Use May Widen

ADHD Patch *from page 1*

"Whether it will be widely accepted or not I think is still an open question," said Dr. Gorman, chairman of the section of clinical pharmacology and therapeutics for the American Academy of Pediatrics.

It is important to note that use of a patch by young children would require intervention by a responsible adult at specific times twice a day, compared with just once a day for oral forms of methylphenidate, said Dr. Gorman, a pediatrician in private practice in Baltimore. The approval applies to children aged 6-11 years.

Approval of the patch—which is called Daytrana and was codeveloped by Shire Pharmaceuticals Inc. and Noven Pharmaceuticals Inc.—had been widely expected after the panel's endorsement. But the panel, citing the patch's potential to cause sensitization to methylphenidate, questioned how strong the warnings on the label would be.

The patch will continue to work for about 2 hours after being removed, 'so it may permit clinicians and families to actually vary the duration of effect.'

Sensitization can occur with any medication delivered using a transdermal patch. People sometimes develop antibodies to the medication in transdermal patches, and when they are later challenged with an oral version of the medication, they may experience an allergic reaction. Theoretically, this could prevent a child who had used the methylphenidate patch from ever taking an oral form of the medication.

Dr. Laughren said such a sensitization reaction had never been seen in 765 patients exposed to methylphenidate patches in short-term trials. In one case that had been thought to involve sensitization, further study showed that sensitization did not occur. However, a separate provocation study with treatment for an extended period of time indicated that sensitization could be a possibility.

At the panel meeting, Shire cited two studies of children aged 6-12 years with ADHD—a 2-day laboratory classroom study of 93 children and a pivotal multicenter outpatient study of 274 children that compared the patch with oral methylphenidate (Concerta) and placebo over 7 weeks. Significant improvements in behavior were seen within 2 hours of application of the patch (left on for 9 hours) and persisted for 3 hours after removal, the company said.

The label instructions call for the patch to left on for a maximum of 9 hours, but Dr. Biederman said that it can be left on for longer than 9 hours for a longer duration of effect. "We know from the early studies that the patch continues to work for about 2 hours after it's removed," he said. "So it may permit clinicians and families to actually vary the duration of effect, depending on the individual needs of the particular day, week, or month."

Normally, the patch is to be applied to alternating areas of the child's thighs each morning and removed later that day. But in the provocation study, patches were applied to a single area and left on continuously for days at a time, and 13% of patients did develop sensitivity.

For that reason, the label of the product as it will be released contains advice for physicians on how to recognize and manage sensitization. Redness at the patch site is very common and does not by itself indicate sensitization. But if there is something beyond redness—such as edema, papules, or vesicles—a dermatologist would need to examine that child to determine whether sensitization had actually occurred.

The patch will be available in four dosages: 10 mg, 15 mg, 20 mg, and 30 mg. ■

Study Reinterpreted: OCD Responds to Skilled Therapy

BY JEFF EVANS
Senior Writer

NEW YORK — Cognitive-behavioral therapy, when provided by a skilled therapist, can be just as effective as an SSRI or combined treatment for children with obsessive-compulsive disorder, Dr. Daniel S. Pine said at a psychopharmacology update sponsored by the American Academy of Child and Adolescent Psychiatry.

To reach that conclusion, Dr. Pine interpreted data from the Pediatric OCD Treatment Study differently than did the study's investigators.

The Pediatric OCD Treatment Study is the only published trial that compares cognitive-behavioral therapy (CBT) with an SSRI for the treatment of pediatric OCD, said Dr. Pine, chief of the section on development and affective neuroscience in the mood and anxiety disorders program at the National Institute of Mental Health.

In the study, 112 patients were randomized to receive sertraline (Zoloft), cognitive-behavioral therapy (CBT), a combination of the two modalities, or placebo for 12 weeks. Patients were treated at one of three sites, and were enrolled primarily at two of the sites (JAMA 2004;292:1969-76).

"There were robust site differences in the response to treatment," he said. "When you look very carefully at the data that are published, what you see was that one site had a massive response to CBT and there was no benefit of adding an SSRI to CBT." The other site had a "very weak" response to CBT, an "okay" response to an SSRI, and a "robust" response to the combination treatment, he noted.

The averaged data for the three sites showed a statistically significant benefit of combination therapy over CBT alone, sertraline alone, and placebo. The investigators concluded that pediatric patients with OCD should receive combination therapy.

"Personally, I think that's a misreading of the study," Dr. Pine said. "I think what the study really tells us is that really well-executed CBT in kids with OCD is every bit as good as monotherapy [with an SSRI] and is every bit as good as combination therapy; however, not-so-great CBT really needs an SSRI to work."

"It would be wonderful if CBT was always the same across therapists, patients, and cities, but it's not, and this study really shows it," he added.

CBT might be the preferred method for treating pediatric OCD, especially in patients without a history of attention-deficit hyperactivity disorder or major depression, because the availability of a CBT therapist will vary depending on geographic location and the fact that there are "tremendous site differences in CBT," he said.

"This recommendation only applies to the case where you have access to a very skilled CBT therapist who has worked with pediatric anxiety disorders," Dr. Pine explained.

An SSRI should be used if a skilled CBT therapist is not available or if a child has a severe anxiety disorder and will not undergo the crucial part of CBT that involves exposure to the feared stimulus, he advised. ■

CLINICAL CAPSULES

Borderline Traits Tracked in Teens

Borderline personality disorder appears to encompass a much broader range of psychopathology in adolescent inpatients than in hospitalized adults, reported Dr. Daniel F. Becker of the University of California, San Francisco, and his colleagues.

The investigators interviewed 123 adolescent inpatients, aged 13-18 years, who were a mean age of 15.9 years. Most (104) were white; 67 (54%) were boys (Compr. Psychiatry 2006;47:99-105).

Based on interviews, borderline personality disorder (BPD) was diagnosed in 65 adolescents—45% of boys and 65% of girls—and four factors associated with BPD presentation accounted for 67% of the overall variance.

Factor 1 reflected negative or self-deprecating aspects of BPD presentation, such as suicidal threats and gestures, and feelings of emptiness or boredom. Factor 2 covered affective dysregulation or irritability, including uncontrolled anger. Factor 3 reflected interpersonal problems, such as unstable relationships. Factor 4 reflected impulsiveness.

These factors suggest that BPD in teens may be associated with Axis I disorders, and more research is needed on the heterogeneity of BPD, the investigators noted.

The existence of the four BPD factors that appear to differ from those reported for similar studies in adults raises "the question whether BPD is different in its nature and underlying structure in adolescents," the authors wrote.

Methylphenidate and Cell Abnormalities

Methylphenidate is associated with significant increases in cell abnormalities when given to children at therapeutic levels, reported Dr. Randa A. El-Zein of the University of Texas M. D. Anderson Cancer Center, Houston, and colleagues.

Data from 12 children showed significant increases in several genotoxic end points after 3 months of daily treatment with methylphenidate. The children, whose average age was 9 years, received doses ranging from 20 mg/day to 54 mg/day (Cancer Letters 2005;230:284-91).

Peripheral blood lymphocyte samples were collected from the children at baseline and after 3 months of treatment and evaluated for cell abnormalities.

Compared with baseline values, the children demonstrated a threefold increase in the mean number of chromosomal abnormalities, from 1.7 per 50 cells to 5.1 per 50 cells. They also showed a 4.3-fold increase in the mean number of sister chromatid exchanges (the number of crossover events in a chromosome pair), from 6.1 to 26.3, and a 2.4-fold increase in micronuclei frequencies per 1,000 cells, from 3.6 to 8.5.

Despite the small sample size, the investigators said, their study was "remarkable in the consistency of the increase of every type of cytogenetic end point monitored, in every child receiving the drug." The study opens the door for further larger studies that address these issues in order to establish the safety of methylphenidate, as well as possible replacement drugs, for treating ADHD, they said.

Psychosocial Support, Pregnant Teens

Pregnant adolescents who receive interdisciplinary prenatal and postpartum care and psychosocial support have lower rates of rapid pregnancy recurrence, Amanda Melhado reported at the annual meeting of the Society for Adolescent Medicine.

In a prospective study of a "global care" model, Ms. Melhado, Dr. Maria José Carvalho Sant'Anna, and Dr. Verônica Coates of Faculdade de Ciências Médicas da Santa Casa in São Paolo, Brazil, compared the outcomes of 30 adolescents who received specialized prenatal medical care and psychoeducational support with those of 39 age-matched adolescents who received standard prenatal care only. All of the young women in the study were 18 years old or younger at the time of conception and gave birth in the maternity ward of the same hospital between July 1, 2004, and June 30, 2005.

No significant differences were found between the two groups with respect to marital status or relationship with the babies' fathers, Ms. Melhado said. More than half of the young women in both groups were not married at the time of the study.

The psychoeducational support component included group and individual sessions with a team of providers—including mental health professionals, obstetricians, and pediatricians—focusing on such topics as self-esteem, contraception, relationships, and infant development.

As of March 2006, the rate of pregnancy recurrence among the young women who received the intervention was 3%, compared with 15% in the standard care group.

—Heidi Splete with staff reports