Original Article

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The Efficacy of Vitamin E in the Treatment of Tardive Dyskinesia: A Double-Blind Placebo Controlled Study

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Abstract

Our aim in this study was to investigate the efficacy of vitamin E in the treatment of tardive dyskinesia in a group of chronic schizophrenic patients. Thirty-eight chronic schizophrenic inpatients with tardive dyskinesia were selected for a double-blind trial of Vitamin E versus placebo (Vitamin E: N=18). Tardive dyskinesia was rated by a blind-trained rater using the Abnormal Involuntary Movement Scale (AIMS) at baseline and after treatment. The AIMS scores in the Vitamin E cohort decreased significantly after treatment while the AIMS scores in the placebo cohort were not different after placebo. The results replicate the short-term effectiveness of Vitamin E in the treatment of tardive dyskinesia in a larger group of chronic schizophrenic patients.

Key words: Vitamin E, antioxidant therapy, tardive dyskinesia, neuroleptic medication, chronic schizophrenia.

Tardive dyskinesia (TD) is a chronic and debilitating side effect of neuroleptic medication. Unfortunately, radical effective treatment is not yet available.[1]

Various theories have been suggested for the etiology of TD. Recently, it has been speculated that persistent TD is caused by free radical toxicity in some areas of the brain, especially in the basal ganglia. This toxicity leads to destabilization of neural membranes through lipid perioxidation.[2] Neuroleptic medications have been shown to increase, at least initially, the turnover of catecholamines, especially dopamin (DA) in the brain.[3] Increased DA metabolism could lead to greater production of cytotoxic free radicals.[4] A recent investigation suggested possible involvement of free radicals in regional monoamine metabolism in the brain during chronic neuroleptic use.[5] Chronic fluphenazine administration caused significant increases in DA, norepinephrine (NE) and serotonin (5-HT) concentrations in some areas of the brain, especially basal ganglia and significant decreases in their metabolites in the same regions.

Vitamin E, with its antioxidant properties, can neutralize the damaging effects of free radicals.[6] It can attenuate some of the
neuroleptic-induced changes in monoamine metabolism.[5]

Vitamin E is useful in the treatment of many pathologic conditions such as neurological dysfunctions.[7] Its side effects are usually mild and well tolerated. They include nausea, vomiting, abdominal cramps, diarrhea, headache, fatigue and skin rash, if there is a history of allergy to Vitamin E.[8] High levels of Vitamin E are contraindicated in subjects who are receiving Vitamin K antagonists as anti-coagulant therapy.

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Except for this interaction with Vitamin K, there is no specific side effect
associated with high doses of Vitamin E.[7]

In the last 10 years, a few clinical trials have found Vitamin E to be effective in decreasing the severity of TD. Our aim in this study was to investigate the effectiveness of Vitamin E in the treatment of TD in a group of chronic schizophrenic patients.

Materials and methods

The research center was the largest mental hospital in Turkey, Bakirky Neuro-psychiatric Hospital. Some of the in-patients in our hospital were recruited for the study.

The inclusion criteria were a DSM III R diagnosis of chronic schizophrenia, taking neuroleptic drugs for at least a year, having Research Diagnostic Criteria (RDC) for at least mild TD9 and aged between 18 and 70. The exclusion criteria were significant medical or neurological illness, receipt of Vitamin K antagonists, history of allergy to Vitamin E, pregnancy, chronic alcohol and substance abuse, mental retardation and taking other drugs, except neuroleptics and anticholinergics.

Thirty-nine in-patients (22 male and 17 female) met the criteria and were separated into two groups: Vitamin E cohort (N=20) and placebo cohort (N=19). Only one patient did not complete the study because of nausea while taking placebo. This patient was ruled out.

In the Vitamin E group, the mean age of the 20 subjects (11 male and 9 female) was 50.25 taking neuroleptic drugs for 16.88 eptic drugs for 13.43 k treatment period with either Vitamin E or placebo Vitamin E, and the placebo was administered on a fixed dosage schedule of four drages (400 iu/day) of Vitamin E or placebo of identical appearance twice a day. It was rated by a blind-trained rater using the AIMS at baseline and after five weeks.[10]

Fisher's exact test was used to compare placebo drug differences. Other results were also compared by using Mann-Whitrey U test and Wilcoxon test where appropriate. All tests were two-tailed.

Results

As shown in Table 1, there was no statistical difference in AIMS scores between the two groups at baseline (Mann-Whitrey U test, U=231, p=0.05). AIMS scores in the Vitamin E cohort decreased from a mean of 9.65 whereas scores for the placebo cohort did not differ statistically (from a mean of 7.22 on in AIMS scores as criterion for good response; 11 of 20 patients (55%) improved after Vitamin E, whereas only two of 18 patients (11%) improved after placebo. Improvement in Vitamin E cohort was significantly higher than placebo cohort (Fisher's exact test, p=0.0052).

Table 1. Results of the trial of five weeks of treatment with vitamin E versus placebo.

	Vitamin E (N=20)	Placebo (N=18)	P Value
AIMS Score			
at baseline[a]	9.65 +/- 4.02	6.71 +/- 3.55	<0.05
after 5 weeks[b]	7.22 +/- 1.93	6.28 +/- 2.52	>0.05
>33% reduction[c]	11	2	0.0052

a: Wilcoxon test, T=15, P<0.05
b: Wilcoxon test, T=36, P>0.05
c: Fisher exact test, P=0.0052

Discussion

Our study was a double-blind trial of five weeks of treatment with Vitamin E (400 iu/day) versus placebo. We found Vitamin E in the treatment of TD was more effective than treatment with the placebo. Our investigation was based on a relatively larger sample compared to previous studies with smaller samples.

Lohr et al.11 found alpha-tocopherol was effective in TD. Ellcashef et al.[8] demonstrated the efficiency of Vitamin E in TD. Their study was a randomized, double-blind crossover study, but the conclusions were based on a small sample. Cadet and Lohr[12] discussed possible involvement of free radicals in neuroleptic-induced movement disorders and suggested the treatment of TD with Vitamin E. Adler et al.13 reported the positive treatment response of Vitamin E in a parallel design study of 8-12 weeks of treatment with larger doses of Vitamin E (1600 iu/day) versus placebo (N=28). Shriqui et al.14 compared Vitamin E (400 iu/day) with placebo in double-blind randomized crossover study of 27 patients with TD and found that Vitamin E showed no differences from placebo. Egan et al.15 reported that Vitamin E had a minor beneficial effect on TD ratings in a selected group of patients with TD for up to five years and concluded that this effect was not due to an increase in blood levels of neuroleptic
medications.

Our results replicated the findings of other studies except those of Shriqui et al. Although the placebo had a minor beneficial effect on TD ratings, this may be related to decreased stress levels as the patients became more familiar with the experimental procedures. It is well-known that TD can be exacerbated by stress.14 Nevertheless, the decrease of AIMS scores after placebo administration was not significant. In our opinion, Vitamin E may also be effective, if used prophylactically, in the prevention of TD. For this reason, additional research is necessary.

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