

Optimal Dosing of Desvenlafaxine, New Insights in Gambling and Anorexia, and Caffeine-Induced Psychosis

By Eric Hollander, MD

This month's *CNS Spectrums* provides information on optimal dosing of desvenlafaxine, a new understanding of ethnic issues in gambling and gene-environment factors in triplets with anorexia nervosa (AN), and a mechanism whereby caffeine can induce psychosis in vulnerable patients.

As a competitive adenosine antagonist, caffeine affects dopamine transmission and has been reported to worsen psychosis in individuals with schizophrenia and to cause psychosis in otherwise healthy people. Dawson W. Hedges, MD, and colleagues report a case of apparent chronic caffeine-induced psychosis characterized by delusions and paranoia in a 47-year-old man with high caffeine intake. The psychosis resolved within 7 weeks after lowering caffeine intake without use of antipsychotic medication. Clinicians might consider the possibility of caffeineism when evaluating chronic psychosis.

Racial minority groups in the United States are more vulnerable to develop a gambling disorder than whites. However, no national survey on gambling disorders exists that has focused on ethnic differences. Analucía A. Alegría, BA, and colleagues analyzed the National Epidemiologic Survey on Alcohol and Related Conditions, a large (N=43,093) national survey of adults during 2001–2002 period. Prevalence rates of disordered gambling among blacks (2.2%) and Native/Asian Americans (2.3%) were higher than that of whites (1.2%). Demographic characteristics and psychiatric comorbidity differed among black, Hispanic, and white disordered gamblers. However, all racial and ethnic groups evidenced

similarities with respect to symptom patterns, time course, and treatment seeking for pathological gambling. The prevalence of disordered gambling, but not its onset or course of symptoms, varies by racial and ethnic group. These varying prevalence rates may reflect, at least in part, cultural differences in gambling and its acceptability and accessibility. These data may inform the need for targeted prevention strategies for high-risk racial and ethnic groups.

To assess the efficacy and optimal dosing of desvenlafaxine in patients with major depressive disorder, Michael E. Thase, MD, and colleagues conducted a meta-analysis of the nine placebo-controlled registration trials of desvenlafaxine. Patients received fixed- (50, 100, 200, or 400 mg/day; n=1,342) or flexible-doses (100–400 mg/day, n=463) of desvenlafaxine or placebo (n=1,108). Significantly greater improvement with desvenlafaxine versus placebo on the 17-item Hamilton Rating Scale for Depression (HAM-D₁₇) total score was observed for the full data set, the fixed-dose groups, and the flexible-dose group. Rates of response ($\geq 50\%$ decrease from baseline score HAM-D₁₇: 53% vs 41%) and remission (HAM-D₁₇: ≤ 7 : 32% vs 23%) were significantly greater for desvenlafaxine versus placebo. Discontinuation rates due to adverse events increased with dose (4% to 18%; placebo: 3%). Desvenlafaxine demonstrated short-term efficacy for treating major depressive disorder across the range of doses studied. No evidence of greater efficacy was observed with doses >50 mg/day, whereas a strong dose-response effect on tolerability was observed.

The cause of AN is unclear, but it is likely multifactorial, including psychological, familial, environmental, societal, genetic, and other biological factors. Mae S. Sokol, MD, and colleagues report on a case of identical 12-year-old female triplets concordant for AN, which illustrates the importance of addressing these multiple components in evaluation and treatment and the difficulty of determining the relative importance of each factor in the cause of an individual's eating disorder. An overly close relationship and competitiveness between the triplet girls and stressful family dynamics were antecedents to AN. The girls encouraged each other and competed to lose weight. Psychotherapy, parent counseling, nutritional counseling, and psychoeducation led to successful treatment. A literature review of AN twins studies add to our understanding of the relative importance of shared genes and shared environment in the development of AN, and add insight into treating individuals from families with multiple affected relatives.

Clearly, clinicians need to evaluate all available data, including meta-analyses, in order to determine the optimal risk-benefit ratio for dosing new medications. The Thase and colleagues data for desvenlafaxine is helpful in this regard. Racial and ethnic differences may contribute to the varying prevalence and presentation of psychiatric illness. Such ethnic factors are currently being incorporated into the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* process, and Alegria and colleagues' data on pathological gambling is helpful in contributing to this knowledge base. Gene-environment interactions play a unique role in the development of neuropsychiatric illness, and the case study by Sokol and colleagues of triplets with AN help to highlight the complexity of disentangling these cause and effect relationships. Finally, caffeine is widely used and abused in our society, but little consideration has been given to its indirect effects on dopamine transmission leading to psychosis exacerbation. Clinicians need to keep this in mind in evaluating contributing factors for psychosis. **CNS**

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Funding for this supplement has been provided by Wyeth Pharmaceuticals*