Atypicals May Mean Metabolic Changes for Youth

**Atypical Antipsychotics Show Promise for Bipolar Children**

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**Mid-Atlantic Bureau**

Stockholm — Atypical antipsychotics appear to be a good choice for treating children with bipolar disorder, and they also show promise for treating psychotic symptoms in these patients. Joseph Biederman, M.D., reported in a presentation at the annual congress of the European College of Neuropsychopharmacology.

Although rare, childhood bipolar disorder is among the most severely disabling pediatric mental disorders. Because this disorder has been assumed to be extremely rare, no standard treatment options exist. “Children with bipolar disorder are frequently treated with many medications with unclear efficacy and inadequate safety data,” said Dr. Biederman of Harvard Medical School, Boston.

Dr. Biederman undertook an 8-week randomized open-label study of the efficacy of olanzapine (Zyprexa), risperidone (Risperdal), or quetiapine (Seroquel)—the three most widely prescribed drugs in this particular class.

The open-label study included youth between the ages of 5 and 18 years with a DSM-IV diagnosis of psychotic, mood, and/or disruptive behavior disorders who had begun or switched to treatment with one of the three medications within 7 days of the start of the investigation. Exclusion criteria included a history of any eating disorder, active thyroid or severe medical disorder, and pregnancy.

At least 50% of the children in each group showed a marked response to treatment, though weight gain, particularly with olanzapine, was substantial.

“Second-generation antipsychotics are widely used in young patients, but limited comparative data exist on their effects on body composition and lipid metabolism,” said Correll of Zucker Hillside Hospitai in Glen Oaks, N.Y. He, along with his colleagues, prospectively evaluated the relative effects on these factors of olanzapine (Zyprexa), risperidone (Risperdal), or quetiapine (Seroquel)—the three most widely prescribed drugs in this particular class.

The study evaluated the change in body mass index (BMI), fat mass and percentage fat, and waist circumference of all the 174 youth in the study—including 57 on olanzapine, 70 on risperidone, and 47 on quetiapine—increased significantly, Dr. Correll said. The greatest increase in prep-treated and those cotreated with olanzapine experienced extreme weight gain—described as an increase in weight from baseline of 7% or more—compared with 57% and 43% of risperidone and quetiapine subjects, respectively. All of the study participants experienced significant increases in total cholesterol, LDL cholesterol, and triglycerides. A separate analysis comparing pretreated and antipsychotic-naive patients showed that only the olanzapine-induced cholesterol and triglyceride increases remained significant. “Nevertheless, 19.9% of the youths experienced new-onset dyslipidemia, with similar rates for all three drugs,” Dr. Correll reported.

Multiple regression analysis identified the following correlates of weight gain: weight increase at 4 weeks, baseline-to-end increases in leptin, body mass index (BMI), fat mass and percentage fat, and waist circumference of all the 174 youth in the study—including 57 on olanzapine, 70 on risperidone, and 47 on quetiapine—increased significantly, Dr. Correll said. The greatest increase was seen in those youths taking olanzapine followed by risperidone, then quetiapine, he said. Additionally, nearly 81% of the subjects taking olanzapine had increased appetite (29%), gastrointestinal disturbances (18%), and myalgia (10%). Weight gain was highest in the olanzapine group (mean 4.7 kg), significantly greater than the weight gain for risperidone (2.1 kg), quetiapine (1.9 kg), and ziprasidone (0.8 kg).

Some of these medications also appear effective in decreasing psychotic symptoms in pediatric bipolar patients. Dr. Biederman reported in a separate poster. In a similarly designed 8-week open-label trial, 110 children with bipolar disorder were randomized to risperidone, quetiapine, or olanzapine. The children were aged 6-17 years, and 26% had a history of psychosis. By the trial’s end, there was a significant reduction of 10 points on the Brief Psychiatric Rating Scale that did not differ between groups. Differences did emerge in changes measured by the YMRS. All the drugs were associated with significant improvements in symptoms of mania, but only risperidone was associated with a significant improvement in symptoms of psychosis.

Side effects were mild and included increased appetite (28%), gastrointestinal discomfort (20%), headache (18%), sedation (18%), and myalgia (10%). Weight gain was highest in the olanzapine group (mean 4.7 kg). At least 56% of the risperidone group had a mean of 1.97 kg, and those in the quetiapine group gained a mean of 1.4 kg. There was a statistically significant increase in the weight gain in children treated with risperidone (33.9 ng/mL) and olanzapine (5.1 ng/mL), but not quetiapine (0.5 ng/mL), Dr. Biederman said.