Tardive dyskinesia in 2 patients treated with ziprasidone

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Ziprasidone is an atypical antipsychotic drug that is believed to have a low propensity for inducing extrapyramidal symptoms, including tardive dyskinesia (TD). Two of our patients developed TD after 23 months and 34 months of ziprasidone monotherapy, respectively. One of the patients had had earlier exposure to typical antipsychotic drugs, but no other predisposing factors for TD were noted. Therefore, patients on long-term therapy with atypical antipsychotic drugs should be screened periodically for TD.

La ziprasidone est un antipsychotique atypique qui, croit-on, a une faible tendance à produire des symptômes extrapyramidaux, y compris une dyskinésie tardive (DT). Une DT a fait son apparition chez deux patients après 23 et 34 mois, respectivement, de monothérapie à la ziprasidone. Un des patients avait déjà été exposé auparavant à des antipsychotiques typiques, mais on n'a noté aucun autre facteur prédisposant à la DT. Il faudrait donc soumettre à un examen périodique de dépistage de la DT les patients qui suivent une thérapie à long terme aux antipsychotiques atypiques.

Introduction

Ziprasidone is a new antipsychotic drug that exhibits high affinity for serotonergic and dopaminergic receptors and has a higher serotonin-2A ($5\text{-}HT_{2A}$)/dopamine-2 (D_2) receptor-binding ratio than other currently available antipsychotic medications. It is a potent $5\text{-}HT_{2A}$-receptor antagonist and also has moderate affinity for adrenergic and histamine receptors.[1,2] In several clinical studies,[3–6] it has been reported that ziprasidone improves various domains of symptoms in schizophrenia. It is believed to have a low propensity for inducing extrapyramidal symptoms,[1,2] including tardive dyskinesia (TD). We wish to report the occurrence of TD in 2 patients on long-term ziprasidone treatment.

Case 1

A 34-year-old white man, who was diagnosed with schizophrenia in 1991, was prescribed trifluoperazine, 15 mg/d. In 1993, because of a recurrence of paranoid delusions and extreme isolation, treatment with trifluoperazine was ended and the patient was prescribed fluphenazine decanoate, 50 mg, administered intramuscularly every 2 weeks, and after 6 months fluphenazine hydrochloride, 10–30 mg/d, administered orally. Despite this treatment, the patient's auditory hallucinations and delusions of extrasensory perception persisted. The patient developed slight tremors and rigidity. No counteractive measures were undertaken. In 1995, the patient discontinued the fluphenazine and experienced an acute exacerbation of

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psychosis. He was seen twice in the psychiatric emergency department and was treated each time with haloperidol, 5 mg, and, to prevent extrapyramidal symptoms, with benztropine mesylate, 2 mg, administered intramuscularly.

The patient was referred to our clinic in April 1996. There was no family history of mental illness. His mother had died of cancer at the age of 42 years. The patient had never been admitted to hospital for schizophrenia and was physically healthy. Upon psychiatric evaluation, he was found to be experiencing hyperacusis, agitation, violent tendencies, hallucinations and delusions with poor insight. The Abnormal Involuntary Movement Scale (AIMS) examination[7] was completed and then repeated at each subsequent monthly visit; the patient's initial AIMS score was 1. The AIMS consists of 10 items to score abnormal movements and 2 items on the condition of teeth or dentures. The 10 items on abnormal movements are scored from 0 to 4 (0, not present; 1, minimal; 2, mild; 3, moderate; 4, severe). Ziprasidone monotherapy, 40 mg twice daily, administered orally, was initiated with a good response. The dosage was increased to 60 mg, twice daily, on May 14, 1996, and to 80 mg, twice daily, on May 28, 1996. Nine months after initiation of ziprasidone therapy, that is, in January 1997, the patient had attended summer classes, obtained a teaching degree and a teaching job. On Feb. 4, 1999, he came for an unscheduled interview, because one of his fellow teachers mentioned that he was moving his fingers and lips. On examination, he manifested abnormal movements of the jaw, lips and mouth, and the upper extremities. His AIMS score at that time was 9. On Feb. 25, 1999, the patient's ziprasidone dosage was decreased from 160 mg/d to 120 mg/d, and vitamin E was added to his regimen. There was little change in the severity of TD. Psychiatrically, he has been doing well with minimal psychopathology.

Case 2

A 42-year-old white man living with his parents and brother had started manifesting isolative behaviour, fear of meeting people and hearing of voices at the age of 29 years. On June 2, 2000, as a result of parental coercion and the severity of the symptoms, he came to our clinic. At that time, the patient believed that a neighbour had a machine that enabled the neighbour to hear what the patient was saying or thinking. Upon examination, the patient had no abnormal involuntary movements and an AIMS score of 0. He was prescribed ziprasidone, 120 mg/d. The AIMS examination was repeated at each subsequent monthly visit. The patient responded well to ziprasidone treatment. The delusions dissipated, so the same dosage of medication was continued. On May 3, 2002, he exhibited choreoathetoid movements of the fingers, chewing movements of the mouth and abnormal movements of the toes. His AIMS score was 16. As the patient's condition had improved with ziprasidone, he continued with the same dosage with monthly follow-up visits. His AIMS score remained about the same throughout. In June 2002, the TD continued to worsen (AIMS score of 18) and, in particular, his hand movements became severe. Therefore, ziprasidone was discontinued, and the patient was prescribed olanzapine, 20 mg/d, and vitamin E, 400 IU/d.

Discussion

The patients described here had regular findings on AIMS examinations and exhibited no abnormal involuntary movements at the beginning of ziprasidone treatment. In addition, both patients were healthy and did not receive any concomitant medications. Our first patient developed TD about 34 months after initiation of ziprasidone monotherapy, indicating that it must have been related to ziprasidone. He had been exposed to other neuroleptic medications in the past without developing TD. Whether this earlier drug therapy predisposed the patient to develop TD is not known. This patient is still taking ziprasidone. Our second patient, who developed TD after 23 months of ziprasidone monotherapy, did not have any predisposing factors for TD, such as a family history of Parkinson's disease, early severe extrapyramidal symptoms, previous exposure to neuroleptic medications or current difficulty with his teeth, thereby indicating that ziprasidone might have played a significant part in the production of TD. As of today, he still has TD and is taking olanzapine instead of ziprasidone.

Rosenquist et al[8] described a case of TD in a patient who was being treated with ziprasidone, but this patient had had previous TD and was being treated with multiple drugs when he developed TD.

During therapy with atypical antipsychotic drugs, including ziprasidone, the possible occurrence of TD should be kept in mind, and periodic monitoring of patients is imperative.

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References

1. Davis R, Markham A. Ziprasidone. *CNS Drugs* 1997;8:153-9.

2. Tandon R, Harrigan E, Zorn SH. Ziprasidone: a novel antipsychotic with unique pharmacology and therapeutic potential. *J Serot Res* 1997;4:159-77.

3. Daniel DG, Zimbroff DL, Potkin SG, Reeves KR, Harrigan EP, Lakshminarayanan M. Ziprasidone 80 mg/day and 160 mg/day in the acute exacerbation of schizophrenia and schizoaffective disorder: a 6-week placebo-controlled trial. *Neuropsychopharmacology* 1999;20:491-505.

4. Daniel DG, Potkin SG, Reeves KR, Swift RH, Harrigan EP. Intramuscular (IM) ziprasidone 20 mg is effective in reducing acute agitation associated with psychosis: a double-blind, randomized trial. *Psychopharmacology (Berl)* 2001;155(2):128-34.

5. Goff DC, Posever T, Herz L, Simmons J, Kletti N, LaPierre K, et al. An exploratory haloperidol-controlled dose-finding study of ziprasidone in hospitalized patients with schizophrenia or schizoaffective disorder. *J Clin Psychopharmacol* 1998;18:296-304.

6. Keck P Jr, Buffenstein A, Ferguson J, Feighner J, Jaffe W, Harrigan EP, et al. Ziprasidone 40 and 120 mg/day in the acute exacerbation of schizophrenia and schizoaffective disorder: a 4-week placebo-controlled trial. *Psychopharmacology (Berl)* 1998;40:173-84.

7. Guy W, editor. *ECDEU assessment manual for psychopharmacology*. Washington: US Department of Health, Education and Welfare; 1976. p. 534-7. Publication ADM 76-338.

8. Rosenquist KJ, Walker SS, Ghaemi SN. Tardive dyskinesia and ziprasidone. *Am J Psychiatry* 2002;159:1436.