Increased Sexual Aggression Following Ziprasidone Discontinuation in an Intellectually Disabled Adult Man

To the Editor: Persons with intellectual or developmental disabilities have an increased frequency of aggressive and/or problematic behaviors. It has been estimated that over 50% of this population demonstrates some form of aggression, although the overall severity is low.[1] In addition, a comorbid mental illness may be underdiagnosed secondary to cognitive impairments.[2] As confirmed via a PubMed literature search utilizing the terms *ziprasidone* and *sexual aggression*, we report the first case of increased sexual aggression in an intellectually disabled man following discontinuation of ziprasidone.

Case report. Mr A, a 53-year-old white man, diagnosed with *DSM-IV* intermittent explosive disorder and moderate mental retardation, was admitted in 2006 to the present long-term care facility secondary to multiple failed community placements due to aggression and/or inappropriate behaviors. Behaviors leading to placement in the current long-term care facility included a long history of verbal and physical aggression to avoid nonpreferred tasks. Behaviors may have included physical and verbal intimidation (pushing, shoving, grabbing, invasion of personal space with yelling) and elopement from the area. The level of aggression and/or inappropriate behaviors resulted in frequent moves and changes in community provider agencies. Upon admission to the present facility, the dose of ziprasidone (for mood lability) was 240 mg daily. The dose was reduced to 180 mg daily the following month.

Three months following admission, overall adjustment to the new milieu and structured program was going well. However, daily problems with inappropriate comments toward and attempts to touch female staff were reported. The physical aggression, particularly directed at women and characterized by inappropriate touching and grabbing areas of the torso, led to the change of his diagnoses to intermittent explosive disorder and frotteurism (*DSM-IV* criteria). Impulsive, opportunistic sexual behaviors responded well to the structured environment of the facility and verbal redirection by staff. Hypersexuality associated with bipolar disorder was ruled out because no affective symptoms were present. Approximately 16 months following admission, it was determined that ziprasidone was not effectively addressing mood lability. Tapering to discontinuation was initiated.

Rates for inappropriate sexual behavior averaged 2–3 episodes per month prior to discontinuation but markedly increased to 21 episodes the following month. In addition to increased frequency, the severity also markedly increased and included attempts to use extreme force toward female staff. Marked irritability was also apparent. Two months following ziprasidone discontinuation, citalopram was initiated at 20 mg daily to help with sexual aggression. Rates improved: 8 episodes of sexual aggression were reported that month, 4 the following month, and 6 by the third month of citalopram use. Episodes were limited to inappropriate verbal comments and responded to redirection.

Ziprasidone is an atypical antipsychotic with high binding affinity for dopamine, serotonin, and a_1-adrenergic receptors.[3] The affinity for ziprasidone binding to serotonin receptors is higher than at the dopamine sites.[4] Binding at these receptors may produce behavioral effects similar to those produced by selective serotonin reuptake inhibitors (SSRIs). Loss of the serotonergic effects of ziprasidone may represent an unrecognized contributing factor to sexual aggression in this patient that emerged following discontinuation. The authors encourage clinicians evaluating patients with intellectual impairments to consider changes in receptor occupancy a contributing cause if identified problematic behaviors reemerge or new aberrant behaviors present.

REFERENCES

1. Benson BA, Brooks WT. Aggressive challenging behaviour and intellectual disability. *Curr Opin Psychiatry*. 2008;21(5):454–458.
2. Rush KS, Bowman LG, Eidman SL, et al. Assessing psychopathology in individuals with developmental disabilities. *Behav Modif*. 2004;28(5):621–637.
3. Product Information. Geodon (ziprasidone). New York, NY: Roerig: Division of Pfizer, Inc; 2007
4. Preskorn SH. Clinical relevance of relative receptor binding affinity: quetiapine and ziprasidone as examples. *J Psychiatr Pract*. 2007;13(6):393–398.

Nancy C. Brahm, PharmD, BCPP, CGP
nancy-brahm@ouhsc.edu
Gary A. Fast, MD

Author affiliations: University of Oklahoma College of Pharmacy, Clinical and Administrative Sciences, Tulsa (Dr Brahm); and Consultant Psychiatrist, Outpatient Psychiatry, Wichita, Kansas (Dr Fast). ***Potential conflicts of interest:*** None reported. ***Funding/support:*** None reported.
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