

# Be Sure to Balance SSRI Benefits Against Risks

BY KERRI WACHTER  
Senior Writer

WASHINGTON — It is important to balance risks with benefits when considering a selective serotonin reuptake inhibitor to treat a child or adolescent, several experts said at the annual meeting of the American Academy of Child and Adolescent Psychiatry.

The session came soon after the Food and Drug Administration's decision to require pharmaceutical companies to add a black box warning alerting prescribers to the risk of suicidal behavior with antidepressants in pediatric patients.

"I think this is very important. This is not a contraindication. This [warning] box is not telling clinicians that they can't use these drugs. What it's saying is that if a clinician is considering using an antidepressant in a child or adolescent, they need to consider the risk and balance that against the clinical need," said Thomas Laughren, M.D., of the FDA's division of neuropharmacological drug products, Rockville, Md.

Selective serotonin reuptake inhibitors (SSRIs) do appear to work better than

placebo in the short-term therapy of depression in children and adolescents, said Neal Ryan, M.D., of the Western Psychiatric Institute and Clinic in Pittsburgh. This is probably true in general, though fluoxetine is the only one with an indication for children.

Combining an SSRI with cognitive-behavioral therapy (CBT) might even be more effective, according to recent findings. In the Treatment for Adolescents With Depression Study (TADS), SSRIs combined with CBT showed the best results for treating depression. The results also suggested that pharmacotherapy is more effective than psychotherapy alone, but this finding needs to be duplicated in other studies, Dr. Ryan said.

For clinicians, the real problem is how to balance the increased short-term risk—an extra 2 per 100 patients who will either attempt suicide or exhibit suicidality because of the use of an SSRI—and the potentially decreased long-term risk of suicidal thoughts and behavior attributable to depression, Dr. Ryan said.

Clinicians are left with the dilemma of what to do about the next depressed child to come into the office: Pick an SSRI

alone, choose psychotherapy alone, or combine an SSRI with psychotherapy. "I think we're going to have a rich debate on that," Dr. Ryan said.

When considering an SSRI in a pediatric patient, it's important to inform the family of the potential risks and benefits and follow the FDA's monitoring suggestions. "I think also that we need to advocate for more studies. I think we're all scared that we won't get any more data on this question," he said.

Mark Olfson, M.D., of Columbia University, New York, is not optimistic about the prospects for this type of research: "For the foreseeable future, I believe the pharmaceutical industry is going to view this whole area as radioactive and stay away from it."

He does, however, think that this kind of research is necessary. "We need to think about this finding in the context of risks and benefits. So, paradoxically, now is the time that we need more information about what are the benefits of SSRIs in kids," he said.

Future research should focus on which subgroups of patients are at higher risk and when in the course of treatment they

are at higher risk. One strategy would be to monitor depressed children closely for short periods of SSRI therapy, looking for somatic subjective dysphoria, changes in attention, changes in impulsivity, or other indicators of suicidality, Dr. Olfson said.

It's also important to look at the bigger public health picture, Dr. Olfson said. "We need to be clear about the distinctions between suicidal ideation and the suicide attempts that were the subject of the randomized controlled trials analyses and actual suicide or serial suicide attempts that we encounter in practice."

The rates of suicidal ideation and suicide attempts in a normal adolescent population also need to be considered. According to the Centers for Disease Control and Prevention's 2003 National Youth Risk Behavior Survey, 16.9% of normal adolescents in grades 9-12 had seriously considered attempting suicide in the previous 12 months and 8.5% had attempted suicide at least once in that time period.

Those numbers stand in sharp contrast to the comparatively small number of kids who show up in emergency rooms and hospitals after actual suicide attempts, Dr. Olfson said. ■

## No Association Seen Between Suicide, SSRIs Among Children in Sweden

BY MICHELE G. SULLIVAN  
Mid-Atlantic Bureau

STOCKHOLM — In Sweden, there is no evidence of an association between suicide and the use of selective serotonin reuptake inhibitors among children or adolescents; instead, these drugs appear to be associated with a decreased risk of suicide in the general population.

About 95% of suicides in Sweden are investigated in a process that includes a forensic toxicology screen, and antidepressants are among the drugs identified, Göran Isacson,

M.D., said at the annual congress of the European College of Neuropsychopharmacology.

Dr. Isacson compared the toxicologic results from 14,857 suicides that occurred from 1992 to 2000 with those of 26,422 natural or accidental deaths during the same period.

His analysis indicated a decreased association with suicide for three serotonin reuptake inhibitors (SSRIs): fluoxetine (relative risk of 0.91), paroxetine (RR 0.87), and citalopram (RR 0.76). Sertraline showed a slightly increased as-

sociation with suicide (RR 1.05), while fluvoxamine showed a significantly increased association (RR 3.04).

"This increased risk can probably be explained by the fact that fluvoxamine was the first SSRI introduced in Sweden and was prescribed for patients who didn't respond to other medications," Dr. Isacson suggested.

The association between SSRIs and suicide was even lower among children and adolescents, he said. There were 52 suicides among children up to 15 years old. Of those

children, seven were taking antidepressants: five, a tricyclic antidepressant; one, venlafaxine; and one, mianserin. "None of these children were taking an SSRI—the most commonly prescribed antidepressant in this age group," Dr. Isacson said. There were 356 suicides among children aged 15-19 years; 13 children had been taking an antidepressant, but only 6 of that group had been taking an SSRI. "That was not significant when compared to the controls," he said. ■

## Maternal Depression and Infants' Cortisol Response

BY MIRIAM E. TUCKER  
Senior Writer

ORLANDO FLA — Pre- and postnatal depression in women influences neuroendocrine function in their infants, Laura R. Stroud, Ph.D., reported at the annual meeting of the American Psychosomatic Society.

Prenatal depression, reported in approximately 10% of all pregnant women, has been linked with deficits in infants such as attenuated response to social stimuli, excessive crying, increased sleep problems, and lower vagal tone. Moreover, women with prenatal depression are also at increased risk for postnatal depression, which has also been linked to adverse effects in infants. Little is known about the influence of pre- and early postnatal depression on infant neuroendocrine functioning, said Dr. Stroud of Brown University, Providence, R.I.

In the first of two studies, cortisol responses to the Neonatal Intensive Care Unit Network Neurobehavioral Scale (NNNS) were measured in 1- to 2-day-old newborns of 49 nonde-

pressed mothers and 13 mothers who scored high for depression (greater than 11) on the Beck Depression Inventory before delivery.

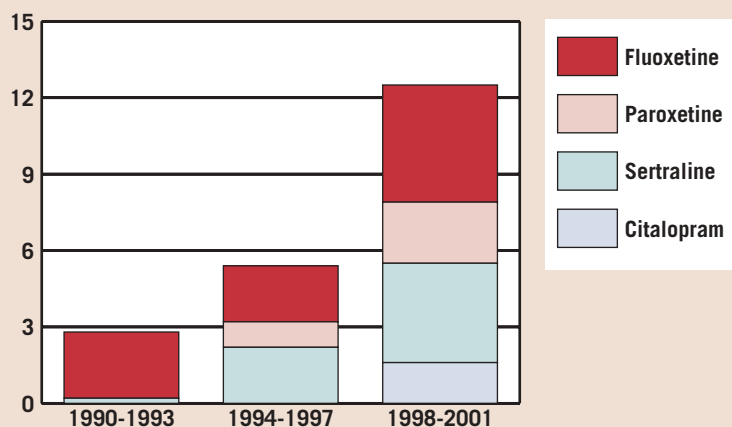
Baseline and poststress cortisol responses were significantly attenuated among the infants of the depressed mothers, compared with those of nondepressed mothers. These results persisted after maternal age, smoking, birth weight, and alcohol use were factored in, Dr. Stroud reported.

In a second study involving 62 different mother-infant pairs, scores higher than 17 on the Center for Epidemiologic Studies-Depression scale, which was used to evaluate postnatal depressive symptoms, were a better predictor than high prenatal depression of cortisol responses to stress in infants at 10-30 days of life. The 13 infants of mothers with high postnatal depression scores showed attenuated baseline but elevated poststress cortisol responses, compared with those of nondepressed mothers.

This study was funded by the National Institutes of Health and the National Alliance for Research on Schizophrenia and Depression. ■

### DATA WATCH

#### Rate of SSRI Prescribing per 1,000 Depressed 5- to 18-Year-Olds



Notes: Based on an analysis of data from the National Ambulatory Medical Care Survey. An SSRI is a selective serotonin reuptake inhibitor.

Source: Linda M. Robison, Washington State University, Pullman