Behavior Modification Can Lower Doses of ADHD Drugs in Children

BY HEIDI SPLETE
Senior Writer

WASHINGTON — Behavior modification can reduce the level of medication needed in school-aged children with attention-deficit hyperactivity disorder, William E. Pelham Jr., Ph.D., said at the annual meeting of the Association for Behavioral and Cognitive Therapies.

Few studies have addressed the issue of how behavioral and pharmacologic therapies should be sequenced in children, said Dr. Pelham, a professor of pediatrics and psychiatry at the State University of New York, Buffalo.

Dr. Pelham, who is also a professor of psychology at the university, and his colleagues have completed two studies funded by the National Institutes of Health that examined dosing and sequencing of behavior modification and medication.

The first study included 154 children aged 5-12 years (130 boys and 24 girls) who participated in a summer day camp program. They were divided for 3 weeks into three behavior modification groups—no behavior modification, low-intensity behavior modification, and high-intensity behavior modification. In addition, the children were divided into four dosage groups for methylphenidate.

Medication was randomized each day, and the program counselors recorded the children's behavior in areas such as failing to comply with staff requests, following activity rules, and exhibiting conduct problems.

When the data were reviewed at summer's end, the lowest dose of medication—0.15 mg/kg three times daily—had a surprising and substantial effect on reducing ADHD impairment. In fact, the maximum incremental value of medication to behavior modification occurred at this low dose.

"There was no incremental value for most children beyond the 0.15 mg/kg dose in combination with behavior modification, but the highest dose—0.6 mg/kg—produced the largest effects in the absence of behavior modification," Dr. Pelham said. This dosage normalized the largest number of children when combined with behavior modification. The effects of behavior modification alone and medication alone were comparable.

"Medication alone does not normalize the children's performance," he explained. "Even at the highest dose of 0.6 m g/kg three times daily, many children were not normalized; the effect of behavior modification is as strong as the effect of medication." Lower doses produce a substantially lower level of side effects—a benefit of using behavior modification as the first-line intervention.

Parents also evaluated the treatment conditions; they ranked a high level of behavior modification therapy, either alone or in combination with medication, as their first choice for managing ADHD.

The investigators conducted a follow-up study to assess the effectiveness of sequencing medication and behavior modification in a school setting. The primary outcome measure was the maintenance of acceptable behavior without medication after summer exposure to both medication and behavioral therapy.

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The study included 128 of the children from the summer program who were randomly assigned to one of three groups. A total of 44 children received high behavior modification treatment, 43 received low behavior modification treatment, and 41 received no behavior modification treatment.

Overall, nearly twice the number of children who received behavior modification remained off medication at school during the fall semester, compared with children who received none (60% vs. 30%).

In addition, about 80% of children who had received behavior modification remained off medication at home. A caveat, however, was that almost all the children (75%) had been taking medication before enrollment in the summer study, which influenced their ability to remain unmedicated, Dr. Pelham noted.

Children who received no behavior modification started taking medication during the school day after 13 weeks, compared with 19 weeks for the low-intensity behavioral therapy group and 20 weeks for the high-intensity behavioral therapy group. Similarly, children who received no behavior modification therapy started taking medication at home after 27 weeks, compared with 38 weeks for the low behavior modification group and 32 weeks for the high behavior modification group.

Dr. Pelham has been a consultant, scientific adviser, speaker, and grant recipient for the following companies: McNeil Consumer Healthcare/ALZA (developers and marketers of the methylphenidate product Concerta), Abbott, Shire, Noven, Eli Lilly, and Cephalon. ■

British Agency Cites Atomoxetine Risks

BY KATE JOHNSON
Montreal Bureau

British physicians are being warned by their country's medical authorities about new risks associated with atomoxetine in the treatment of attention-deficit hyperactivity disorder.

The new risks of seizures and abnormal heart rhythm (QT interval prolongation) were identified by the Medicines and Healthcare Products Regulatory Agency (MHRA), the U.K. equivalent of the Food and Drug Administration (FDA), after a Europewide review of atomoxetine, which is marketed in the United Kingdom and United States as Strattera.

The FDA has not issued similar warnings, although it is evaluating the U.K. data and "will make any necessary label changes as appropriate," said spokesperson Crystal Rice.

The MHRA initiated its Europewide review of Strattera last fall, after new warnings were issued about the drug's potential to cause suicidal thoughts and behavior. Changes were made to the product's label at that time in the United Kingdom and the United States. The British review concluded that "the overall balance of risks and benefits of Strattera remains positive in the treatment of ADHD in children of 6 years and older and in adolescents."

However the MHRA's letter to health care physicians says the product's label is being updated to reflect the new risks, and it offers the following new advice to prescribers:

► Seizures are a potential risk with Strattera and therefore it should be introduced with caution in patients with a history of seizure. Discontinuation of Strattera should be considered in any patient developing seizures or if there is an increase in seizure frequency.

► Reports of QT interval prolongation have been received in association with Strattera. Therefore it should be used with caution in those with congenital or acquired long QT or a family history of QT prolongation. This risk may be increased if Strattera is used concomitantly with other drugs that produce QT prolongation, drugs that can cause electrolyte disturbances, and those that inhibit cytochrome P450 2D6.

The new evidence comes on the heels of a recent FDA panel meeting in which reports of sudden death and nonfatal cardiovascular events in connection with ADHD drugs were discussed. Last month, the panel advised that ADHD drugs carry a black box warning about these potential adverse events. ■

Restless Legs Syndrome Tied to Jump in Depression Incidence

BY JANE SALODOF MACNEIL
Southwest Bureau

SANTA ANA PUEBLO, N.M. — People with restless legs syndrome were three times more likely to have a major depressive disorder in a study of 1,071 Baltimore residents reported by Dr. Hochang Benjamin Lee at the annual meeting of the Academy of Psychosomatic Medicine.

Investigators from Johns Hopkins University in Baltimore found major depressive disorder in 8 of 42 patients (19%) diagnosed with restless legs syndrome (RLS). Only 8.4% of those without RLS met the DSM-IV criteria for depression in diagnostic interviews.

"Depression and anxiety are common in RLS, and vice versa," said Dr. Lee of the Neuropsychiatry and Memory Group at Johns Hopkins. Previous studies suggested a connection, he said, but the new study is "probably the most definitive."

Dr. Lee described many overlaps between the two disorders, both of which are diagnosed on the basis of subjective reports from the patient. He said the two conditions have similar prevalence, occur twice as often in women as in men, present with diurnal variation, and tend to run in families. Both also have a high placebo response rate in treatment trials.

Six of the nine symptoms that the DSM-IV lists for major depressive disorder are common in RLS patients, Dr. Lee said. He cited depressed mood, diminished interest, fatigue or loss of energy, diminished concentration, psychomotor retardation, and insomnia or excessive sleepiness. Indeed, he suggested asking depressed patients who complain of insomnia or excessive sleepiness whether they experience "a creepy crawling feeling" in their legs.

Noting that no guidelines exist for managing depression in RLS patients, Dr. Lee recommended the following strategy:

► If an RLS patient presents with mild depression or dysthymia, treat the RLS first and see whether mood-related symptoms improve. If the patient continues to have depressive symptoms, treat these as well.

► If a severe major depressive disorder occurs along with mild RLS, treat the depression first, preferably with agents that are *not* SSRIs or tricyclic antidepressants.

► If both RLS and depression are severe, however, consider treating the conditions simultaneously, but avoid using most dopamine agonists for RLS because of the possibility of the rare side effect of psychosis.

"Careful consideration is needed for treatment of major depressive disorder in patients with restless legs syndrome," Dr. Lee warned. He ruled out many medications, saying that SSRIs and tricyclic antidepressants should be avoided whenever possible. Both can exacerbate periodic limb movements, which occur in 80%-90% of RLS patients, according to Dr. Lee.

Dr. Lee suggested nefazodone, trazodone, and bupropion as alternatives. These agents have not been reported to exacerbate periodic limb movements, he said, and they may produce improvement. Mirtazapine is sometimes recommended for depression in RLS patients, he added, but reports are conflicting.

Regarding adjunctive treatments for RLS, he said that antipsychotic medications generally exacerbate the syndrome. While atypical antipsychotic agents are less likely to do so, he said there have been reports of risperidone, quetiapine, and olanzapine worsening RLS. Aripiprazole might be worth a trial in this movement disorder, given that it is a partial dopamine agonist. ■