Gambling, hypersexuality, compulsive shopping associated with dopamine agonist drugs

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During a 10-year period, there were 1,580 adverse drug events reported in the United States and 21 other countries that indicated impulse control disorders in patients, including 628 cases of pathological gambling, 465 cases of hypersexuality and 202 cases of compulsive shopping. The total included 710 events associated with dopamine receptor agonist drugs (used to treat Parkinson disease, restless leg syndrome and hyperprolactinemia) and 870 events for other drugs.

Unusual and severe impulse control disorders, including pathological gambling, hypersexuality and compulsive shopping, have been reported in patients taking dopamine receptor agonist drugs. Dopamine receptor agonist drugs, which activate the dopamine receptors, are commonly prescribed and there were 2.1 million dispensed outpatient prescriptions in the fourth quarter of 2012.

The authors analyzed adverse drug event reports for six dopamine receptor agonist drugs marketed in the U.S. Their analysis was based on 2.7 million domestic and foreign adverse drug event reports from 2003 to 2012 pulled from the U.S. Food and Drug Administration's Adverse Event Reporting System database.

The 710 reports (44.9 percent) for dopamine receptor agonist drugs occurred among patients with a median age of 55 years and who were mostly male (65.8 percent). About half of the reported events happened

in the United States. The medications had mostly been prescribed for Parkinson disease in 438 events (61.7 percent) and restless leg syndrome in 169 events (23.8 percent).

"Our findings confirm and extend the evidence that dopamine receptor agonist drugs are associated with serious impulse control disorders; the associations were significant, the magnitude of the effects was large and the effects were seen for all six dopamine receptor agonist drugs. ... At present, none of the dopamine receptor agonist drugs approved by the FDA have boxed warnings about the potential for the development of severe impulse control disorders as part of their prescribing information. Our data, and data from prior studies, show the need for these prominent warnings," Thomas J. Moore, A.B., of the Institute for Safe Medication Practices, Alexandria, Va., and colleagues wrote in their *JAMA Internal Medicine* article.

In a related commentary, Joshua J. Gagne, Pharm.D., Sc.D., of Brigham and Women's Hospital and Harvard Medical School, Boston, writes: "In this issue, Moore and colleagues present compelling results of a disproportionality analysis examining the association between dopamine receptor agonist drugs and impulsive behavior. ... The authors used these data to calculate a proportional reporting ratio (PRR) of 277.6, indicating that the proportion of all adverse event reports involving impulsive behavior was 277.6 times higher for dopamine receptor agonist drugs vs. other drugs."

"Given the limitations of FAERS [U.S. Food and Drug Administration's Adverse Event Reporting System database] and the provocative analysis by Moore and colleagues, is the association between dopamine receptor agonist drugs and impulse control disorders likely a true causal connection and not merely a pattern among random data? With the large PRR that may actually be attenuated by confounding and the emerging evidence from other sources, the likelihood of a causal connection is

high," Gagne concludes.

In another related commentary, Howard D. Weiss, M.D., of Sinai Hospital of Baltimore, and Gregory M. Pontone, M.D., of Johns Hopkins University School of Medicine, Baltimore, write: "The report by Moore and colleagues in this issue highlights the associations between impulse control disorders and dopamine receptor agonist drugs."

"The report raises several questions? How do dopamine receptor agonist drugs trigger the abnormal behaviors seen in patients with impulse control disorders? Why do some patients, but not others, develop these problems? Why was the association not recognized sooner?" the authors continue.

"In summary, physicians have overestimated the benefit and underestimated the risks associated with the use of dopamine receptor agonist drugs in patients with Parkinson disease. In our view, these medications should be used less frequently and with great caution, paying close attention to possible untoward effects on behavior and impulse control."

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