Fluoxetine's Effect on Suicide Events Downplayed

BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

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. "About 83% of those on fluoxetine and the same percentage on the combination of cognitive-behavioral therapy and fluoxetine completed the treatment period—and that says a lot."

TADS included 439 patients aged 12-17 years with major depressive disorder. They were randomized to either 12 weeks of fluoxetine alone, cognitive-behavioral therapy (CBT), CBT with fluoxetine, 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 during the study: 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 therapy 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%), upper abdominal pain (3% vs. 2%), and sedation (2% vs. 0%).

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. Agitation occurred in 1.5% of the fluoxetine groups, 2% of the placebo group, and none of the CBT group. Anxiety occurred in 1% of the fluoxetine groups, none of the placebo group, and 1% 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." ■

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'It is clear that specialty hospitals are not shouldering their burden to provide critical community health care services, such as emergent care or caring for those least able to pay, but instead are exacerbating an existing problem.'

Jeffrey Micklos, p. 65