

Compliance Puts New Spin on Psychosis Treatment

Adolescents with prodromal psychosis had better outcomes with antidepressants than antipsychotics.

BY DIANA MAHONEY
New England Bureau

ATLANTA — Adolescents with prodromal psychosis who were being treated with second-generation antipsychotic drugs had significantly higher rates of medication noncompliance than adolescents who had the same early symptoms and were taking antidepressants, according to early results from a naturalistic treatment study.

Preliminary findings from the ongoing Recognition and Prevention (RAP) program at the Zucker Hillside Hospital in Glen Oaks, N.Y., and Schneider Children's Hospital in New Hyde Park, N.Y., also showed that the medication-noncompliant adolescents were 10 times more likely to convert to full psychosis during a 5-year follow-up period than adolescents who remained on their prescribed regimen, Barbara Cornblatt, Ph.D., said at the annual meeting of the American Psychiatric Association.

"While the second-generation antipsychotics may have a positive effect in treating symptoms, if adolescents won't stay on them, the drugs cannot possibly be effective," said Dr. Cornblatt, director of the RAP program.

"On the other hand, it seems that the antidepressants are more tolerated and have some kind of protective effect, though exactly what that may be is not yet clear," she said.

The RAP program began in 1997 and

typically serves adolescents between the ages of 12 and 18 who fall somewhere on the prodromal psychosis continuum and have been referred to the stand-alone RAP clinic for treatment.

The objective of the research arm of the RAP program is to gain insight into the natural history and developmental course of psychotic disorders, as well as to understand the effects of different medications at different phases of the illness using a naturalistic vs. randomized control format.

"Our researchers treat patients as they would if they were in private practice with respect to selecting drug and behavior therapy. We give them no input; there's no ideation of our hypotheses. When they prescribe medication, it's based on the symptoms being displayed, not the notion of prevention," Dr. Cornblatt said.

To date, 152 patients at a mean age of 15 years have completed the baseline research procedures and have been divided into one of three subgroups:

► Clinical high-risk negative patients, who meet prodromal criteria but have only exhibited nonspecific negative symptoms, such as anhedonia and lack of affect.

► Clinical high-risk positive patients, who have attenuated positive prodromal symp-

toms (delusions and hallucinations, as well as disorganized thoughts and speech).

► Clinical high-risk "slip" patients, "who are just slipping into first-episode psychosis," Dr. Cornblatt explained.

The adherence/conversion data come from a sample of 50 clinical high-risk positive patients who had at least 1 year of follow-up and available adherence rates. Although no significant differences were found in baseline symptoms, 22 of the patients were prescribed antidepressants, 11

received monotherapy with second-generation antipsychotics (either olanzapine or risperidone), and 17 received combination therapy of antidepressants and antipsychotics.

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DR. CORNBLATT

"For purposes of reporting outcome, the two groups that received antipsychotic medications were combined because we didn't find any difference between the baseline characteristics or outcome between combination [and] monotherapy," Dr. Cornblatt said.

During the follow-up period, investigators found that 13 of the 50 patients developed psychoses. Of the 13 who converted, 12 were receiving antipsychotic medication.

"In other words, nearly half the patients being treated with antipsychotics converted, compared with 1 out of 22 patients on antidepressants," Dr. Cornblatt noted.

The only major difference that was not-

ed between these two groups, other than the class of medication they received, was noncompliance to medication. Approximately 64% of adolescents prescribed antipsychotics were noncompliant, compared with 18% of those prescribed antidepressants alone.

"In general, the females in the study were more compliant with medication, and the older boys were the least compliant, suggesting that the earlier therapy is introduced, the more successful it might be," Dr. Cornblatt said.

The low conversion rate in this study among those adolescents who stayed on their antidepressant medication and the high conversion rate among those who were medication noncompliant generate several hypotheses.

"It's possible that the negative symptoms set up some sort of biologic vulnerability, and maybe going to antidepressants directly affects these underlying negative components," Dr. Cornblatt said.

"It's also possible that, although noncompliance doesn't cause positive symptoms, it could act as a trigger that makes them worse or more likely to progress to psychosis," she said.

Although the outcome data from this investigation are "obviously not the final word because the study was not randomized, it does make the case that treating prodromal individuals with antidepressants does not cause any damage and might have some kind of positive effect," she said.

"And it also points to medication noncompliance as a possible stressor, and one that we might be able to deal with," Dr. Cornblatt noted. ■



Symptoms of Pediatric Delirium Often Overlooked, Mistreated

BY JANE SALODOF MACNEIL
Southwest Bureau

SANTA ANA PUEBLO, N.M. — Pediatric delirium is rarely discussed in the medical literature and hardly ever diagnosed in practice, but Dr. Susan Beckwitt Turkel contends that children may be as vulnerable as elderly patients.

"I think when we say that children don't get delirium, it is because it is very rarely diagnosed by pediatricians, and most consultation-liaison psychiatrists don't bump into it," Dr. Turkel said at the annual meeting of the Academy of Psychosomatic Medicine.

Pediatric delirium "is probably very common, and when it does occur, it is typically mistreated," said Dr. Turkel, chief of neuropsychiatry and child adolescent psychiatry at Childrens Hospital Los Angeles.

She speculated that age-related changes in the cholinergic systems may put children and the elderly at risk for delirium. "It may have something to do with the development of the cholinergic system in the brain and then the decline of cholinergic system in the brain," she said.

Children present with many of the characteristic symptoms in the DSM-IV, but, because pediatricians think in a developmental context, they describe "behavioral regression," according to Dr. Turkel.

She suggested many children become delirious while running high fevers from common conditions such as ear infections that are treated at home.

At Childrens Hospital, a tertiary care referral center, she and a colleague reviewed 84 cases involving very sick chil-

dren who were the subject of psychiatric-liaison consultations from 1991 through 1995 (J. Neuropsychiatry Clin. Neurosci. 2003;15:431-5).

Delirium was identified in 45 males and 39 females, ranging in age from 6 months to 18 years. Their length of stay ranged from 1 to 255 days, with an average of 41 days.

Infection was the most common cause of delirium, but mortality was higher in children with organ failure, autoimmune diseases, or a recent transplant. Overall, the mortality rate was 20%.

All of the children had impaired attention and fluctuating symptoms, often described as "waxing and waning." Nearly all had impaired alertness, confusion, sleep disturbance, and impaired responsiveness. Exacerbation at night and disorientation also were common.

Apathy and agitation were documented in more than two-thirds of the children. Only about half had memory impairment. Fewer than half hallucinated, and none had perceptual disturbance, delusion, paranoia, or hypervigilance.

"These are not things you see in children," Dr. Turkel said, adding that when children do hallucinate, the experience is more likely to be auditory than visual.

Dr. Turkel said she has since compared the children with 968 adults, aged 30-100 years, in 10 published delirium studies. "Overall, you see the same symptoms in toddlers, children, adolescents and adults, but maybe at different rates," she said, noting that the articles concerning adults were not consistent with each other in reporting data.

As many adult diagnostic techniques cannot be used with very young children, she suggested asking pediatric hospital patients where they are.

"If they tell you they are at home or at school, you can tell they are disoriented," she said. "They don't have the same specificity you get from an adult."

Sometimes a child will talk to someone who is not there, she said. Mood changes, irritability, and sleep changes also are clues.

"The inattention may not be picked up, but we get the consult because they are not sleeping," she said. "They nap a little while, and wake up really cranky."

Dr. Turkel described her approach to delirium treatment as multifactorial. Physicians treat the underlying condition, she said, but also look for sedating and anticholinergic medications that may be playing a role.

She said she works closely with the child's family, advising parents that their job is to tell children where they are each time they wake up irritable and confused. "You tell them ... 'You are in the hospital, you are sick, and mommy is here.' That is often enough to calm them down," she said.

Positioning the children near a window can help them distinguish day from night, she added.

If these interventions do not work, Dr. Turkel said she gives the child a small dose of an atypical antipsychotic medication.

Benzodiazepines and anticholinergic agents should be avoided, she said, as they can make delirium worse and even precipitate delirium. ■