

Fluoxetine's Effect on Suicide Events Downplayed

BY MICHELE G. SULLIVAN
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TORONTO — Few suicide attempts occurred during the Treatment for Adolescents with Depression Study (TADS), but suicide-related events were more common in both fluoxetine arms than in the placebo arm, Graham J. Emslie, M.D., reported at the joint annual meeting of the American Academy of Child and Adolescent Psychiatry and the Canadian Academy of Child and Adolescent Psychiatry.

But, Dr. Emslie said this should be tempered with another of the study's conclusions. Almost 30% of the adolescents had suicidal ideation at the study's outset; at 12 weeks of treatment, suicidal behavior had improved in about 86% of the fluoxetine arms, compared with 77% of those in a cognitive-behavioral therapy-only arm.

"If you talk to the press, you would assume people are dying in the [United States] from these medicines, but in fact they are well tolerated," said Dr. Emslie,

chief of the University of Texas Southwestern's division of child and adolescent psychiatry, Dallas. "About 83% of those on fluoxetine and the same percentage on the combination of cognitive-behavioral therapy (CBT) and fluoxetine completed the treatment period—and that says a lot."

TADS included 439 patients aged 12-17 years with major depressive disorder. Patients were randomized to 12 weeks of fluoxetine alone (10-40 mg/day), cognitive-behavioral therapy (CBT), CBT with fluoxetine (10-40 mg/day), or to placebo.

Combination therapy was superior to either fluoxetine or CBT alone in reducing symptoms of depression, and fluoxetine alone was superior to CBT alone.

Suicide-related events occurred in nine patients in the fluoxetine-only arm, five in the combination therapy arm, five in the

CBT-only arm, and two in the placebo arm. There were five suicide attempts: two in the combination arm, two in the fluoxetine arm, one in the CBT-only arm, and none in the placebo arm.

New suicidal ideation was most common in the fluoxetine-only arm (three cases). There were no new cases in the combination therapy arm, one in the CBT-only arm, and two in the placebo arm.

Suicidal ideation worsened in 13% of those in the fluoxetine arm, 15% of those in the CBT-only arm, 7% of those in the placebo arm, and 5% of those in the combination arm. "There were few attempts, but there was some increase in ideation," Dr. Emslie said. He noted that TADS was a flexible-dose study and that the addition of CBT to fluoxetine was associated with lower doses of the drug. "CBT appears to decrease the

amount of drug that they need, and keeping the dose lower for longer appears to be a good idea."

Physical adverse events were more common in the fluoxetine arms, compared with placebo. Insomnia occurred in 4% of those taking fluoxetine and 1% of those in the placebo group. Rates were similar for vomiting (3% vs. 1%) and upper abdominal pain (3% vs. 2%).

Those taking fluoxetine also reported more psychiatric symptoms than those on placebo. Mania occurred in 2% of the fluoxetine groups, 1% of the placebo group, and none of the CBT-only group. Irritability occurred in 3% of the fluoxetine groups, 1% of the placebo group, and none of the CBT group. The total psychiatric event rate was 11% for fluoxetine, 5.5% for combination therapy, 4.5% for placebo, and 1% for CBT.

However, Dr. Emslie noted, "There's no evidence that the drug was doing this. These symptoms vary. They go up and down with time." ■

There were two suicide attempts in the combination arm, two in the fluoxetine arm, and none in the placebo arm.

Study Examines Impact of Drug Warnings in Canada

BY DOUG BRUNK
San Diego Bureau

SAN DIEGO — A specific warning issued in June 2003 by the United Kingdom Committee on Safety of Medicines that advised physicians not to use paroxetine in patients younger than 18 years of age significantly influenced how the drug was prescribed in young patients in Ontario.

Yet subsequent, more generalized warnings about selective serotonin reuptake inhibitors (SSRIs) issued in the United States and Canada did not influence antidepressant prescription trends in any age group of Ontario residents, Paul A. Kurdyak, M.D., reported during a poster session at the American Psychiatric Association's Institute on Psychiatric Services.

The finding suggests that, at least for the population studied, specific drug warnings influence prescribing habits more do than general warnings.

"From a policy perspective, vague warnings don't do anything in Ontario," Dr. Kurdyak, a research fellow in the department of psychiatry at the University of Toronto, said in an interview. "I don't know about the United States. It might be different there because you're more litigious here than we [in Canada] are."

In a study supported by AstraZeneca Pharmaceuticals and the Canadian Institute of Health Research, Dr. Kurdyak and his associates analyzed new antidepressant prescriptions dispensed by the Ontario Drug Benefits Program between April 1998 and March 2005. Three age groups were studied: younger than 20 years, 20-65 years, and 66 years and older.

The investigators conducted a time-series analysis to assess the impact of five advisory dates on the prescription of antidepressants. Those dates were:

► **June 10, 2003.** UK Committee on the Safety of Medicine advises against the use of paroxetine in patients under 18 years of age with depression.

► **Oct. 27, 2003.** The U.S. Food and Drug Administration issues a more general public health advisory emphasizing that newer antidepressants should be used with caution in children.

► **March 22, 2004.** The FDA issues a public health advisory about the need to closely monitor patients of all ages for worsening depression or suicidality after initiation of antidepressant therapy.

► **June 3, 2004.** Health Care Canada follows suit with a similar warning.

► **Oct. 15, 2004.** The FDA issues a black box warning for the use of antidepressants in pediatric patients.

Analysis revealed that the mean number of monthly new prescriptions for any SSRI per 10,000 individuals was 5.5 for patients younger than 20 years; 29.7 for patients aged 20-65 years, and 16.4 for patients aged 66 years and older.

"The number of new prescriptions for SSRIs as a group did not change after any antidepressant warning in any age group," the investigators wrote in their poster. "However, the rate of new paroxetine prescriptions in patients younger than 20 years of age declined by 54% immediately following the first UK warning for paroxetine in June 2003."

That particular warning "had no effect on new paroxetine prescriptions in the other age categories, [and] no warnings influenced new prescription rates for any other antidepressants in any other age group," they added. ■

Obesity Is Not a Risk Factor For Chronic Daily Headache

BY DEBBIE LERMAN
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PHILADELPHIA — Children and adolescents who were overweight or obese were not found to have an increased risk for chronic daily headache in a study on CDH risk factors in a pediatric population. CDH was defined in the study as headaches occurring on 15 or more days per month for more than 3 months.

Female gender, psychiatric comorbidity, caffeine use, and analgesic overuse were the only factors found in the study to increase CDH risk. These surprising results were reported by Elza Vasconcellos, M.D., at the annual meeting of the American Headache Society.

"Based on what we know about CDH in grown-ups, we expected a high correlation between high body mass index (BMI) and CDH risk in the pediatric population," Dr. Vasconcellos, who is director of the Miami Children's Hospital headache center, said in her presentation. But the results of the study did not bear out this hypothesis.

To identify risk factors associated with the development of CDH, the researchers examined the medical records of 226 patients, aged 6-18 years, with a diagnosis of headaches or migraines. After factoring out the patients with nonchronic headaches, the investigators compared 53 patients with CDH and 146 control patients with nondaily headaches (110 with migraines, 18 with tension-type headaches, and 18 with other or mixed-types).

They also compared the BMI and percentage of overweight patients (defined as BMI

less than or equal to the 95th percentile of the sex-specific BMI-for-age growth chart) in both headache groups with a control group of 100 healthy pediatric patients who were seen for well-child visits at a pediatric clinic.

The researchers found that 35% of the children with CDH were overusing analgesics more than 15 days per month, compared with none of the patients with nondaily headaches.

Of the children with CDH, 34% had a comorbid psychiatric condition, compared with 19% of non-CDH patients. There were significantly more females in the CDH group than the non-CDH group (66% vs. 46%), and more children in the CDH group said they consumed caffeine (in an answer to a yes/no question) than did children in the non-CDH group (95% vs. 80%).

The two groups (CDH vs. non-CDH) were not significantly different in terms of age, sleep hours, handedness, stress, parental marital status, learning difficulties, head trauma, or abnormal neuroimaging.

The researchers found no significant differences between the CDH and non-CDH groups in terms of obesity or overweight. They also found no significant differences in obesity or overweight between all the children with headaches and the control group of healthy patients.

Despite the lack of a significant link between obesity and CDH in this study, Vasconcellos still believes overweight might play an important role in headaches in children and adolescents. "Overall, a significant proportion of the children who visit headache clinics are overweight," she said in an interview. ■



The results are surprising since 'a significant proportion of the children who visit headache clinics are overweight.'

DR. VASCONCELLOS