Prazosin for Pediatric PTSD

There is little evidence available to guide treatment of posttraumatic stress disorder in young children. SSRIs are considered first-line treatment for adult PTSD, but controlled trials of sertraline have not found it more effective than placebo in young patients. Although not FDA approved for PTSD treatment, the alpha-antagonist prazosin has been shown to be effective in adults and adolescents with PTSD but has not been evaluated in prepubertal children.

A 7-year-old boy presented with PTSD associated with a sexual assault. The child was experiencing insomnia, recurrent nightmares, and intrusive and hyperarousal symptoms. He had been receiving 5 mg/day dexmethylphenidate for comorbid ADHD. Supportive psychotherapy did not improve the PTSD symptoms, and his Clinical Global Impression-Severity (CGI-S) Scale* score was 5. He was started on 1 mg prazosin at bedtime. His CGI-S score quickly decreased to 2, and he was judged to be much improved. Over nearly a year of follow-up, the child reported no nightmares, normal sleep latency, less hyperarousal, and gradual improvement in avoidant symptoms. Treatment was well tolerated, he experienced no orthostatic hypertension or excessive sedation, but weight gain and increased body mass index were noted. Intrusive and hyperarousal symptoms recurred during a 5-day lapse in medication, but they resolved when prazosin was restarted.

Strawn J, Keeshin B: Successful treatment of posttraumatic stress disorder with prazosin in a young child [letter]. Annals of Pharmacotherapy 2011; doi 10.1345/aph.1Q548. From the University of Cincinnati, Ohio; and Cincinnati Children’s Hospital Medical Center, Ohio. The primary study author disclosed a financial relationship with a commercial source.

Drug Trade Names: dexmethylphenidate—Focalin; prazosin—Minipress; sertraline—Zoloft

*See Reference Guide.

Atypical Antipsychotics and Diabetes Risk

In a retrospective cohort study, second-generation antipsychotics were associated with a 4-fold increase in diabetes risk in children and adolescents. However, the association was inconsistent and requires additional investigation.

Methods: Investigators analyzed data from 3 large health plans that enrolled >700,000 youths, aged 5–18 years. Patients newly prescribed a second-generation antipsychotic between 2001 and
2008 were compared with 2 other groups: children not exposed to any antipsychotic medication (a 4:1 match) and all youths with a new prescription for an SSRI or a tricyclic antidepressant. Diabetes onset was defined as a diabetes diagnosis or dispensing of a diabetes medication within the first year after prescription of a psychotropic drug (or an equivalent index date) in children with no previous history of diabetes. (Metformin monotherapy in adolescent girls was not included as an outcome.) For a secondary analysis, the definition of diabetes was expanded to include an abnormal glucose laboratory test.

**Results:** A total of 9636 children and adolescents started therapy with an atypical antipsychotic. About 60% were male, and 46% were aged 15–18 years. There were 12 cases of incident diabetes in this group, compared with 26 cases in >38,000 healthy controls and 19 cases in >26,000 youths prescribed an antidepressant. Patients prescribed an antipsychotic were 4 times as likely as controls to have onset of diabetes (incidence rate ratio,* 4.24; 95% confidence interval, 1.95–8.72). Their diabetes incidence was also elevated in comparison to youths receiving an antidepressant, although not significantly (rate ratio, 1.74; 95% confidence interval, 0.77–3.78).

Regardless of psychotropic medication exposure, diabetes was more likely to occur in children and adolescents with autism, disruptive behavior disorders, and mood disorders. No other patient characteristics were associated with diabetes risk.

When the investigators used the expanded definition of diabetes that included an abnormal glucose test, the size of the risk elevation did not change in children receiving an atypical antipsychotic compared with unmedicated controls. Using this outcome measure, antipsychotic and antidepressant medications were associated with equivalent risks for diabetes (rate ratio, 0.81).

**Discussion:** The results of this study differed depending on the choice of comparison group and definition of diabetes. Interpretation of the results is also limited by the small sample of identified cases, which did not allow comparison of individual drugs or doses, and by the inability to distinguish between type-1 and type-2 diabetes in an administrative database. Antipsychotic drugs would be expected to influence risk only for type-2 diabetes; thus the reported results may be an underestimate of the true effect.

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**Antidepressants, Stimulants, and Mania**

The growing use of stimulants and the advent of approved antidepressants in pediatric patients have led to concerns that these agents may precipitate mania or accelerate the onset of bipolar disorder. Published evidence was reviewed, and according to the results, stimulants do not appear to induce mania in children with ADHD, even those at risk for bipolar disorder. The results also suggest that if needed, antidepressants can be beneficial but should be used cautiously in this at-risk population.

The common concern that stimulants can induce mania in at-risk children without a diagnosis of bipolar disorder is based on case reports, which are subject to publication bias. Results of 4 longitudinal studies indicate that the risk of inducing mania with stimulants is low. In fact, some research suggests stimulants may even protect against the development of bipolar disorder in children with ADHD and manic symptoms. In children with both bipolar disorder and ADHD, the onset of the latter typically occurs before development of bipolarity and may even represent a distinct precursor form of the disorder. Use of stimulants does not appear to precipitate mania onset even in this high-risk group.
Among children with a diagnosis of bipolar disorder, depending on age, up to 85% have comorbid ADHD. Clinical trials (n=4) have been conducted to assess the effects of adding stimulants or atomoxetine (Strattera) to mood stabilizers in children with bipolar disorder and stabilized mood. Overall, the agents were beneficial for ADHD symptoms, but adverse mood or behavioral effects occurred in 2.5–10% of children receiving ADHD pharmacotherapy. However, these resolved rapidly when the stimulant or atomoxetine was withdrawn. The authors recommend stabilizing mood as fully as possible before cautiously adding stimulants, while monitoring closely for the emergence of mania and suicidality.

Published case reports suggest that treatment-emergent mania or hypomania may appear within 2 weeks to 1 year in children prescribed antidepressants. Rates of mania are relatively low in large-scale pediatric clinical trials of SSRIs, but they are higher in patient populations that may be at elevated risk, such as those with a family history of bipolar disorder. When prescribing antidepressants for children, clinicians should take a careful history for prior antidepressant-induced mania; psychosis; age of onset of depressive symptoms; family history of mood disorders; and red flags such as changes in sleep, irritability, and psychotic features.

In children with bipolar depression, SSRIs should be added only after mood stabilization. The issue of whether antidepressants can induce rapid cycling in children has not been investigated. SSRIs can induce suicidal ideation and behavior in up to 25% of children and adolescents with bipolar disorder. There is little evidence for efficacy of non-SSRI drugs, but psychotherapy may be worth considering in adolescents with bipolar depression. If dangerous behaviors or full-blown, treatment-emergent mania occurs, SSRI therapy should be tapered and a mood stabilizer started.

Goldsmith M, Singh M, Chang K: Antidepressants and psychostimulants in pediatric populations: is there an association with mania? Pediatric Drugs 2011;13:225–243. From Stanford University School of Medicine, Calif. The review was conducted with no external funding. The primary author disclosed financial relationships with commercial sources.

**Soda Consumption Linked to Increased Violence**

High consumption of carbonated, non-diet soft drinks was associated with violent behavior in Boston high-school students, according to a survey.

**Methods:** The Boston Youth Survey is a biennial pencil-and-paper survey of 9th–12th-grade students in Boston public schools. The present analysis is based on responses from the 1618 students who responded to a question about intake of non-diet soda during the prior 7 days. A 12-oz can was considered a single serving, and a 20-oz bottle was considered 2. Students who consumed ≥5 servings during the prior week were classified as high consumers.

**Results:** High consumers of soft drinks (nearly 30% of the sample) were more likely than other adolescents to report carrying a gun or knife (40% vs 27%) and to report that they engaged in violence against other adolescents, dates, or other children in the family (26–57% in frequent soda consumers vs 16–39% in others). The magnitude of the association with violence was similar to that reported for alcohol and tobacco. In an analysis with soda consumption divided into quartiles, there appeared to be a dose-response relationship with both weapon-carrying and all types of violence.

Asian youths, who made up 8% of the sample, were the only ethnic group that showed significant differences in soft-drink consumption, with much less consumption than others. High consumption of soft drinks was equally likely in boys and girls and in black or multiracial youths (who comprised 50% of the sample), Hispanics (representing 33%), and whites (9%). The number of soft drinks consumed was not associated with body mass index or with 2 behaviors indicative of problems: insufficient sleep and not having dinner with the family. Youths with high soda consumption were more likely than others to report alcohol and tobacco use.
Discussion: A small number of previous studies have linked sugar or soft-drink consumption with poor mental health and antisocial behavior. The underlying mechanism is unknown. Caffeine or other additives may be a factor. It is also possible that high soft-drink consumption may be substituted for more nutritious foods or may mask an underlying organic problem, such as low blood sugar or micronutrient deficiencies. Consumption may also reflect behavioral or socioeconomic variables not measured in this survey.

Solnick S, Hemenway D: The 'Twinkie defense': the relationship between carbonated non-diet soft drinks and violence perpetration among Boston high school students. *Injury Prevention* 2011;doi 10.1136/injuryprev-2011-040117. From the University of Vermont, Burlington; and Harvard School of Public Health, Boston, Mass. Funded by the Centers for Disease Control and Prevention. The authors disclosed no competing interests.

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Clinical Global Impression Severity (CGI-S) Scale: A 7-point rating of the severity of illness. A score of 1 corresponds to a rating of normal; 2=borderline mentally ill; 3=mildly ill; 4=moderately ill; 5=markedly ill; 6=severely ill; 7=extremely ill.

Rate Ratio: A comparison of the rates of a disease/event in two groups that differ by demographic characteristics or exposure history. The rate for the group of primary interest is divided by the rate for a comparison group.
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