

For Girls on Risperidone, Don't Measure Prolactin

BY PATRICE WENDLING
Chicago Bureau

NEW YORK — A 6-year-old girl with autism is treated with risperidone 0.5 mg twice daily, and after 2 months of treatment her behavior is improved, and there are no noted side effects. But her serum prolactin is clearly elevated for her age at 45 ng/mL. What should you do?

Nothing. In fact, her serum prolactin shouldn't have been measured in the first place, Dr. Harold E. Carlson said at a psychopharmacology update sponsored by the American Academy of Child and Adolescent Psychiatry.

Secretion of prolactin is primarily regulated by tonic inhibition by dopamine, which is secreted by the hypothalamus and acts on D2 dopamine (DA) receptors in the pituitary gland. Most antipsychotics have D2 DA antagonist activity and therefore raise serum prolactin.

Atypical antipsychotics vary in their affinity for the D2 DA receptor and in their propensity to cause hyperprolactinemia, which is characterized by amenorrhea and oligomenorrhea in women of reproductive age, breast enlargement or engorgement in women and men, galactorrhea, decreased libido, erectile dysfunction, osteoporosis, failure to enter or progress through puberty, and possibly hirsutism in women.

The young autism patient is prepuber-

tal and has no ovarian function, so there is nothing for her prolactin to inhibit, said Dr. Carlson of the division of endocrinology at the State University of New York at Stony Brook. In the absence of estrogen priming, it is unlikely she will have breast enlargement or galactorrhea.

Moreover, prolactin levels often spontaneously decrease over time despite con-



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DR. CARLSON

tinued antipsychotic therapy, even at the same dosage. A post hoc analysis of data from five clinical trials in 700 children and adolescents, aged 5-15 years, reveals that prolactin levels in children receiving long-term risperidone (Risperdal) tend to peak within the first 2 months and then steadily decline to values within or very close to normal within 3-5 months (*J. Clin. Psychiatry* 2003;64:1362-9).

A similar trend in prolactin levels was identified in a large 52-week unpublished study involving 542 children conducted by Dr. Christoph U. Correll and his colleagues at the Zucker Hillside Hospital in

Glen Oaks, N.Y., Dr. Carlson reported.

Risperidone is the most potent prolactin elevator, followed by haloperidol (Haldol), olanzapine (Zyprexa), ziprasidone (Geodon), and quetiapine (Seroquel). Clozapine (Clozaril) is relatively neutral, and aripiprazole (Abilify)—a partial D2 DA agonist—suppresses prolactin below baseline levels. It is sometimes useful to combine aripiprazole or a prolactin-neutral agent if discontinuation of a prolactin-raising antipsychotic is not an option, Dr. Carlson said.

First and foremost, inquire about menstruation, nipple discharge, sexual functioning, and pubertal development in all patients receiving antipsychotics; if they are normal, there is no need to measure serum prolactin, he said.

If prolactin is elevated in an asymptomatic patient, perform a pregnancy test and check thyroid-stimulating hormone and serum creatinine to rule out other causes of hyperprolactinemia. Because estrogen enhances prolactin responsiveness, women and postpubertal girls have greater drug-induced prolactin elevations than do men. In general, the higher the serum prolactin, the more likely it is for the patient to be symptomatic, Dr. Carlson said.

If serum prolactin is less than 200 ng/mL in patients with clinical features of hyperprolactinemia, try reducing the dose of the antipsychotic or switch to a more

prolactin-sparing drug. If prolactin is greater than 200 ng/mL, or remains elevated after switching agents, that is the only time to perform an MRI scan of the sella turcica to look for a pituitary adenoma or parasellar tumor, Dr. Carlson said.

Some patients have been alarmed about recently reported surveillance data identifying 77 reports of pituitary tumors occurring in patients receiving antipsychotic agents—particularly risperidone—since 1968 (*Pharmacotherapy* 2006;26:748-58). The data raise obvious questions, said Dr. Carlson, but he added that the report provided no information on the type of tumor, response to changes in therapy, or patient outcomes.

In addition, the patients may have incidental pituitary tumors, which are found in roughly 10% of normal adults on routine MRI. "We really are awaiting a systematic and exhaustive study to determine if there is a causal or coincidental association," he said. "I favor coincidental."

If a patient's MRI is normal, estrogen and testosterone could be replaced to treat hypogonadism, or medication could be given for osteoporosis, if needed. A few patients with antipsychotic-induced hyperprolactinemia have been concurrently treated with dopamine agonists with partial resolution of the hyperprolactinemia. But Dr. Carlson cautioned that in some patients, psychosis is occasionally worsened. ■

Risk of PTSD Is Higher in Those With History of Family Problems

BY TIMOTHY F. KIRN
Sacramento Bureau

SAN DIEGO — A high proportion of America's youth experience or witness a violent event, and a family history of substance abuse or mental health problems increase the risk that these youth will develop posttraumatic stress disorder or depression.

Those are the findings of a 7- to 8-year follow-up of subjects in the National Survey of Adolescents, Rochelle F. Hanson, Ph.D., said at a conference sponsored by the Chadwick Center for Children and Families at Children's Hospital and Health Center, San Diego.

The follow-up found that both experiencing/witnessing violence and a family history of substance abuse, mental health problems, or depression could put an adolescent at risk of PTSD or depression. They carry a risk individually, but in combination are worse. And clinicians who care for a victim should be aware of this, said Dr. Hanson, the director of clinical operations at the National Crime Victims Research and Treatment Center at the Medical University of South Carolina, Charleston.

"It is important to assess family environment because it does seem to be associated with risk for later mental health problems," she said.

PTSD risk was almost five times higher in those who experienced a rape if they also had a family history of alcohol/drug or mental health problems.

The follow-up reinterviewed 1,753 of the survey's initial 4,023 subjects, who were interviewed first when they were adolescents. Most of the subjects grew up in a central city area, and exposure to violence was fairly common. The violence defined in the survey had to be significant—more than a fistfight and a bloody nose, Dr. Hanson said.

In the follow-up interview, 8% reported having experienced a sexual assault, 20% reported having experienced a physical assault, and 35% had witnessed violence. In the initial survey, 37% of the respondents reported having witnessed violence.

An analysis of the responses from the second survey found that if individuals experienced or saw a physical assault, their risk of developing posttraumatic stress disorder symptoms was more than two times higher if they also had family alcohol/drug or mental health problems.

The risk was almost five times higher in those who experienced a rape if they also had a family history of alcohol/drug or mental health problems.

The findings for depression were similar.

The survey found that 25% of individuals who experienced a sexual assault had PTSD symptoms and about 15% who experienced a physical assault had PTSD. ■

Thimerosal Exposure During Pregnancy Not Linked to Autism

Exposure to thimerosal-containing Rh immunoglobulin during pregnancy is not associated with an increased risk of having a child with an autism spectrum disorder, said Dr. Judith H. Miles and T. Nicole Takahashi.

Overall, 214 mothers of 230 children receiving treatment for an autism spectrum disorder at the autism clinic at the University of Missouri-Columbia were not more likely to be Rh-negative than were 65 mothers of children receiving other medical genetic treatment there (15.4% vs. 15.4%), said Dr. Miles and Ms. Takahashi of the university (*Am. J. Med. Genet. A* 2007;doi:10.1002/ajmg.a.31846).

The proportion of Rh-negative women was similar among other controls, including 15.2% among all patients at the university hospital whose blood was typed between April 1, 2005, and March 31, 2006, and 17.7% among blood donors at the Missouri Illinois Regional Red Cross in calendar year 2005, they reported.

Mothers of children with an autism spectrum disorder were also not more likely than the control patients receiving other medical genetic treatment to have been exposed to antepartum thimerosal-

containing Rh immunoglobulin (13.9% vs. 14.8% of those pregnant prior to 2002) or to have an Rh-incompatible pregnancy (61% vs. 50%).

These findings provide further evidence that exposure to ethylmercury in thimerosal does not explain the increased prevalence of autism in recent years.

"We hope this report ... will offset some of the decreased compliance with immunization recommendations which is known to increase morbidity and mortality from childhood infectious diseases," wrote Dr. Miles and Ms. Takahashi.

They also emphasized the importance of these findings in terms of the international use of thimerosal-containing vaccines, which are more affordable because they allow the preservation of multidose vials.

The investigators also failed to identify an association between thimerosal-containing Rh immunoglobulin and various autism characteristics, including clinical diagnosis, IQ, gender, dysmorphology status, head size, and regressive versus early-onset autism spectrum disorder.

—Melinda Tanzola