Atomoxetine Improves ADHD, Anxiety Disorder

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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 with less than 25% improvement in anxiety during the first 2 weeks of the trial, those on atomoxetine (55 patients) had a significant improvement in ADHD scores 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 scores 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 those on atomoxetine, compared with those on placebo.

Decreased appetite was the only adverse event that occurred more frequently in the atomoxetine group.

In the second trial, adolescents 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, though patients could go up to a dose of 1.8 mg/kg each day. Both placebo and atomoxetine were given once a day.

The response of ADHD symptoms 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 ADHD and depression scores at 9 weeks were analyzed as change from baseline, with last observation carried forward. Treatment emergent mania was described as a patient who started with a score of less than 15 on the mania scale, and at the end point the score was 15 or greater.

"Atomoxetine really helped depression. There was a considerable reduction in the depressive rating scales. The other side of the story is, so did placebo," Dr. Sumner said. Placebo showed a very strong effect on depressive symptoms that was independent of its effect on ADHD.

"So this was inconclusive. There was no evidence—that was separable from placebo—that atomoxetine had any benefit in reducing depressive symptoms," he said.

Two patients in each group had treatment emergent mania, a result that was not interpretable. In terms of adverse events, nausea and decreased appetite were more common in the atomoxetine group. Importantly, there were no adverse events involving suicidal ideation or suicidal behavior in either group. ■

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