Antipsychotics Tied to Adverse Metabolic Events

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Antipsychotic medications are associated with adverse metabolic and cardiovascular events in children and adolescents who are treated in usual-care settings, according to a report.

In a retrospective cohort study, children who are treated with antipsychotics, particularly those who were also receiving antidepressants or mood stabilizers, were two to three times more likely than those not taking the drugs to develop metabolic disruption and cardiovascular abnormalities, notably obesity, type 2 diabetes, cardiomegaly, nonspecified heart disease, tachycardia, nonspecified arrhythmia, and orthostatic hypotension/syncope, reported Dr. Roger S. McIntyre of the University of Toronto and his associates.

When assessing the risk-benefit profile of this class of drugs, physicians "need to give careful consideration to possible metabolic disruptions or cardiovascular toxic effects, especially in individuals with comorbid metabolic conditions and those receiving concomitant psychotropic medications," the investigators said.

They examined adverse events among children and adolescents who were included in the South Carolina Medicaid database in 1996-2005. In all, 4,140 patients were prescribed atypical or conventional antipsychotics (aripiprazole, ziprasidone, quetiapine, risperidone, olanzapine, haloperidol, or fluphenazine). A random sample of 4,500 children who were not treated with antipsychotics served as controls.

The treated children and adolescents had primary diagnoses of ADHD, conduct disorder, oppositional-defiant disorder, major affective disorder, schizophrenia, and other psychotic disorders. Comorbid conditions included convulsions, CNS disorder, organic brain syndrome, severe mental retardation, substance-related disorder, and congenital heart defects. Nearly 80% of these patients were concomitantly taking antidepressants that can induce weight gain, and many were taking psychostimulants, SSRIs, and mood stabilizers.

Compared with controls, the patients who were treated with antipsychotics were more likely to develop obesity (odds ratio, 2.13), type 2 diabetes (OR, 3.23), cardiovascular conditions (OR, 2.70), and orthostatic hypotension (OR, 1.64). Girls, adolescents, and patients on combination therapy were at highest risk of these adverse effects, Dr. McIntyre and his associates said (Arch. Pediatr. Adolesc. Med. 2008;162:929-35).

Children treated with antipsychotics also were two to three times more likely than those not taking the drugs to develop cardiovascular abnormalities.

"Of major public health concern is that, by the end of the study period, 25% of the sample had [one to three] comorbid chronic medical conditions (metabolic and cardiovascular) in addition to their psychiatric disorder," they added.

"We can speculate that the antipsychotic treatment may have predisposed or exacerbated metabolic changes subsequently leading to cardiovascular events. Other hypothetical mechanisms could be ECG changes (such as QT-interval prolongation), procoagulation effects, or direct effects on blood pressure via adrenoreceptor antagonism," the investigators noted.

The study findings show that "psychiatric and primary care practitioners need to familiarize themselves with the potential for cardiometabolic toxic effects associated with antipsychotics in pediatric populations, and use them sparingly in children displaying early-onset risk factors," Dr. McIntyre and his colleagues said.

Dr. McIntyre has received research grants from, served on advisory boards of, served on speakers bureaus of, and participated in CME activities of Eli Lilly & Co., the Stanley Medical Research Institute, the National Alliance for Research on Schizophrenia and Depression, AstraZeneca, Biovail Corp., Bristol-Myers Squibb Co., the France Foundation, GlaxoSmithKline, Janssen-Ortho Inc., Organon, Lundbeck, Pfizer Inc., Solvay/Wyeth, Shire PLC, 13CME, and Physicians Postgraduate Press Inc. ■