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.

Serum 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 antagonistic 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 prepubertal 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 continuing antipsychotic therapy, even at the same dosage. A postmarketing surveillance study 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A similar trend in prolactin levels was identified in a large 52-week unpublished study involving 542 children conducted by Dr.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. The dopamine D4 receptor 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 to check for the stimulatory effects of estrogen and serum creatinine to rule out other causes of hyperprolactinemia. Because estrogen enhances prolactin responsiveness, women in the postpubertal growth phase tolerate greater drug-induced prolactin elevations than 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 paraspinal 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 outcome.

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

If a patient’s MRI is normal, estrogen treatment should 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 or 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.

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

Thimerosal Exposure During Pregnancy Not Linked to Autism

BY DR. CARLSON

“With History of Family Problems” she said. 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 39% had witnessed violence. In the initial survey, 37% of the respondents reported having witnessed violence.

An analysis of the responses found that if individuals experienced or saw a physical assault, their risk of developing posttraumatic stress disorder 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 among those who experienced a sexual assault had PTSD symptoms and about 15% who experienced a physical assault had PTSD.

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