Medication and Diagnostic Issues

This section of Focus on Childhood and Adolescent Mental Health presents timely information on the topics of polypharmacy, the olanzapine safety profile, the role of conduct disorder in the development of substance use disorder in adolescents with bipolar disorder, and autistic spectrum disorder symptoms in a group of adolescent suspects of sex offenses.

Recent attention has focused on the use of polypharmacy for children with psychiatric disorders. McIntyre and Jerrell examine the use of polypharmacy for treatment of major depressive disorder in children and adolescents using data obtained from the South Carolina Medicaid program between the period January 1996 and December 2005. Consistent with clinical expectations, they found that the likelihood of psychotropic polypharmacy increased when there were comorbid psychiatric disorders, with odds ratios ranging from 1.5 for 1 comorbid disorder to 9.8 for 6 comorbid disorders compared to an odds ratio of 0.4 for major depressive disorder alone.

With regard to antidepressant use, individuals were switched from tricyclic antidepressants to selective serotonin reuptake inhibitors (SSRIs) in 1996 and 1997 and from SSRIs to serotonin-norepinephrine reuptake inhibitors between 1998 and 2005. Of note, the use of antidepressants declined between 2002 and 2005, which was prior to the U.S. Food and Drug Administration warning regarding suicidality. An increase in the use of concomitant antipsychotics was found over time. Given the significant extent of polypharmacy in this sample, it is critical that further controlled trials be conducted to determine the efficacy and safety of combination medication treatments for children and adolescents with major depressive disorder.

With the increased use of atypical antipsychotics in youths, it is essential for clinicians to be informed about the safety profile of these medications in this population. Kryzhanovskaya and colleagues from Lilly Research Laboratories report olanzapine safety data for a total of 633 adolescents aged 13–17 years old with schizophrenia or bipolar I disorder and compare the findings to adult data. The adolescent olanzapine-treated sample included data from 2 double-blind placebo-controlled trials with open-label extension phases and 2 open-label studies. The mean daily dose of olanzapine in these trials ranged from 2.5 mg to 20.0 mg with a mean daily dose of 10.6 mg/day.

The most common adverse events in olanzapine-treated adolescents were increased weight (31.7%), somnolence (19.8%), increased appetite (17.4%), headache (16.7%), and sedation (14.1%). Of particular concern, more adolescents than adults had significant weight gain (7.4 kg vs. 3.2 kg) and gained ≥ 7% of their baseline weight (65.1% vs. 35.6%) at 32 weeks and had significantly greater increases in prolactin levels (4.7 µg/L). Adolescents treated with olanzapine had statistically significant baseline-to-endpoint mean changes in all metabolic parameters. Twelve percent of olanzapine-treated adolescents had alanine aminotransferase levels 3 times greater than the upper limit of normal compared to 2% of placebo-treated adolescents. There were no suicides in the adolescent olanzapine-treated patients. Although the overall safety profile was

similar between adolescents and adults, the findings of greater weight gain and elevated prolactin levels in adolescents are of significant concern. Clinicians will need to carefully weigh the risk-benefit ratio prior to consideration of the use of olanzapine in adolescents. It is also important to recognize that the database did not include children, and the safety profile of olanzapine in this younger age group remains to be determined.

Wilens and colleagues answer the important clinical question of whether conduct disorder mediates the development of substance use disorder in adolescents with bipolar disorder. The sample included 105 adolescents with bipolar disorder and 98 non–mood disorder control subjects based upon structured diagnostic interviews. Lifetime criteria for conduct disorder were met by 55% of the bipolar sample. No significant differences were found in the risk for substance use disorder between those adolescents with bipolar disorder and those adolescents with bipolar disorder and preexisting conduct disorder.

A comparison of adolescents with early-onset conduct disorder to those with late-onset conduct disorder found no difference in the age of development of substance use disorder. The investigators conclude that bipolar disorder in adolescents increases risk for substance use disorder; however, early-onset conduct disorder does not substantially increase the risk for substance disorder beyond that which is found for bipolar disorder alone. It is noteworthy that those adolescents with bipolar disorder and conduct disorder had a lower global assessment of functioning and more complicated substance use disorders including drug plus alcohol use disorders.

'T Hart-Kerkhoffs and colleagues raise the issue of whether suspects of sex offenses have more symptoms of autistic spectrum disorder that may lead to social misjudgment and inappropriate sexual behavior than those youths without autistic spectrum disorder. The study was conducted in the Netherlands and included 175 adolescent males suspected of sex offenses, 114 adolescent males with autistic spectrum disorders, and 500 adolescent males without psychiatric disorders. The Children's Social Behavior Questionnaire was used to evaluate symptoms of autistic spectrum disorder in this sample.

It was found that the juvenile sex offenders had significantly higher levels of autistic spectrum symptoms than the control group, but those scores were significantly lower than those of the group with autistic spectrum disorders ($p < .05$). In a comparison of subgroups of sex offenders, solo peer offenders and child molesters had higher levels of autistic spectrum disorder symptoms than group sex offenders. With regard to autistic spectrum disorder symptomatology, lack of social understanding and repetitive and stereotyped behavior were higher in the juvenile sex offender group compared to the control group. Since the findings from this study were based upon a questionnaire that was completed by parents or caregivers, it is important for future studies to include structured diagnostic interviews to further clarify whether there is an increased diagnosis of autistic spectrum disorders in adolescents who have committed sexual offenses.

Karen Dineen Wagner, M.D., Ph.D.
Deputy Editor
kwagner@psychiatrist.com

Editor's Note: We encourage authors to submit papers for consideration as a part of our Focus on Childhood and Adolescent Mental Health section. Please contact Karen D. Wagner, M.D., Ph.D., at kwagner@psychiatrist.com.