EXPERT COMMENTARY

Antipsychotics and Kids: Data Mostly Reassuring

Figuring out the safest treatments for pediatric patients with psychiatric disorders has never been more challenging. This is particularly the case for young patients with psychotic disorders, bipolar disorder, autism, and disruptive behavior disorders.

BY CHRISTOPH U. CORRELL, M.D.

However, strong new efficacy data emerging for second-generation antipsychotics in the treatment of these young patients are reassuring, at least regarding efficacy. We now have data from randomized, placebo-controlled trials in more than 3,500 children and adolescents with psychosis, bipolar mania, autism, and aggression. The numbers are clear: These medications work. Between 2 and 10 patients need to be exposed to second-generation antipsychotics to get 1 additional responder, compared to placebo. These results are comparable to those found in adult studies.

The strongest effect sizes were found for aggression/irritability in autism and disruptive behavior disorders, followed by bipolar mania, and finally, schizophrenia—which is most difficult to treat.

Most of the available data, however, come from short-term trials, and controlled long-term and maintenance study data are largely absent.

Still, the reality is that youth who are treated with second-generation antipsychotics are particularly vulnerable for numerous adverse effects. Compared with adults, children and adolescents seem to have higher risks of sedation, withdrawal dyskinesias, and elevations of prolactin, weight gain, and dyslipidemia.

This risk profile raises these questions: How sick does a child need to be—short of frank psychosis—to justify the use of antipsychotics? What other, lower-risk pharmacologic treatments or non-pharmacologic treatments should troubled children receive and fail first before a second-generation antipsychotic is used?

As always, when such difficult questions of individualized risk-benefit evaluation are raised, these decisions must be made on a case-by-case basis. Relevant related questions for the clinician and family are: Can the kid stay in or go back to school? Is the youngster able to maintain close relationships with peers? Is the family environment threatened by the child's behavior and level of symptomatology? It is relevant to recognize that if a child stagnates, he or she is really falling behind peers and age-normed expectations.

Children are expected to grow, develop, expand. If they cannot function in school, or with family and peers, that is a big problem. Another factor is distress. If the family is distressed, that constitutes a problem that ultimately will affect the child as well as any existing siblings.

Despite the risks associated with medications, starting with lower risk approaches, such as using behavioral therapy, often proves impractical, especially in the more severely affected youth. For example, some patients or families can be so disorganized that they might not come in for therapy. Or the child is so aggressive or disorganized that the family does not want to deal with him or her.

When medication is started, the best approach is to use those with the best risk-to-benefit ratio, with the aim to maximize efficacy while minimizing adverse effects.

It appears to be general consensus, both in adult and pediatric psychiatry, that the efficacy of medications in treating psychosis and mania is difficult to predict, whereas the side-effect profiles are much easier to predict. If one chooses a lower side-effect agent first, one is more likely to see a positive effect than if one reserves it after higher-risk agents have failed already. This is because prior nonresponse predicts future nonresponse. One should consider reserving higher-risk agents for those patients who do not respond to agents with a more favorable benefit-to-risk ratio. This way, patients who are likely to respond to numerous agents will end up being stabilized on the lower-risk agents.

Based on the available data and the biggest concern about the long-term risk of weight gain and metabolic abnormalities, it appears that aripiprazole and ziprasidone currently have the best data for having a more favorable risk-benefit ratio. But neither agent is weight neutral; they also can be associated with relevant weight gain.

But the weight generally starts to flatten out earlier, while the efficacy is most likely similar to the other agents. Will those two medications help all patients? They are unlikely to be able to be helpful and well tolerated for every patient. This is not surprising, considering the heterogeneity of patients and their response to medications. Not even clozapine benefits all patients with psychosis.

See related articles on pages 14 & 15.

Recent data finding little evidence for superior efficacy of second-generation antipsychotics over first-generation antipsychotics in adults (N. Engl. J. Med. 2005 353:1209-23) and youth (Am. J. Psychiatry 2008;165:1420-31) with schizophrenia while showing relatively little weight gain increased debates about whether high- or mid-potency antipsychotics also constitute a relatively safe treatment option for youngsters.

However, data suggesting a significantly greater risk for parkinsonism, akathisia, and tardive dyskinesia and a lack of evidence for lower weight gain compared to aripiprazole and ziprasidone do not seem to argue sufficiently for first-generation antipsychotic use as a first-line strategy in youth.

Prescribing antipsychotics to anyone—especially children and adolescents—is a sobering task. The reality, however, is that some seriously ill patients need these medications to restore their functionality. If we choose to use these powerful medications, however, it is also our job to monitor each patient's treatment outcomes. This is particularly relevant when it comes to monitoring body weight, and fasting blood glucose and lipids. Such monitoring should be performed at the time of initiation of antipsychotic treatment, at 3 months and 6-monthly thereafter (J. Acad. Child Adoles. Psychiatry 2008;47:9-20).

Healthy lifestyle instruction and treatment, as well as psychosocial interventions, should be used to optimize outcomes. Moreover, medications should only be used for as long as needed.

Without such individualized approaches that adjust the treatment regimen based on quantified outcomes, we cannot optimize the treatment in youth who are developing and changing because of the environment they grow up in, their psychiatric condition(s), and the treatments we prescribe. ■

DR. CORRELL *is a child and adolescent psychiatrist affiliated with the department of psychiatry at the Zucker Hillside Hospital, Queens, N.Y. He reports serving as a consultant, adviser, and/or safety monitor for several pharmaceutical companies, including Actelion, AstraZeneca, Bristol-Myers Squibb, Eli Lilly, GlaxoSmithKline, Hoffmann-La Roche, Lundbeck, Medicure, Ortho-McNeil-Janssen, Otsuka, Pfizer, Schering-Plough, Supernus, Takeda, and Vanda. He is seeking referrals for a 6-month study in New York and three other sites that aims to understand how best to reduce weight gain in youth aged 8-19 who have gained >10% of body weight during antipsychotic treatment. Treatment is free, and subjects will be reimbursed for their time and effort. For more information, e-mail him at ccorrell@lij.edu.*

LETTERS

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LETTERS

Two Sides to Chronic Pain Problem

Although I don't disagree that there may be some undertreated chronic pain out there, prescription medication abuse, diversion, and misuse is such a huge problem in my practice and in the country as a whole, that I feel we are on dangerous ground when we proclaim we are undertreating pain ("Chronic Pain Called a Public Health Problem," CLINICAL PSYCHIATRY NEWS, December 2009, p. 4).

I do see the dilemma of untreated pain, but there is also a massive problem of medication misuse and diversion. We frequently only look at one side of the problem, and I think that it is unwise to discuss one side without the other.

Roger Hill, M.D., M.P.H.
Glen Alpine, N.C.

Correction

An article about a study on the impact of the economic downtown on the prevalence and treatment of addiction in the United States ("Economic Woes Are Taking Toll on Addiction Services," December 2009, p. 56) incorrectly reported the city in which the investigators are based. Paul Roman, Ph.D., and Amanda J. Abraham, Ph.D., are with the University of Georgia, Athens.