Antipsychotics' Side Effects More Common in Young

BY JANE SALODOF MACNEIL
Southwest Bureau

PARIS — A series of studies in children and adolescents suggests that they may be more vulnerable than adults to some side effects of antipsychotics, Dr. Celso Arango warned at the annual congress of the European College of Neuropsychopharmacology.

Dr. Arango, head of the adolescent unit at Hospital Gregorio Marañón in Madrid, cited dyskinesia, hyperprolactinemia, sleepiness and sedation, and weight gain among the side effects identified by the investigations at his hospital.

Despite a sixfold increase from 1993 to 2002 in the prescribing of antipsychotics to youths in the United States, he said, little is known about these drugs' safety and tolerability in children and adolescents. Long-term effects on sexual development, age-specific requirements in dosing, and impact on cognition have not been adequately studied in young patients, Dr. Arango said.

"Children and adolescents may not only be more vulnerable to some side effects but also some side effects may specifically interfere with functioning and induce lack of adherence in this population," he said.

Singling out the potential impact on learning, he cautioned, "Some of these side effects may mean that our patients do not gain what they should be gaining [from school] because they cannot pay attention in class or they are too sleepy."

The first study described by Dr. Arango followed 110 patients for 1 year. Their average age was 14.5 years, and 60% were males. Only about one-third were being treated for psychotic disorders. Affective disorders and eating disorders accounted for about 14% of the population. Other diagnoses included pervasive development disorders, tic disorders, attention-deficit hyperactivity disorder, and mental retardation.

Many patients were prescribed more than one antipsychotic during the course of the year: 45% were given a first-generation antipsychotic, 84% a second-generation agent, and 9% both combined. Other psychotropic drugs also were prescribed.

Preliminary analysis of extrapyramidal symptoms showed a significant increase in dyskinesia, rising from 30.9% of 110 patients to 47.8% of 86 patients between the first and second visits. By the third visit, it fell back to 33.3% of 54 patients. Twenty percent of patients had never before taken an antipsychotic, Dr. Arango added; 11.8% of them experienced dyskinesia.

He also reported that hyperprolactinemia was found in 81% of serum samples taken at baseline and that youths treated with first-generation antipsychotics had significantly higher scores on a Parkinsonism subscale. Risperidone (Risperdal) was associated with a significantly higher number of dystonic episodes, he said, and with increases in prolactin and body mass index (BMI).

Treatment with olanzapine (Zyprexa) also led to a significant increase in BMI.

The second study compared 60 patients on antipsychotics for less than 1 month with 66 patients treated for more than 1 year. The average age was 15.6 years.

Dr. Arango reported finding mild dyskinetic movements in 21.7% of short-term patients and 37.9% of long-term patients. Tic-like eye movements, jerky finger and wrist movements, jerky arm movements, and rigid masked facial expression were significantly more common in the young people on antipsychotics for more than a year.

'Some side effects may specifically interfere with functioning' in children and adolescents.

DR. ARANGO

The third study, also reported in a poster at the meeting, was the only one to show no ill effects of antipsychotic use. Dr. Arango's group performed electrocardiograms on 111 consecutive adolescents (mean age 14.9 years) who were treated with antipsychotics for more than 2 weeks after admission to an inpatient unit. None had a pathologically prolonged QTc interval, and no relevant cardiovascular side effects were detected.

The fourth study, also reported in a poster, randomized 24 first-episode adolescent psychosis patients to quetiapine and 26 to olanzapine.

The two groups, stratified by age (mean age 15.9 years) and gender, included patients diagnosed with schizophrenia, bipolar disorder, and other psychotic disorders. Sixteen patients in each arm completed the 6-month study.

None of the dropouts was attributed to adverse events.

Dr. Arango reported that whereas significantly more patients on olanzapine experienced rigidity, diminished sexual desire was significantly more common with quetiapine. Both groups gained weight during 6 months of treatment, but the patients on olanzapine gained significantly more: 16.5 kg on average vs. 5.4 kg.

In addition, a review of subjective side effects showed about 70% of patients in both groups complaining of sleepiness and sedation. More olanzapine patients reported concentration difficulties and failing memory. Constipation and palpitations/tachycardia were cited more often by those on quetiapine (Seroquel).

The fifth study followed 67 patients in the first-episode clinic at Dr. Arango's unit for 6 months. The population comprised 22 patients on risperidone, 20 on olanzapine, and 25 on quetiapine. Their mean age was 15.7 years, about two-thirds were males, and none had previously taken an antipsychotic. About half had schizophrenia.

The male patients gained more weight, the patients' HbA_{1c} was related to changes in BMI, and those on olanzapine had significantly increased systolic blood pressure.

In conclusion, he recommended that clinicians assess risk/benefit ratios carefully when prescribing antipsychotics to children and adolescents, especially if the patient has a nonpsychotic disorder. He also urged frequent reconsideration of whether these medications need to be continued in patients who are not psychotic and said that all young patients should be monitored for adverse metabolic and endocrine effects. ■

Autism Disorders More Prevalent Than Thought in England

BY MARY ANN MOON
Contributing Writer

The prevalence of autism and related disorders was found to be "substantially greater" than expected in a screening of nearly 57,000 children in England.

The prevalence of autism spectrum disorders was 116 per 10,000 population. Previous estimates from research published in the past 6 years pegged the prevalence at only 30-90 cases per 10,000.

Before that, prevalence was widely accepted to be only four to five cases per 10,000, according to Dr. Gillian Baird, who is affiliated with Guy's and St. Thomas' NHS Foundation Trust, London, and her associates (Lancet 2006;368:210-15).

These findings indicate that autism spectrum disorders are not the rare anomalies that the public has always considered them to be but instead affect about 1% of children aged 9-10 years, they added.

In an editorial comment accompanying their report, Dr. Hiroshi Kurita of Zenkoku Ryoiku Sodan Centre, Tokyo, speculated that the recent surge in prevalence is more likely attributable to improved case ascertainment rather than to a true increase in the disorders (Lancet 2006;368:179-81).

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Dr. Baird and her associates screened a population cohort of 56,946 children born 1990-1991 in 12 districts in South Thames, England.

The subjects were aged 9-10 years at assessment, "an age when it is likely that all true cases of autism spectrum disorders, or at least those in whom the condition was causing significant functional impairment, would have come to the attention of health and education services."

They used data from the special needs register of the department of child health services to identify those who might have an autism spectrum disorder.

The registry also listed all children who attended special schools or mainstream schools and whose files contained a statement of educational needs indicating they had language, learning, behavior, or medical problems requiring intervention.

The researchers also collaborated with local clinicians to search registers of children known to various therapy services for having social or communicative impairment or autism spectrum disorders.

In all, they identified 255 children with a current diagnosis of autism spectrum disorders and another 1,515 considered to be potential candidates for the diagnosis.

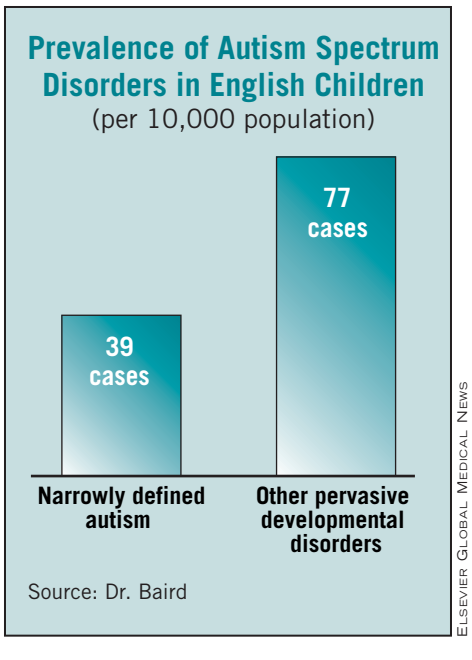
The investigators screened these subjects using a parent-report questionnaire on characteristic autistic behavior. They then conducted detailed clinical assessments of a random sample of 255 subjects (223 boys, 32 girls). This included in-person observation and scoring on two diagnostic tools, the autism diagnostic interview–revised (ADI-R) and the autism diagnostic observation schedule–generic (ADOS-G); it also included review of teacher reports, psychometric testing results, and other extensive case material.

Based on these results, Dr. Baird and her associates estimated the prevalence of autism spectrum disorders to be 116 per 10,000 population.

When the data were broken down into subtypes, the prevalence of narrowly defined autism was 39 per 10,000, and the prevalence of other pervasive developmental disorders was 77 per 10,000.

The National Autistic Society, the leading charity for people with autism spectrum disorders in the United Kingdom, says there are about 520,000 people with autism spectrum disorders in the U.K.

Mounting evidence shows that genetic factors may play a prominent role in the causes of autism spectrum disorders. In addition, twin studies have suggested a genetic vulnerability to ASD. The disorders can be diagnosed in young toddlers and even in infants. But screening advances have not yet filtered to clinical practice. ■



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