The Effects of Eight-Week Treatment with High Dose Vitamin E on Serum Cholesterol and Triglyceride Level of Patients with Schizophrenia on Olanzapine: A Placebo Controlled Study

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Objective: To study the effects of a high dose alpha-tocopherol on serum total cholesterol (TC), triglyceride (TG), and the high density lipoprotein (HDL) levels of patients with schizophrenia receiving olanzapine.
Method: Thirty six adults diagnosed with schizophrenia based on DSM-IV who were taking olanzapine for a minimum of thirty days entered this eight-week, double blind, placebo-controlled study. Patients were randomized to receive alpha-tocopherol 400IU or placebo capsules twice a day for 2 weeks, then three times a day for 6 more weeks. Fasting total cholesterol (TC), triglyceride(TG), and HDL levels were measured at the baseline and weeks 4 and 8.
Results: TC, TG and HDL levels did not change significantly during this study. There were no significant differences in TC, TG and HDL levels between the two groups at the baseline and weeks 4 and 8.
Conclusion: High-dose vitamin may not improve triglyceride and cholesterol levels in patients who are already on olanzapine. Further studies with greater number of patients and for a longer duration are needed.

Key Words:
Cholesterol, Olanzapine, Schizophrenia, Triglyceride, Vitamin E

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Atypical antipsychotics including olanzapine have been reported to cause metabolic adverse effects including weight gain and lipid profile changes (1-3).
Accumulating evidence suggests that clozapine and olanzapine result in weight gain and elevated triglyceride levels (2). There are some hypotheses for lipid dysregulation including weight gain, changes in diet, and the development of glucose intolerance (1). Vitamin E is reported to improve lipid peroxidation and, therefore, may be useful in reducing high lipid profile (4, 5).
We present an eight-week study that assessed the effects of a high dose alpha-tocopherol on serum total cholesterol (TC), triglyceride (TG), and the high density lipoprotein (HDL) levels of patients with schizophrenia receiving olanzapine.

Materials and Method

Thirty six adults diagnosed with schizophrenia based on DSM-IV (6) who were taking olanzapine for a minimum of thirty days entered this eight-week, double blind, placebo-controlled study. Exclusion criteria included receiving electroconvulsive therapy within six months or any medications affecting lipid profile (e.g. other antipsychotics, tricyclic antidepressants, birth control pills, etc) within two weeks prior to the initiation of the study, suffering diabetes mellitus, a history of hypercholesterolemia, hypertriglyceridemia, cardiovascular, or/and hematologic disorders documented in patient records, and pregnancy or

Table1. Plasma Total cholesterol, triglyceride, and High-Density Lipoprotein levels (mg/dl) of the patients during the study

TC Levels (mg/dl) [Mean±SD,SEM]				
Groups	**Baseline**	**Week 4**	**Week 8**	**P value**
Vitamin E	179.46±52.32;13.51	190.86±59.11;15.26	185.53±49.59;12.80	0.846
Placebo	208.68±40.33;10.08	201.31±39.63;9.90	193.31±32.83;8.20	0.520
TG Levels (mg/dl) [Mean±SD,SEM]				
Groups	**Baseline**	**Week 4**	**Week 8**	**P value**
Vitamin E	154.46±46.52;12.01	162.80±55.91;14.43	149.13±49.37;12.74	0.760
Placebo	151.18±61.46;15.36	168.18±90.33;22.58	154.75±69.16;17.29	0.795
HDL Levels (mg/dl) [Mean±SD,SEM]				
Groups	**Baseline**	**Week 4**	**Week 8**	**P value**
Vitamin E	44.15±6.18;1.59	43.40±6.56;1.69	43.25±7.54;1.94	0.927
Placebo	46.12±6.42;1.60	43.90±5.30;1.32	42.03±6.82;1.70	0.189

breast-feeding. Patients were educated not to change their diet during the course of the study. An informed consent was obtained from all patients/guardians. Patients were randomized by blocked randomization to receive alpha-tocopherol 400IU or placebo capsules twice a day for 2 weeks, then three times a day for 6 more weeks. Fasting TC, TG, HDL levels were measured at the baseline and weeks 4 and 8 .

Data were analyzed using one way ANOVA and independent sample t-test via utilizing SPSS version 11.5 .

Results

Thirty one patients between 18 to 49 years of age completed the study. These patients received olanzapine for the treatment of schizophrenia for a minimum of 1 month. Eight males and 7 females with a mean age of 34.93 +/- 10.02 years received high-dose vitamin E and ten males and 6 females with a mean age of 32.81 +/- 12.65 years received placebo. Age and sex were not significantly different between the two groups. None of the patients reported any side effects that could be related to vitamin E. Five patients were dropped out of this study; 4 due to not being compliant and one due to the familial hyperlipidemia. As illustrated in table1, overall, TC, TG and HDL levels did not change significantly during this study. There were no significant differences in TC, TG and HDL levels between the two groups at the baseline and weeks 4 and 8.

Discussion

Clozapine and olanzapine have been reported to increase TG levels and to a higher extent when compared with risperidone (1, 2). The present study was designed to assess the effects of 8 week treatment of high dose vitamin E on plasma TG and TC levels of patients with schizophrenia who had been on olanzapine for at least 1 month. This study showed that overall, olanzapine had no significant effect on TC, TG or HDL levels.

To our knowledge, other studies in which the baseline TG levels were increased in patients receiving olanzapine, have measured lipid levels before initiation of olanzapine and compared it with the levels after patients were initiated on olanzapine. However, patients in this study were already on olanzapine for at least 1 month before entering the study. Since no significant changes were observed in the levels of TC, TG and HDL in patients of this study, one can speculate that lipid levels of patients on olanzapine may increase in the first month of treatment and stays stable thereafter. Furthermore, a recent study by Roberts II et al on patients with polygenic hypercholesterolemia suggested that vitamin E at doses of 1600 IU and 3200 IU per day resulted in significant percent reduction n plasma concentration of F2-isoprostane, a biomarker of free-radical-mediated peroxidation of lipid, after 16 weeks of supplementation (7). High-dose vitamin E may have a role in reducing TC or TG and increasing HDL levels in hyperlipidemic patients.

Considering the results of this study, it may not be vise to add high-dose vitamin E in order to improve triglyceride and cholesterol levels in patients who are already on olanzapine. It should be mentioned that this study did not note any adverse reactions related to vitamin E. Further studies with greater number of patients and for a longer duration are needed to confirm the results of this study and to assess the preventive effects of high-dose vitamin E on increasing TG and TC levels in patients who are going to be started on olanzapine.

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