Tool Helps Spot Bipolar Prodrome in Children

Questionnaire asks patients to rate 39 symptoms that can emerge before the first manic episode.

BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

TORONTO — Many children with bipolar disorder experience a lengthy prodromal phase of clinically significant symptoms before their first manic episode; in almost 70% of these children, the prodrome begins with a drop in school functioning, often accompanied by racing thoughts, irritability, and anger, and can last for almost 1 year.

Recognizing such a prodrome could help facilitate an early intervention program for children who are at risk of developing bipolar disorder, Dr. Christoph Correll reported at the joint annual meeting of the American Academy of Child and Adolescent Psychiatry and the Canadian Academy of Child and Adolescent Psychiatry.

"The sufficient duration and severity of this prodrome enables the development of early identification and prevention programs," wrote Dr. Correll, a psychiatrist at the Zucker Hillside Hospital, Glen Oaks, N.Y. However, "prospective studies are required to validate these findings and to test effective interventions."

Dr. Correll characterized the onset of bipolar disorder in 51 patients by interviewing the patients and/or their parents with his newly created Bipolar Prodrome Symptoms Scale–Retrospective Version.

The questionnaire asks parents and patients to rate 39 putatively prodromal symptoms that can emerge before the occurrence of a syndromal manic or hypomanic episode.

The scale—an in-person structured interview with patient or parent alone—takes between 1 and 1.5 hours to complete. It was developed based on DSM-IV criteria for major depressive disorder and bipolar disorder, a review of the literature, input from experts in the areas of schizophrenia prodrome and bipolar disorder, and open questioning of young patients and their caregivers.

Dr. Correll also drew the symptoms that the scale assesses from several retrospective studies that have identified some possibly prodromal traits, including depressed mood or hopelessness, hyperactivity, mood swings, increased or decreased energy, irritability or anger dyscontrol, argumentativeness, decreased sleep, crying spells, inappropriate behaviors, and overtalkativeness.

The patients' mean age was 16 years; the mean age at first manic episode was 13 years.

The patients experienced a mean of 13 of the prodromal symptoms, which preceded the first full manic episode by nearly 1 year.

In more than half of the patients, the most commonly reported symptoms that were at least moderately severe were a drop in school functioning, irritability or anger, racing thoughts, mood swings, inattention, depressed mood, and anger outbursts or tantrums.

At least moderately severe symptoms of increased energy, psychomotor agitation, overtalkativeness, and social isolation occurred in more than 40% of patients.

The most common presenting symptoms were a drop in school functioning, mood swings, depressed mood, irritability or anger, social isolation, and racing thoughts.

About one in five patients reported presenting symptoms of oppositionality, anhedonia, being overly cheerful, psychomotor agitation, or inattention.

The lag between first manic episode and bipolar disorder diagnosis was about 20 months, but the lag between onset of prodromal symptoms and diagnosis was twice that long—a mean of 41 months.

In most patients (59%), the prodromal onset was slow and marked by gradual deterioration; 29% of patients experienced a slow onset with quick deterioration, while only 12% experienced a rapid onset of illness.

The newly developed scale will be useful not only in assessing a possible prodrome, but in research as well, Dr. Correll said in an interview.

In most patients (59%), the prodromal onset was slow and marked by gradual deterioration.

DR. CORRELL

"It can be used in future studies to determine different patterns of symptom onset and contributing factors to symptom onset, as well as to identify characteristics that may define a person who may be at ultrahigh risk for the development of bipolar disorder," he said.

He is also working on a prospective version of the scale, which he hopes will be a valuable predictive tool. "We have already used the data from this study to develop a prospective version of the scale," Dr. Correll said.

"We are now in the process of validating the scale and criteria that predict conversion to bipolar disorder in patients considered to be at clinical risk for the development of bipolar disorder," he commented. ■

Dearth of Evidence in Guiding Tx Of Bipolar Depression in Teens

BY JEFF EVANS
Senior Writer

NEW YORK — Because of the current lack of data and consensus on the treatment of bipolar depression in children and adolescents, pharmacotherapeutic options need to be discussed with family members on a case-by-case basis, Dr. Gabrielle A. Carlson said at a psychopharmacology update sponsored by the American Academy of Child and Adolescent Psychiatry.

No controlled studies of bipolar depression in children or adolescents exist and no results from such trials can be expected for the foreseeable future, said Dr. Carlson, director of child and adolescent psychiatry at the State University of New York at Stony Brook. A few recent open-label trials with lithium and lamotrigine (Lamictal) provide all the data that are available on pharmacotherapy in these patients.

In one study, a 6-week open trial of lithium in hospitalized adolescents with bipolar depression, 13 of the 27 patients had a 50% reduction in Children's Depression Rating Scale–Revised (CDRS-R) scores at some point during the study. At the end of the 6 weeks, however, only 8 patients met the study's response criteria, defined as a CDRS-R score of 28 or less and a Clinical Global Impressions (CGI) score of 2 or less. Most of the patients' improvement occurred during the first 2 weeks of the trial, when they were in the hospital.

In an open study of 20 adolescents with bipolar I, II, or depression not otherwise specified, 16 patients responded to lamotrigine after 8 weeks, as defined by a CGI score of 2 or less. Eleven patients were in remission after 8 weeks. Seven of the patients also were taking other psychotropic medications.

"Until there are placebo-controlled trials [of children and adolescents] in bipolar depression, don't get too excited because we all know that there are high rates of placebo response in depression," Dr. Carlson said.

When treating a first-episode case of depression, clinicians should consider that bipolar disorder is prevalent in only 5% of children and adolescents who have a parent with the condition, according to one study, whereas unipolar depression and other affective disorders are prevalent in 9% and 27% of children and adolescents with such parents, respectively, she said.

Clinicians will need to consider different scenarios when treating a first episode of major depression in adolescents and children with bipolar disorder, or even recurrent unipolar major depression in pediatric patients with a history of bipolar disorder in their families. In both cases, the clinician will have to decide on whether to prescribe an antidepressant—which requires a discussion of its risks and benefits in light of the black box warning on suicidal ideation—or a mood stabilizer that may not be needed, Dr. Carlson said. ■

Quetiapine May Help Manage Depression in Bipolar Adolescents

TORONTO — Quetiapine appears to improve symptoms of depression and suicidal ideation in adolescents with bipolar disorder, mood disorder, and those at familial risk of developing bipolar disorder, according to a poster presented at the joint annual meeting of the American Academy of Child and Adolescent Psychiatry and the Canadian Academy of Child and Adolescent Psychiatry.

Dr. Melissa DelBello of the University of Cincinnati and her colleagues presented the results of three studies of the drug in bipolar adolescents aged 12-18 years.

Study 1 included 30 adolescents hospitalized with mixed or manic episodes.

The patients were randomized to divalproex or divalproex plus quetiapine (mean dose 423 mg/day) for 6 weeks.

Those in the combination group experienced a greater mean decrease in depression scores from baseline than did those in the divalproex-only group (from 50 to 24 vs. 50 to 34, respectively).

Study 2 included 50 patients hospitalized with bipolar I disorder (94% mixed, 6% manic episodes).

They were randomized to quetiapine (Seroquel) monotherapy (mean dose 417 mg/day) or divalproex monotherapy for 4 weeks.

Mean depression scores in the quetiapine group decreased from 52 to 25. Dr. DelBello did not analyze the divalproex response in this study.

Study 3 included 25 hospitalized adolescents with a mood disorder and with at least one parent with bipolar disorder.

The adolescents received quetiapine monotherapy (mean dose 447 mg/day) for 12 weeks. Mean depression scores decreased from 40 to 29.

In the three studies, 65 patients who took quetiapine alone had major depression. Overall, their mean suicidality score decreased from 3.0 to 1.5.

The suicidality score increased, however, in two of the patients, both of whom were taking quetiapine.

Quetiapine was well tolerated alone and in combination with divalproex, Dr. DelBello said.

Sedation (mostly mild and transient) was the most common adverse event, followed by dizziness and gastrointestinal upset. No patients discontinued therapy because of adverse events.

The poster was sponsored by AstraZeneca.

—Michele G. Sullivan