Rapid Response of Disabling Tardive Dyskinesia to Amantadine: A Case Report

To the Editor: About 20% of patients treated with standard neuroleptic drugs are affected with tardive dyskinesia (TD), and approximately 5% are expected to develop TD with each year of neuroleptic treatment.[1] The majority of patients with TD have a mild disorder, but about 5%–10% suffer impairment from the dyskinesia.[2] The evidence in relation to the atypical antipsychotics suggests that these drugs present a significantly lower risk for TD in comparison to first-generation antipsychotics.[3] Reports suggest that the risk of TD is lowest with clozapine, followed by quetiapine.[4] The severity of TD and the absolute need for neuroleptic therapy often dictate the treatment approach. Although there is no currently effective treatment for TD, amantadine has been reported to be beneficial, possibly because of its glutamatergic effects.[4,5]

Herein, I report a patient with disabling TD due to quetiapine that responded rapidly to amantadine. To my knowledge, this report is the first description of rapid improvement of quetiapine-induced TD by amantadine.

Case report. Ms A, a 57-year-old retired librarian, was hospitalized in the fall of 2009 with long-standing history of treatment-resistant *DSM-IV-TR*–defined major depressive disorder, recurrent, severe episode without psychotic features. For 6 weeks, she was treated with fluoxetine (60 mg/d), duloxetine (120 mg/d), quetiapine (400 mg/d), and clonazepam (2 mg/d) and underwent bilateral electroconvulsive treatment (ECT) once per week.

At this hospitalization, her 17-item Hamilton Depression Rating Scale (HDRS)[6] score was 40 and her Abnormal Involuntary Movement Scale (AIMS) score was 10.[7] Her blood workup for the causes of refractory depression revealed no abnormalities. Ms A denied consent for ECT. She was switched from fluoxetine to paroxetine treatment (increased to 40 mg/d), and clonazepam was increased to 3 mg/d. Quetiapine was continued as an augmenting agent and was increased to 600 mg/d. She had no change in depressive symptoms and was noted to be more anxious and agitated during the following 4 weeks (HDRS score = 38 and AIMS score = 16). Therefore, paroxetine treatment was switched to mirtazapine treatment (increased to 45 mg/d) and duloxetine treatment was switched to venlafaxine extended release treatment (increased to 300 mg/d).

The patient continued to worsen over the next 3 weeks. Gradually, varieties of repeated stereotypic abnormal movement became evident. She was noted to have dyskinetic blinking, frowning, lip smacking, puckering, chewing, jaw clenching, mouth opening, and facial grimacing movements. She also had stereotypic and involuntary movements of hands and toes. These movements would aggravate when she became more anxious and would disappear while she was sleeping. She was unable to interact because her speech was broken, repetitive, and nonfluent. Ms A became incapacitated to the extent that she was not able to communicate with others and take care of her daily routine activities. Her HDRS score was 38 and AIMS score increased to 41.

At that time, findings of electroencephalogram and magnetic resonance imaging of the head with and without contrast were within normal limits. Clonazepam was increased to 5 mg/d, and vitamin E 1,600 units was added. The neurology department was consulted the following week when no change in her condition was noted. They stopped vitamin E and administered amantadine 400 mg/d in 4 divided doses. Within 3 days she started to improve, and her AIMS score reduced to 18 in 5 days. Clonazepam was decreased to 1 mg 2 times daily. Then, a gradual taper of quetiapine was started at the rate of 100 mg/wk. She agreed to ECT treatments and was discharged after 2 weeks, at which time her HDRS and AIMS scores were 15 and 14, respectively.

During the office follow-up, quetiapine was completely stopped in the next 4 weeks. Amantadine was then tapered gradually to 100 mg/d without any worsening of TD. She has been stable for the last year, and her AIMS score at 1-year follow-up was 12.

Tardive dyskinesia is the most serious consequence of long-term neuroleptic administration, and all known approaches to its treatment are relatively unsuccessful.[5] Amantadine is a commonly used drug in neurology, but psychiatrists are generally less experienced with its use. There has been very little research on the use of amantadine in TD, and the patient population studied was on treatment with typical antipsychotics only.[8–14] An 18-week, double-blind, crossover study by Angus et al[14] demonstrated that amantadine is significantly better than placebo in the management of TD and that there is little risk of exacerbating psychosis. Using amantadine to treat TD has produced a rapid improvement in dyskinesia without emergence of psychosis even with prolonged administration. More studies are needed to prove the utility of amantadine in atypical antipsychotic–induced TD. Meanwhile, a trial of amantadine for a short period (1–2 weeks) in a patient with debilitating TD may be useful.

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