Update on Pediatric Bipolar Disorder

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Bipolar disorder (BPD): no child should be treated unless diagnosis established; close follow-up and knowledge of child and family important; developmental stage of child must be considered; some children with BPD misdiagnosed with attention-deficit/hyperactivity disorder (ADHD) or oppositional behavioral disorder; onset of BPD typically in adolescence; prevalence 1% to 2%; most studies indicate that BPD begins before 25 yr of age; 70% of patients have mood symptoms before 18 yr of age.

Presentation: in patients who do not meet strict criteria for BPD I or II, bipolar disorder not otherwise specified (BP-NOS) diagnosed if hypomania lasts <4 days or mania lasts <7 days; these children should be treated; children with mood and behavioral disorders or temper outbursts may or may not have BPD; following them may clarify diagnosis.

Case 1: 13-yr-old boy presented with depression early in life and 2 severe manic episodes; child referred by school and police for behavioral issues; he ultimately did well on combination of lithium andquetiapine (Seroquel).

Case 2: girl presented with 2-yr history of 2- to 10-day episodes of major depression (tearfulness, low energy, insomnia, lack of motivation, irritability, frustration, and temper tantrums) and 2- to 3-day episodes of high activity (extreme happiness, giggling, talkativeness, high energy, and sleeping 3 to 4 hr nightly); this 9-yr-old responded well to treatment for BPD.

Diagnosis: may be challenging; children may be depressed, manic, or hypomanic or have mixed presentations that complicate diagnosis; many children also have ADHD, oppositional behavior, or substance abuse; symptoms of ADHD and BPD overlap (eg, hyperactivity, impulsivity), so may be difficult to disentangle unless clinician knows child and family well; children often have increased energy and may be irritable, labile, or destructive, but symptoms vary.

Speaker’s study: design — study recruited children 6 to 18 yr of age whose parents had BPD I or II; children matched with controls randomly selected from community and assessed every 2 yr; population — 233 parents and 143 controls recruited; parents with BPD had more substance abuse, anxiety, disruptive behaviors, and ADHD; unclear whether psychopathology in these children caused by living with parents with BPD or by BPD itself; findings — when ≈400 children of these parents compared with 250 children of controls, children whose parents had BPD showed more mood disorders, Axis I disorders, BPD, and ADHD; after adjusting for family conflict, demographics, and parental psychopathology, BPD still more common in children of affected families; data analyzed over 10 yr; diagnosis of bipolar spectrum disorder (including BP-NOS) made in 23% of offspring of parents with BPD and 3% of children of controls (rate of BPD in controls similar to that expected in community); BPD I or II diagnosed in 12% of children whose parents had BPD.

Risk factors: study assessed whether development of BPD predictable; children with threshold manic episodes, major depressive episodes, and disruptive behavioral disorders at risk for BPD; when only children with new onset of BPD included, main risk factor threshold manic episodes; incidence of BPD increased when parent developed BPD before 18 yr of age; development of BPD more likely in children with anxiety, depression, and affective lability; if child has anxiety, depression, affective lability, and subsyndromal manic symptoms, and parent had early onset of BPD, risk for BPD in child ≈50%; children of parents with BPD may also have ADHD, substance abuse, and anxiety.

Longitudinal study: in multicenter longitudinal study of children with BPD, 438 patients evaluated every 6 to 9 mo; population — mean age 13 yr; 50% of children male, 80% white, and 40% living with both biological parents; mean age at onset of mood symptoms 9 yr; mean duration of illness 3 yr; mean score on Global Assessment Scale (GAS) 55; 60% of children had BPD I, 35% had BP-NOS, and 7% had BPD II; findings — many children had subclinical symptoms, mixed episodes, irritability, switching of polarity, hallucinations, ADHD, and oppositional defiant disorder; young age at presentation associated with worse outcomes, numerous admissions, and polypharmacy; affected children often experienced family conflicts, academic problems, physical and sexual abuse (in 20%); psychotic symptoms (30%), significant suicidal ideation (76%), and attempted suicide (40%-50%); only 19% had substance abuse, but mean age of children in study 13 yr; over time, ≈40% expected to develop substance abuse.

Outcomes: survival analysis — over course of 4-yr study, 80% of children recovered, but 60% of those had recurrences; over 8 yr, conversion to BPD I observed in 25% of patients with BPD II and in 45% of those with BP-NOS; many children with BP-NOS did as poorly as those with BPD I; subsyndromal mania should be followed and treated; duration of illness — over 4 yr, children euthymic 40% of time and had syndromic or subsyndromic symptoms 60% of time, especially mixed symptoms and depression; other findings — compared to adults with...
BPD I (who were in another long-term study), children with BPD I and II spent significantly less time being well and had more mixed presentations, rapid cycling, and changes of polarity; in Kraepelin study (1921), most patients <30 yr of age had mixed episodes; speaker’s study, although confounded by treatment, verified these findings; in 367 subjects studied over 4 yr, 24% of children euthymic for 80% of time; 20% persistently did poorly; another group initially did poorly but improved, contradicting beliefs about lifelong nature of BPD; some children continue to do well and can stop treatment; Kraepelin found that some children had no more episodes for 20 yr; this information may provide hope for families; poor functioning despite stable mood — speaker analyzed children who did persistently well, ie, who maintained stable moods; in subgroup of 56 children, functioning poor due to family conflicts, poor neighborhoods, low socioeconomic status, comorbid ADHD, and substance abuse; risk factors for poor outcomes include early onset of disorder, severe depressive or manic symptoms, suicidality, subsyndromal episodes, comorbid disorders, sexual abuse, and family history of substance abuse and mania

Psychotherapy: children with BPD I or II or BP-NOS need psychopharmacology and psychotherapy; education — part of treatment; educating parents may help them understand why child has difficulty controlling his behavior; study in teenagers with major depression showed that Beck Depression Inventory scores of 25 to 30 fell to 5 to 6 with education alone in 30% of patients; psychotherapy — increases adherence and treats depression; approaches include cognitive behavioral therapy, family-focused therapy, group approaches, and dialectic behavioral therapy

Pharmacotherapy: randomized controlled trials (RCTs) evaluating mood stabilizers for acute mania or mixed episodes report response rates of 50% to 60% and remission in 25% to 50%; effect sizes of mood stabilizers in children range from 0.2 to 0.5; drugs less effective than in adults, possibly because children have more mixed episodes (which usually do not respond to lithium and valproate); in children, lithium works better than valproate; topiramate, carbamazepine, and oxcarbazepine not effective; in multicenter study, lithium superior to placebo; difference between groups not large, but some individuals responded well to lithium; children respond well and quickly to atypical antipsychotics (however, some children in large RCTs may not actually have bipolar illness); in multicenter study, 70% responded acutely to risperidone, 30% to lithium, and 20% to valproate; other studies confirm that children respond well to atypicals; children tend to relapse when treatment is discontinued prematurely; rate of relapse 90% after stopping lithium (vs 40% in children who continued treatment); in some studies, combination of lithium and valproate better, but sample size small and result preliminary; long-term effects of medications in children unknown; side effects include increased glucose and cholesterol; atypical antipsychotics increase risk for diabetes in dose-dependent fashion; other side effects extrapyramidal symptoms, neuroleptic malignant syndrome (NMS), and elevated prolactin; body mass index and hemoglobin A1c should be followed

Bipolar depression: very few studies have assessed treatment of bipolar depression; RCT that compared quetiapine with placebo in children had negative result; management depends on severity of hypomania; studies support monotherapy with selective serotonin reuptake inhibitors; lamotrigine useful; children who function better when hypomanic may be allowed to remain hypomanic but should be taught which symptoms to report

Comorbid disorders: should be treated; in children with ADHD, stimulants do not worsen BPD; if child has ADHD and diagnosis of BPD in doubt, ADHD should be treated; in some cases, symptoms of BPD disappear

Summary: unlike adults, children gain weight on aripiprazole (Abilify); unknown how long to give continuation treatment

Suggested Reading


Diagnosing and Managing Dangerous Psychiatric Disorders

Kim Nordstrom, MD, JD, Assistant Professor, University of Colorado Denver School of Medicine; Medical Director, Psychiatric Emergency Services, Denver Health Medical Center; President, American Association for Emergency Psychiatry, Denver

Triaging: when determining whether patient should be admitted to medical or psychiatric service, psychiatrist should evaluate chief complaint, timing and severity of symptoms, and vital signs (VS); once situation less acute, history should be explored

Serious conditions: factors associated with life-threatening medical conditions include new onset of symptoms in youth or later years, sudden onset, delirium, fluctuating course, disorientation, abnormal VS, and focal neurologic examination

Case 1: 44-yr-old man with long history of major depression presented with 1 day of no talking or moving, minimal recognition of his wife, and confusion; patient could follow commands but initiated no actions on his own

Case 2: 65-yr-old woman had high fever, autonomic instability, hallucinations, and no psychiatric history

Case 3: 20-yr-old man brought to emergency department by police for aggressive behavior; patient threatening personnel; heart rate 110 bpm but VA otherwise normal

Catatonia: any of these 3 patients could have catatonia; patients with retarded catatonia appear withdrawn; 3 forms of catatonia exist; failure to treat other forms of catatonia may allow progression to malignant catatonia; third form excited catatonia; many medical and psychiatric disorders, including neuroleptic malignant syndrome (NMS), cause catatonia

Retarded catatonia: symptoms include decreased movements, rigidity, posturing, and waxy flexibility; benzodiazepines initial treatment for every form of catatonia; patients with schizophrenia may need higher doses; electroconvulsive therapy (ECT) second-line treatment for retarded or withdrawal catatonia; underlying cause should be treated; differential diagnosis includes hypoactive delirium; retarded catatonia usually has medical cause

Excited catatonia: using antipsychotic in patient with agitation from excited catatonia (eg, case 3) problematic; patients have increased motor agitation; condition differentiated from other causes of agitation by repetitive movements and other symptoms of catatonia; patients may alternate between excited and retarded catatonia; Bush-Francis Catatonia Rating Scale not
widely used in clinical setting but may help clinician recall other symptoms of catatonia; 60% to 80% of patients respond to monotherapy with benzodiazepines; high doses may be required; psychiatrist should begin with 1 to 3 mg, 3 times daily, and increase dose quickly; barbiturates not standard of care; ECT used for second-line treatment

Malignant catatonia: as with NMS, symptoms include autonomic instability, fever, and rigidity; motor signs may be present; initial treatment ECT, but benzodiazepines also often used; supportive care for immobile patients may include compression stockings and heparin; high fever may necessitate rebalancing of electrolytes

Management: high doses of benzodiazepines may be used if tolerated; if diagnosis questionable, give test dose of lorazepam (Ativan); patient with catatonia should respond within minutes to intravenous (IV) administration; treatment continued for 4 to 10 days; although other benzodiazepines may be used, lorazepam considered standard of care; no absolute contraindications to ECT

Case 4: 20-yr-old woman with history of psychosis during pregnancy presented with presumed psychosis at 18 wk gestation; patient hospitalized for 2 wk for vomiting and treated with IV fluids, potassium, and antiemetics; patient incontinent and not speaking, eating, or walking; she had wide-based gait with slow, short steps, nystagmus, difficulty expressing words, decreased sensation to painful stimuli, and increased tone in lower extremities; magnetic resonance imaging showed abnormalities in thalami; diagnosis—patient had Wernicke encephalopathy from altered nutritional status; classic triad of ataxia, eye changes, and altered mental status found in only 20% of patients; Caine criteria nutritional deficiency, oculomotor abnormalities, cerebellar dysfunction, and altered mental status; presence of 2 of these 4 criteria 85% sensitive and 100% specific for Wernicke encephalopathy; Caine criteria should be used instead of triad; patient improved on thiamine but had persistent deficits; unclear whether thiamine must be given before glucose

Case 5: 19-yr-old male brought in by police for waving and screaming at cars from interstate highway; history unobtainable; patient treated with haloperidol (Haldol) and midazolam (Versed); patient shouting and unable to answer questions; heart rate slightly elevated; glucose normal; differential diagnosis broad; patient had stimulant intoxication; treated with fluids and rest; support for stimulant intoxication may include medical intervention if patient tachycardic; initial phase of treatment includes benzodiazepines (rather than antipsychotics); patients may demonstrate euphoria, irritability, overconfidence, sexually inappropriate behavior, disorganization, psychosis, or aggression; withdrawal phase more difficult to manage; patients may become dysphoric and suicidal; in emergency setting, treatment focused on agitation and supportive care during intoxication; during withdrawal, safety plan should be developed and detoxification managed

Suggested Reading


Acknowledgments

Dr. Birmaher was recorded at the 21st National Psychopharmacology Update, presented by Nevada Psychiatric Association and held February 10-13, 2016, in Las Vegas, NV. Dr. Nordstrom spoke at the Sixth Annual National Update on Behavioral Emergencies, presented by Sinai Health System and the Rosalind Franklin University of Medicine & Science, and held December 3-4, 2015, in Las Vegas, NV. For information on the 22nd National Psychopharmacology Update, scheduled for February 12-19, 2017, in Las Vegas, visit npvpsychiatry.org. To learn about the next National Update on Behavioral Emergencies, scheduled for December 7-9, 2016, in Las Vegas, visit behavioralemergencies.com. The Audio Digest Foundation thanks the speakers and the sponsors for their cooperation in the production of this program.

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1. Which of the following is the most common time of onset of bipolar disorder (BPD)?
   (A) Childhood  (C) Early adulthood
   (B) Adolescence  (D) Middle age

2. A study by Birmaher et al compared ≈400 children of parents with BPD to 250 children of controls. Approximately what percent of offspring of parents with BPD developed bipolar spectrum disorder over a 10-yr period?
   (A) 3%  (B) 12%  (C) 23%  (D) 80%

3. In the study described in Question 2, what was the main risk factor for new onset of BPD in children of parents who had BPD?
   (A) Disruptive behavior  (C) Substance abuse in the family
   (B) Major depressive episodes  (D) Threshold manic episodes

4. In a multicenter, longitudinal study of 438 children, which of the following was most common among children with BPD?
   (A) Significant suicidal ideation  (C) Substance abuse
   (B) Physical/sexual abuse  (D) Psychosis

5. In a study of children with BPD, what was the percentage of children with BPD II whose condition converted to BPD I within 8 yr?
   (A) 19%  (B) 25%  (C) 45%  (D) 60%

6. Which of the following statements about treating children with BPD with mood stabilizers is correct?
   (A) Children tend to respond better than adults
   (B) Valproate is more effective than lithium
   (C) The rate of response is ≈50%
   (D) Topiramate is often effective

7. A randomized, controlled, multicenter study that evaluated multiple drugs for treating children with BPD found that children were most likely to respond acutely to:
   (A) A combination of valproate and lithium
   (B) Valproate
   (C) Carbamazepine
   (D) Risperidone

8. Which of the following had a negative result in a study vs placebo and is NOT recommended for treating children with bipolar depression?
   (A) Selective serotonin reuptake inhibitors
   (B) Lamotrigine
   (C) Quetiapine

9. Which of the following should the psychiatrist use as initial treatment for a patient with excited catatonia?
   (A) Glucose  (C) Electroconvulsive therapy
   (B) Benzodiazepines  (D) Barbiturates

10. The Caine criteria for Wernicke encephalopathy include all the following, EXCEPT:
    (A) Decreased sensation to painful stimuli  (C) Altered mental status
    (B) Cerebellar dysfunction  (D) Nutritional deficiency

Answers to Audio Digest Psychiatry Volume 45, Issue 19: 1-D, 2-B, 3-A, 4-C, 5-D, 6-A, 7-B, 8-D, 9-C, 10-B

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