria for both attention-deficit hyperactivity disorder (ADHD) and anxiety disorder (generalized anxiety separation anxiety, or social phobia disorder), were randomized to receive either atomoxetine (87 patients) or placebo (89 patients) in a 12-week trial. The mean age of the patients was roughly 12 years, and boys outnumbered girls 3:1. The target dose of atomoxetine was 1.2 mg/kg per day (split and given twice a day), said Calvin Sumner, M.D., of Eli Lilly.

ADHD symptoms were assessed using the ADHD Rating Scale (ADHDRS). The Pediatric Anxiety Rating Scale total score and the Multidimensional Anxiety Scale for Children (which allows children to rate their own anxiety) were used to assess anxiety symptoms. The last observations were carried forward as a way to minimize any placebo effect, those randomized to receive atomoxetine actually received placebo for the first 2 weeks of the trial. Any patients who had a 25% reduction in anxiety score during that period were allowed to finish the trial but not included in the final analysis.

For the analysis that excluded patients who had a 25% improvement in anxiety score during the first 2 weeks of the trial, those on atomoxetine (55 patients) had a significant improvement in ADHD symptoms from baseline to the end point, compared with those on placebo (58 patients). When all patients were considered, there was a significant improvement in ADHD symptoms for patients on atomoxetine, compared with those on placebo.

In the smaller analysis, there also was a significant improvement in anxiety scores for those on atomoxetine, compared with those on placebo.

Among all patients, a significant improvement in anxiety scores was seen for the ADHD symptoms. Among those on placebo.

Also looking at the full group, the children who received atomoxetine had a greater perceived reduction in anxiety symptoms, compared with those who received placebo, as measured by the Multidimensional Anxiety Scale for Children.

In the second trial, children had to meet the clinical definition of both ADHD and major depressive disorder. “These were kids who really had major depression,” Dr. Sumner said.

The patients, aged 12-18 years, were randomized to receive 9 weeks of treatment with atomoxetine (72 patients) or placebo (70 patients). Boys outnumbered girls 3:1.

The target atomoxetine dose was 1.2 mg/kg each day, through patients were titrated up to a dose of 1.8 mg/kg each day. Both placebo and atomoxetine were given once a day. The response of atomoxetine dose was measured using the 18-question ADHDRS. Depressive symptoms were measured using the Children’s Depression Rating Scale. Patients were assessed using the Young Mania Rating Scale, as a way of determining whether the depression experienced by these adolescents was a heralding event for bipolar disorder or true depression.

The finding corroborates and extends existing literature linking low total cholesterol and aggressive behavior in adults. Low cholesterol may be a risk factor for aggressive behavior, a risk marker for other biologic substances or genotypes that predispose to such behavior, or a biologic marker for poor prognosis. In any case, if confirmed by prospective studies, these findings may assist pediatricians in contributing to schools and to violence prevention, the investigators said (Am J Epidemiol. 2005;161:691-9).

The data come from 4,852 children and adolescents aged 6-17 years (mean 16) whose mothers were interviewed by National Health and Nutrition Examination Survey (NHANES III), conducted during 1988-1994.

None attended special schools or classes as a result of intellectual or physical health impairment. Serum cholesterol was measured, and a variety of neuropsychiatric tests administered. The proportion who had ever been suspended from school was 15.38% among children with serum cholesterol levels less than 145 mg/dL, compared with 6.25% among those with cholesterol levels of 145 mg/dL and above. After adjustment for age and gender, the odds ratio for school suspension for low vs. high cholesterol was 1.71.

On the other hand, serum cholesterol was not predictive of ever seeing a psychologist, being shy when meeting new persons, or having difficulty getting along with others: for children.

Possible biologic mechanisms to explain the association between serum lipids and violence involve the role of cholesterol metabolism and aggressive behaviors. The causal relationship remained significant even after accounting for potential confounds such as alcohol and tobacco consumption, the investigators said.