FDA Guide on Antidepressants Offers Challenges

Complying with schedule in agency's medication guide 'almost impossible' for first 12 weeks.

BY JOYCE FRIEDEN
Associate Editor, Practice Trends

MONTREAL — Prescribing antidepressants to children comes with its own set of challenges, Dr. Neil S. Kaye said at the annual meeting of the American Academy of Psychiatry and the Law.

For one thing, it's difficult to comply with the visit schedule suggested by the Food and Drug Administration, said Dr. Kaye, a psychiatrist in private practice in Wilmington, Del.

The agency's "Medication Guide: About Using Antidepressants in Children and Teenagers" recommends: "After starting an antidepressant, your child should generally see his or her health care provider:

- ► Once a week for the first 4 weeks.
- ► Every 2 weeks for the next 4 weeks.
- ► After taking the antidepressant for 12 weeks.
- ► More often if problems or questions arise."

After 12 weeks, "we get to become providers again," Dr. Kaye said, noting that the visit schedule goes back to whatever the physician thinks is appropriate.

"You'll see it's almost impossible to comply" with that schedule for the first 12 weeks, Dr. Kaye said. "Nobody has enough time slots; there aren't enough doctors available; and managed care does not really want to pay for that."

Dr. Kaye wrote to one senator complaining about the recommendations. "He said …his office's view after contacting the FDA was that the FDA didn't really intend for that to be what is said and done, even though it's what they've written," Dr. Kaye said.

Physicians need to alert parents that their children may get worse initially, 'either because of the drug or because the drug has not yet started and the disorder is still going on.'

Doctors need to make themselves available to parents whose children are taking these drugs, Dr. Kaye continued. "When you look at cases that have been litigated, one of the major issues is doctors and their staffs not returning phone calls in a timely manner," he said.

"That breeds anger, that breeds malpractice, that breeds bad outcomes. We need to return patients' [and parents'] calls. It sounds simple, but it needs to be said."

Physicians also need to alert parents that their children may get worse initially, "either because of the drug or because the drug has not yet started and the disorder is still going on," he said.

"And we need to let everyone know what [side effects] to watch for," including akathisias, restlessness, and induction of hypomania.

Dr. Kaye noted that the media have really jumped on the story of problems with prescribing antidepressants. "As of Sept. 8, there were more than 3.6 million Internet articles on this topic," he said. "This is hot."

Unfortunately, the media have done an effective job of scaring people away from antidepressants, according to Dr. Kaye, who has consulting arrangements with many pharmaceutical companies.

"Twenty-five percent of people surveyed say that antidepressants are harmful to someone who's depressed and suicidal," Dr. Kaye said. "That's a big number of people who will be driven away from what could be life-saving treatment because of the hype and what the media has done."

How have physicians responded to the hype? "We're scared," he said, noting that there has been a big drop in the number of antidepressants being prescribed.

And the number of doctors willing to prescribe them seems to be decreasing as well.

"Pediatricians and primary care doctors are saying, 'This is too litigious; we're not going near this—you have to see a specialist,'" Dr. Kaye said. "And of course there aren't enough psychiatrists to take on those patients in a timely manner, so a crisis is being developed, without a doubt."

A study released last year by Medco Health Systems Inc., the pharmacy benefit manager, showed a 10% dropoff in prescribing antidepressants for patients younger than 18 years in 2004.

Medco reported that no difference was seen in the dropoff rate between primary care physicians and psychiatrists. ■

Combo Tx Surpasses Fluoxetine or Therapy Alone, TADS Results Show

BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

TORONTO — Fluoxetine combined with cognitive-behavioral therapy was more effective in improving functioning, global health, and quality of life in depressed adolescents than was either treatment alone, Dr. Benedetto Vitiello said at the joint annual meeting of the American Academy of Child and Adolescent Psychiatry and the Canadian Academy of Child and Adolescent Psychiatry.

However, he noted, although symptoms of depression might have improved, many patients remained functionally impaired after 12 weeks of treatment, even with the most effective therapy. "It's not really surprising that function doesn't improve as quickly as symptoms," he said in an interview. "You would expect symptoms to improve first, and then to see a gradual improvement in function."

Dr. Vitiello, chief of the child and adolescent treatment and preventive intervention research branch of the National Institute of Mental Health, presented a secondary analysis of the Treatment for Adolescents with Depression Study (TADS). The TADS trial included 439 patients aged 12-17 years with major depressive disorder. Patients were randomized to either 12 weeks of fluoxetine alone (10-40 mg/day), cognitive-behavioral therapy (CBT) alone, CBT with fluoxetine (10-40 mg/day), or placebo.

The study found that combination therapy reduced the symptoms of depression better than did fluoxetine or CBT alone. But when the main outcome measure was function, rather than symptoms of depression, the results were not as robust, he concluded. "The data seem to show that treatment effects on function lag behind those on symptoms."

In the analysis, functional outcomes were measured with the Children's Global Assessment Scale (CGAS), the Pediatric Quality of Life Enjoyment and Satisfaction Questionnaire (PQ-LES-Q), and the Health of the Nation Outcome Scales for Children and Adolescents (HONOSCA). Baseline scores showed moderate impairment, Dr. Vitiello said. Average scores were 50 (ideal score, 100) on the CGAS, 17 (ideal, 0) on the HONOSCA, and 43 (ideal, 75) on the PQ-LES-Q.

After 12 weeks of treatment, the combination therapy was clearly superior to any of the other arms on the basis of these measurements, he said. Average scores on the CGAS improved to 65 in the combination therapy group, 60 in the fluoxetine-only group, and 57 in the CBT-only and placebo groups.

HONOSCA scores declined (showing improvement) in all arms. However, the only statistically significant decline occurred in the combination therapy group. On the PQ-LES-Q, the most improvement occurred in the combination therapy group, with the average score increasing to 55.

"Combination therapy was consistently superior to the other arms in improving function in all three measures," Dr. Vitiello said.

Even with these improvements, however, most patients didn't regain normal function. Only 35% of those in the combination therapy group attained a CGAS score higher than 70, representing normal function, although 71% of those in this group were classified as responders when assessing their symptoms of depression.

In the fluoxetine-only group, only 20% of patients attained normalization, although 61% were classified as responders. "It's quite a dramatic difference when you take the level of function as the outcome," Dr. Vitiello said.

The numbers were significantly lower in the other groups—13% of those in the CBT-only arm and 19% of those in the placebo arm attained normalized function.

"It was quite disappointing that CBT had only a 13% recovery rate," Dr. Vitiello said. ■

Full-Scale IQ Gap Found Between XXYY, XXY Males

SAN DIEGO — Verbal and full-scale intelligence quotient measures for males with XXYY syndrome are significantly lower than for males with XXY syndrome, but performance IQ is not significantly different between the two groups, results from a small study show.

Although previous reports have noted more cognitive and behavioral problems in XXYY males than in XXY males, this is the first study to directly compare the cognitive and behavioral features of the two syndromes, Dr. Nicole R. Tartaglia said at the annual meeting of the Society for Developmental and Behavioral Pediatrics.

She and her associates recruited 16 males with XXYY syndrome and 9 males with XXY syndrome from national organizations for patients with sex chromosome aneuploidy.

The males were 5-20 years old, and all of the families underwent a clinical interview and completed the Behavioral Assessment System tool.

The investigators obtained information on cognitive function either by reviewing patients' medical records or by administering to the subjects the children's intelligence scale in the Wechsler Abbreviated Scale of Intelligence.

XXYY males were found to have significantly lower verbal and full-scale IQs compared with XXY males, but there were no significant differences between the two groups on mean performance IQ scores, said Dr. Tartaglia, who is a fellow in the department of pediatrics at the University of California, Davis.

XXYY males were more likely than their XXY counterparts to have problems with hyperactivity, aggression, conduct, and depression, she said.

XXYY males were also more likely to have significantly lower adaptive functioning than were males with XXY.

Dr. Tartaglia noted that a limitation of the study is its small sample size.

XXY syndrome occurs in about 1 in 800 males whereas XXYY is much less common, occurring in about 1 in 17,000 males.

—Doug Brunk