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Vitamin E Treatment for Olanzapine Induced Tardive Dyskinesia in an Adolescent with Bipolar Disorder

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To the Editor,

Atypical antipsychotics have increasingly been used for the management of various psychiatric disorders of childhood and this may have important health consequences, including tardive dyskinesia (TD) (1-4). The symptoms of TD in pediatric patients may be more complex than in adults and this may be related to shorter and episodic treatment durations (3). TD in children and adolescents may be a serious concern for both the patient and the family. The relationships between olanzapine, TD and oxidative stress may be controversial. There have been case reports of TD due to olanzapine, as well as its use in treating TD (5). Here, we report a case of TD in an adolescent with Bipolar Disorder, which arose after prolonged use of olanzapine and may have responded to a treatment regimen with vitamin E.

Case

An 18-year-old male was brought to our department with complaints of involuntary movements of the tongue, jaw, lips and neck. The complaints had been present for 4 months, regardless of his use of the drug. They increased with stress and were abolished during sleep. No signs or symptoms of dystonia, tics, akathisia or parkinsonism seemed to accompany the movements. Both the patient and the family reported that he did not use alcohol or drugs either before or after the complaints.

He had been diagnosed with Bipolar I Disorder 3 years ago and started on olanzapine 20 mg/day. No other antipsychotics had been used for treatment in the past. At the time of presentation for treatment, he had been receiving olanzapine 10 mg/ day regularly for the last year and had had no affective symptoms for the past 3 months. The family history was negative for psychotic and movement disorders. The movements corresponded to a score of 20 on the Abnormal Involuntary Movements Scale (AIMS). The severity score was judged to be 4. Neurological and laboratory investigations, including a drug screen, were all within normal limits. Accordingly, the patient was diagnosed to have Tardive Dyskinesia according to the DSM-IV criteria. Olanzapine was suspected as a cause, but the patient required the drug to be continued out of concern of a relapse, therefore the dose was reduced to 5 mg/day while paying attention to affective symptoms and vitamin E (alpha-tocopherol) was started at the same time, at a dose of 1600 IU/day. After a month of treatment, the involuntary movements reduced while there was no relapse of affective symptoms. AIMS evaluation at the 12th week of treatment denoted a score of 5 and a severity score of 1 with most of the movements being minimal. Further assessments at the 16th, 20th and 24th weeks of the treatment revealed that the treatment gains had been maintained without affective relapses.

Discussion

Risk factors for TD are thought to include female gender, advanced age, prolonged use of antipsychotics, negative symptoms, affective disorders, organic brain syndromes, mental retardation, comorbid alcohol and drug abuse, and, previous signs of parkinsonism due to treatment (6). Other than a long term treatment with olanzapine and being diagnosed with bipolar disorder, our patient displayed none of the risk factors for TD.

Hypotheses proposed to explain TD include hypersensitivity in striatal dopamine receptors after prolonged treatment with antipsychotics, a reduced gamma-amino butyric acid (GABA) turnover, an increase of GABA binding sites in one or more areas of the basal ganglia, neurotoxicity due to chronic

treatment with antipsychotics culminating in structural damage, striatal disorganization as a result of changes in the ratio of D1 and D2 receptors, noradrenergic hyperactivity, cholinergic hypoactivity, and, lastly changes in serotonin and/or neuropeptides (6). Blockade of presynaptic dopaminergic receptors may elevate glutamatergic neurotransmission, leading to increased production of free radicals and oxidative stress and culminating in death of medium spiny interneurons located in striatum. According to this hypothesis, anti-oxidants including vitamin E may be potential treatment options for TD and the response of our patient to treatment may support this (7,8). Previous reports suggested that vitamin E treatment of TD might be especially beneficial for patients displaying abnormal movements for 5 years or less, or who had dystonia and buccolingual movements and our case may also support these positions (7,9). The lack of adverse events associated with vitamin E in our patient with TD is also similar to previous reports (8). However, our results are not in accordance with those from a large, multi-site trial of vitamin E in elderly patients receiving antipsychotics which showed that it may not help with TD (10). This discrepancy may be explained by the age difference between the sample of that study and our patient or by the duration of treatment received.

A recent meta-analysis of studies evaluating use of vitamin E for treatment of TD concluded that it might protect against worsening of symptoms but that there was no evidence for treatment effects; although the authors reported that limited size of samples and methodological problems including randomization may have affected the results (11). Contrarily, another, older systematic review reported modest improvement in symptoms of TD with use of vitamin E (12). Soares and McGrath also reported that no trial-based information on the effect of vitamin E for patients with early onset of TD exists and when our observation is considered in the light of this information, it may be argued that children and adolescents with TD might benefit from anti-oxidant treatment more than adults (11).

Alternatively; the reduction in TD may be due to reduced dose of the olanzapine, to the waxing and waning course of the TD or to a spontaneous remission, which is more common in younger patients (13). In conclusion, this case illustrates that children and adolescents using atypical antipsychotics such as olanzapine might develop TD and that they may benefit from dose reduction or adjunctive treatment with vitamin E. Further studies on the effects of various alternative agents, including vitamin E, for treatment and prevention of TD in pediatric patients may be warranted.

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