Resolution of Ziprasidone-Related Tardive Dyskinesia With a Switch to Aripiprazole

Sir: Tardive dyskinesia (TD) is a serious, potentially irreversible side effect of antipsychotic medications. Prevalence rates of 20% with the typical antipsychotics have been reported.[1] Although the risk is smaller, treatment with atypical antipsychotic agents still poses a risk of TD. There is 1 report of ziprasidone-related TD in a patient who had other risk factors for TD, including advanced age, female gender, and affective illness.[2] However, the report did not address the management of the patient's TD. We report a case of ziprasidone-related TD that resolved after a switch to aripiprazole therapy was made.

Case report. Ms. A, a 52-year-old African American woman, was admitted for a psychotic exacerbation. She had a 20-year history of DSM-IV paranoid schizophrenia treatment characterized by frequent relapses, noncompliance with treatment, multiple antipsychotic trials, and hospitalizations. Her past history of TD was not known; however, over the past few years she had gained weight and had also been diagnosed with diabetes. There was no history of any illicit drug abuse.

Ziprasidone 60 mg p.o. b.i.d. was initiated in December 2002 during Ms. A's hospitalization, with good control of her psychotic symptoms. Within 2 months of initiation of treatment with ziprasidone, she was noted to have buccal-oral tardive dyskinesia and had an Abnormal Involuntary Movement Scale (AIMS)[3] score of 3. Vitamin E was added at a dose of 800 mg twice a day to manage the TD. She was discharged home on treatment with vitamin E 800 mg p.o. b.i.d. and ziprasidone 60 mg p.o. b.i.d. During Ms. A's follow-up outpatient visits, although her psychotic symptoms were stable, TD persisted. She had also discontinued vitamin E. After 12 months of ziprasidone therapy, a decision to switch to aripiprazole 15 mg/day was made. Over the next 2 months, her tardive dyskinesia gradually but completely remitted, and her symptoms of schizophrenia remained stable. Her AIMS score dropped to zero.

Aripiprazole is an atypical antipsychotic drug with a unique mechanism of action; it inhibits central dopaminergic neuron activity by a partial agonistic effect on the presynaptic D_2 dopamine autoreceptor and also acts as an antagonist at postsynaptic D_2 dopamine receptors. Through this mechanism, aripiprazole exerts activity as a dopamine agonist in hypodopaminergic states, while acting as a dopamine antagonist when dopaminergic activity is increased.[4] Alteration of the sensitivity of dopaminergic receptors to dopamine in the corpus striatum has been studied in experimental models, and it has been proposed that the lingual-facial-buccal dyskinesia seen in humans could be the human equivalent of stereotyped behavior seen in experimental animals with chronic chlorpromazine pretreatment.[5] There is also evidence from basic science studies that aripiprazole causes little D_2 receptor up-regulation.[6] Therefore, it is plausible that aripiprazole, by virtue of its dopamine agonistic activity, can potentially normalize D_2 dopamine receptor up-regulation. These properties may play a role in both prevention of the emergence of TD and the treatment of TD.

There is 1 other report of improvement of TD with aripiprazole in which improvement continued even after a conventional antipsychotic was added to the patient's regimen.[7]

We propose that for schizophrenic patients who have tardive dyskinesia and who do not desire clozapine treatment or cannot be prescribed clozapine due to medical contraindications, aripiprazole may provide alternate pharmacotherapy to treat psychoses and tardive dyskinesia. However, more research is needed in this direction.

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REFERENCES

1. Kane JM, Smith JM. Tardive dyskinesia: prevalence and risk factors, 1959 to 1979. Arch Gen Psychiatry 1982;39:473–481
2. Keck ME, Muller MB, Binder EB, et al. Ziprasidone-related tardive dyskinesia [letter]. Am J Psychiatry 2004;161:175–176
3. Psychopharmacology Research Branch, National Institute of Mental Health. Abnormal Involuntary Movement Scale (AIMS). In: Guy W, ed. ECDEU Assessment Manual for Psychopharmacology, Revised. US Dept Health, Education, and Welfare publication (ADM) 76-338. Rockville, Md: National Institute of Mental Health; 1976:534–537
4. Burris KD, Molski TF, Xu C, et al. Aripiprazole, a novel antipsychotic, is a high-affinity partial agonist at human dopamine D2 receptors. J Pharmacol Exp Ther 2002;302:381–389
5. Kalwans HL Jr, Rubovits R. An experimental model of tardive dyskinesia. J Neural Transm 1972;33:235–246
6. Inoue A, Miki S, Seto M, et al. Aripiprazole, a novel antipsychotic drug, inhibits quinpirole-evoked GTPase activity but does not up-regulate dopamine D2 receptor following repeated treatment in the rat striatum. Eur J Pharmacol 1997;321:105–111
7. Duggal HS. Aripiprazole-induced improvement in tardive dyskinesia [letter]. Can J Psychiatry 2003;48:771–772

Ashish Sharma, M.D.
Sriram Ramaswamy, M.D.
Creighton-Nebraska Psychiatry Residency Program
Vijay K. Dewan, M.D.
Department of Psychiatry
University of Nebraska Medical Center
Omaha, Nebraska