Atypicals May Mean Metabolic Changes for Youth

BY DIANA MAHONEY
New England Bureau

BERLIN — The most common second-generation antipsychotics prescribed to young people with various psychotic, mood, and behavioral disorders adversely affect all components of body composition and lead to dyslipidemia in this patient population, a study has shown.

Youths who have never taken antipsychotics and those cotreated with olanzapine (Zyprexa) and divalproex (Depakote) who experience significant early weight gain are at highest risk for the metabolic changes, Christoph U. Correll, M.D., said in a presentation at the 16th World Congress of the International Association for Child and Adolescent Psychiatry and Allied Professions.

"Second-generation antipsychotics are widely used in young patients, but limited comparative data exist on their effects on body composition and lipid metabolism," said Dr. Correll of Zucker Hillside Hospital 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 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. All subjects were assessed at baseline and monthly for height, weight, body mass index, total fat mass and percentage fat (via bioimpedance measurement), and waist circumference. In addition, fasting blood leptin, prolactin, and antipsychotic serum levels were measured at baseline, week 4, and week 12.

After 12 weeks of treatment, the weight, body mass index (BMI), fat mass and percentage fat, and waist circumference of all of 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 all measures was seen in those youths taking olanzapine, followed by risperidone, then quetiapine, he said. Additionally, nearly 81% of the subjects taking 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, antipsychotic naive status, olanzapine treatment, and divalproex cotreatment.

With respect to lipids, predictors for both cholesterol increase and for triglyceride increase were low baseline cholesterol level, antidepressant cotreatment, and 12-week BMI change. Male gender was a predictor for cholesterol increase only.

"What we're seeing is that these drugs have an impact on all aspects of body composition, and they lead to dyslipidemia, which further increases the cardiovascular risk profile. We're not suggesting they shouldn't be used because obviously these drugs have an important role, but they should be used carefully, and these side effects should be monitored regularly.

"Pretreatment dietary and lifestyle counseling, particularly among those at highest risk, cannot be overlooked," Dr. Correll concluded. ■

Atypical Antipsychotics Show Promise for Bipolar Children

BY MICHELE G. SULLIVAN
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 poster session 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.

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

Dr. Biederman undertook an 8-week randomized open-label study of the efficacy of olanzapine (Zyprexa), risperidone (Risperdal), quetiapine (Seroquel), and ziprasidone (Geodon) in children with bipolar disorder. The 103 patients were aged 6-17 years. At baseline, they were all markedly impaired according to the Young Mania Rating Scale (YMRS). By the study's end, the mean dosages were 7.5 mg/day for olanzapine, 250 mg/day for quetiapine, 1.4 mg/day for risperidone, and 56 mg/day for ziprasidone.

After 8 weeks, there were no statistically significant differences between the groups in response. At least 50% of the children in each group showed a marked response (either a Clinical Global Impression rating of much or very much improved or a 30% reduction in symptoms).

Half the children in both the olanzapine and ziprasidone groups experienced a robust response to the therapy (Clinical Global Impression rating of much or very much improved and a 30% reduction in YMRS scores). The rate of robust response was higher in the quetiapine (55%) and risperidone groups (75%).

Weight gain over the study was substantial but varied significantly across study groups. Olanzapine was associated with an increase (4.9 kg) that was 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 (29%), gastrointestinal discomfort (20%), headache (18%), sedation (18%), and myalgia (10%). Weight gain was highest in the olanzapine group (mean 4.7 kg). Those in the risperidone group gained 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 prolactin levels in subjects treated with risperidone (33.9 ng/mL) and olanzapine (5.1 ng/mL), but not quetiapine (0.5 ng/mL), Dr. Biederman said. ■