

Vitamin B6 for tardive dyskinesia?

Gerald Martone, MS, MSN, PMHNP-BC

Mr. Martone is a psychiatric mental health nurse practitioner, Alaska Psychiatric Institute, Anchorage, Alaska.

Disclosure

The author reports no financial relationships with any company whose products are mentioned in this article, or with manufacturers of competing products.

Although antipsychotics have revolutionized the treatment of severe mental illnesses, adverse effects often present a substantial obstacle to adherence. One of the most tenacious and difficult-to-treat adverse effects is tardive dyskinesia (TD), a neuromotor syndrome with characteristic involuntary repetitive movements, typically of the muscles of the jaw, lips, and tongue. In addition to spasms and grimacing, patients can have choreoathetoid movements of the neck. In more extreme presentations, some patients can have difficulty breathing. TD is a largely irreversible condition. It is often a disfiguring lifelong disability that can further stigmatize patients who already suffer scorn and derision. TD usually has a delayed onset after a patient is started on an antipsychotic.¹ The syndrome is more commonly associated with first-generation antipsychotics, but affects up to 20% of patients who are treated with second-generation antipsychotics.¹ In the United States, TD affects as many as 500,000 patients.¹

There are several palliative interventions for TD, but the evidence for a consistently reliable treatment is weak. Branched-chain amino acids, ginkgo biloba, melatonin, and vitamin E have been investigated as interventions. Other approaches include switching to an alternate antipsychotic such as clozapine, adjusting the antipsychotic dose, using anticholinergic medications, adjunctive amantadine, gamma aminobutyric acid agonists, or adding tetrabenazine.

The FDA recently approved two vesicular monoamine transporter 2 (VMAT2) inhibitors, deutetrabenazine and valbena-

zine, for addressing symptoms of TD. However, these medications can cost tens of thousands of dollars per year, and also carry the risk of adverse effects such as sedation, akathisia, urinary retention, constipation, and muscle pain.² When treating a patient who develops TD, one might consider other potentially effective therapies with low adverse effect profiles that may be more cost-effective than existing treatments. The bioactive form of vitamin B6 (pyridoxine), pyridoxal-5-phosphate, has been used to treat various antipsychotic-induced movement disorders. Preliminary evidence suggests that vitamin B6 may help reduce the symptoms of TD.

A recent Cochrane Database Review (2015)³ of pyridoxal-5-phosphate treatment for TD found a significant improvement in symptoms compared with placebo. Although the studies included in this review were limited by modest sample sizes and short follow-up periods, 2 of the investigations revealed improvements of >40% in extrapyramidal symptoms with vitamin B6 compared with placebo.

Lerner et al (2001)⁴ conducted a randomized, double-blind, placebo-controlled crossover trial in which 15 inpatients with schizophrenia who met the criteria for TD were assigned to vitamin B6, 400 mg/d, or placebo for 4 weeks. After a 2-week washout period, the placebo group was given vitamin B6 and vice versa. Compared with placebo, mean scores on the parkinsonism and dyskinetic movement subscales of the Extrapyramidal Symptom Rating Scale were significantly better in the third week of treatment with vitamin B6.



Discuss this article at
www.facebook.com/MDedgePsychiatry

continued from page 42

Lerner et al (2007)⁵ later conducted a separate crossover study using the same design with a washout period. This trial included a larger sample size (50 inpatients with DSM-IV diagnoses of schizophrenia or schizoaffective disorder and TD) and the dosage of vitamin B6 was increased to 1,200 mg/d over 26 weeks. Patients who received vitamin B6 experienced a significantly greater decrease in Extrapyramidal Symptom Rating Scale scores compared with those in the placebo group.

Umar et al (2016)⁶ published a case review of a 29-year-old woman with treatment-resistant schizophrenia with TD who was treated with clozapine, 400 mg/d. She was started on vitamin B6, 450 mg/d, for 4 weeks, and then her dose was increased to 600 mg/d. At 6 months, she experienced a 78% reduction in the severity of her TD symptoms, as measured by the Abnormal Involuntary Movement Scale. The authors reported that this improvement was maintained for 1 year after vitamin B6 was stopped.

Miodownik et al (2008)⁷ reported in a study of 89 patients with schizophrenia that those with TD (n = 40) had diminished amounts of vitamin B6 in their plasma compared with patients without symptoms of motor disturbances (n = 49).

Vitamin B6 has been known to improve other psychotropic-induced movement disorders. In a study of lithium-induced tremors, treatment with pyridoxine, 900 to 1,200 mg/d, resulted in “impressive improvement until total disappearance of tremor.”⁸ Lerner et al (2004)⁹ also reported significant improvement for patients with neuroleptic-induced akathisia who were treated with vitamin B6.

Some proposed mechanisms of action

Pyridoxal-5-phosphate is a coenzyme in the synthesis of dopamine and other neuro-

transmitters. This might explain in part the biochemical mechanism of vitamin B6 in attenuating motor symptoms following long-term dopamine blockade. Chronic neurotransmitter antagonism may result in an upregulation of dopamine receptors in response. This compensatory reaction might create a dopamine receptor super-sensitivity in the nigrostriatal pathways.¹⁰

Another potential mechanism of action might be vitamin B6's potent antioxidant properties and its scavenging of free radicals. The neurotoxicity of oxidative stress has been implicated in various movement disorders and psychiatric conditions.

In all of the studies described here, patients continued to receive daily antipsychotic treatment. In these trials, the adverse effects of vitamin B6 were minimal or negligible. In one study, vitamin B6 was reported to have had a better adverse effect profile than placebo.⁴

References

1. Carbon M, Hsieh CH, Kane JM, et al. Tardive dyskinesia prevalence in the period of second-generation antipsychotic use: a meta-analysis. *J Clin Psychiatry*. 2017; 78(3):e264-e278.
2. Smith Mosley LL, Mosely II JF, Fleischfresser JR, et al. Vesicular monoamine transporter type 2 (VMAT2) inhibitors in the management of tardive dyskinesia. *Clin Med Rev Case Rep*. 2017;4(12):1-5.
3. Adelufosi AO, Abayomi O, Ojo M. Pyridoxal 5 phosphate for neuroleptic-induced tardive dyskinesia. *Cochrane Database Syst Rev*. 2015;(4):CD010501.
4. Lerner V, Miodownik C, Kapstan A, et al. Vitamin B(6) in the treatment of tardive dyskinesia: a double-blind, placebo-controlled, crossover study. *Am J Psychiatry*. 2001;158(9):1511-1514.
5. Lerner V, Miodownik C, Kapstan A, et al. Vitamin B6 treatment for tardive dyskinesia: a randomized, double-blind, placebo-controlled, crossover study. *J Clin Psychiatry*. 2007;68(11):1648-1654.
6. Umar MU, Isa AA, Abba AH. High dose pyridoxine for the treatment of tardive dyskinesia: clinical case and review of literature. *Ther Adv Psychopharmacol*. 2016;6(2):152-156.
7. Miodownik C, Meoded A, Libov I, et al. Pyridoxal plasma level in schizophrenic and schizoaffective patients with and without tardive dyskinesia. *Clin Neuropharmacol*. 2008;31(4):197-203.
8. Miodownik C, Witztum E, Lerner V. Lithium-induced tremor treated with vitamin B6: a preliminary case series. *Int J Psychiatry Med*. 2002;32(1):103-108.
9. Lerner V, Bergman J, Statsenko N, et al. Vitamin B6 treatment in acute neuroleptic-induced akathisia: a randomized, double-blind, placebo-controlled study. *J Clin Psychiatry*. 2004;65(11):1550-1554.
10. Miller, BJ. Tardive dyskinesia: a review of the literature. *Psychiatric Times*. <http://www.psychiatrictimes.com/articles/tardive-dyskinesia-review-literature>. Published June 27, 2017. Accessed July 31, 2018.

Preliminary evidence suggests that vitamin B6 can help alleviate symptoms of tardive dyskinesia