THE EFFECT OF VITAMIN E SUPPLEMENTATION ON LIPID PROFILE AND OXIDATIVE STRESS MARKERS IN HEMODIALYSIS PATIENTS

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Abstract

INTRODUCTION: Dyslipidemia and oxidative stress are thought to be important mechanisms in pathogenesis of disease in hemodialysis patients. This study was designed to investigate the efficacy of oral vitamin E supplementation on lipid profile and oxidative stress in hemodialysis patients.

METHODS: The study group consisted of 26 uremic patients (10 women and 16 men), 16-68 years of age undergoing maintenance hemodialysis three times a week (12 hours/week), lasting a range of 6-108 months, at Vali-e-Asre Hospital in Birjand (Iran). Total Antioxidant Capacity (TAC), lipid peroxidation, cholesterol, triglyceride, high-density lipoprotein and low-density lipoprotein levels were determined before and after oral vitamin E supplementation, 400 mg/d for 90 days.

RESULTS: Vitamin E supplementation caused a significant decrease in ThioBarbituric Acid Reactive Substances (TBARS) level as a marker for lipid peroxidation (2.97±0.52 vs. 2.55±0.44, P<0.001) and a significant increase in plasma TAC (1252±348 vs. 1398±372, P<0.01). Although there was a decrease in the level of lipid profile, there were no statistically significant differences in the means of cholesterol, triglyceride, high-density lipoprotein and low-density lipoprotein before and after vitamin E supplementation among patients.

CONCLUSION: Our results indicated that oral vitamin E supplementation might be able to modify oxidative stress by an increase in TAC, and a decrease in lipid peroxidation; that could be considered as a preventive strategy in hemodialysis patients

Keywords: Antioxidant capacity, lipid peroxidation, lipid profile, vitamin E, hemodialysis.

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Introduction

Dyslipidemia and lipid oxidation are well known risk factors of cardiovascular disease (CVD). The generation of free oxygen radicals is a major pathogenic factor for tissue damage in many clinical conditions.[1] It is generally thought that uremia and dialysis are responsible for the imbalance between formation of reactive oxygen species and antioxidant defense systems, that results in oxidative stress in these situations.[2-5] The antioxidant reserve in uremic patients is also significantly lower than in normal subjects.[6] Among the proposed causes of atherogenesis and CVD, oxidative stress during hemodialysis is regarded as one of the critical determinants.[7] Attempts to improve the patients prognosis with antioxidant therapy has been made in the general population and in patients with renal disease.[8] Vitamin E is an effective chain-breaking lipid-soluble antioxidant in biologic membranes and has been widely used in the defense against oxidative stress.[9,10] Long-term supplementation of vitamin E reduced ex vivo low-density lipoprotein(LDL) oxidizability and in vivo lipid peroxidation level.[11] Beneficial effects of vitamin E administrated orally have also been suggested

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in hemodialysis or peritoneal dialysis patients.[12,13] However, the results of clinical trials have not been so consistent with result from routine use of vitamin E supplements in the general population and particularly in hemodialysis patients. Therefore we investigated thelipid-lowering effect and also the protective effect of vitamin E on oxidative stress markers and prevention of lipid peroxidation in the patients on maintenance hemodialysis, to verify the beneficial effect of this vitamin, specifically in hemodialysis patients.

Materials and Methods

The study group consisted of 26 uremic patients (10 women and 16 men),16-68 years of age undergoing maintenance hemodialysis three times a week (12 hours/week), lasting 6-108 months, at Vali-e-Asr Hospital in Birjand (Iran). All dialysis patients underwent therapy with oral vitamin E, 400 mg daily for 90 days. The studies were approved by the Local Institutional Review Committees and all subjects gave informed consent and participated in the study voluntarily. Fasting blood samples (10 ml) were collected in heparinized tubes in the morning just before dialysis. Plasma samples were separated and stored at -70°C.

Determination of the total antioxidant capacity (TAC) was performed by FRAP assay. The procedure described by Benzie and Strain was followed[14] the method is based on the reduction of a ferric-tripyridyltriazine complex to its ferrous, colored form in the presence of antioxidants. Aliquots of 50 µl plasma were mixed with 2.5 ml FRAP reagent and the absorbance of reaction mixture at 593 nm was measured spectrophotometrically after incubation at 37°C for 10 minutes. Standard curve was prepared using different concentrations (100-1000 µmol/l) of $FeSO_4.7H_2O$.

Thiobarbituric acid reactive substances (TBARS) assay for lipid peroxidation was conducted. Plasma TBARS were measured as an index of lipid peroxidation using the method as described by Satoh.[15] Malonyl dialdehyde (MDA), an end product of fatty acid peroxidation reacts with TBA to form a colored complex that has maximum absorbance at 532 nm. Briefly, plasma samples were mixed with trichloroacetic acid (20%) and the precipitate was dispersed in H_2SO_4 (0.05 M). TBA (0.2% in 2 M sodium sulfate) was added and heated for 30 minutes in boiling water bath. TBARS adducts were extracted by n-butanol and absorbance was measured at 532 nm. Tetramethoxypropane solution was used as standard. TBARS level of plasma was expressed as µmol/l.

Cholesterol and triglyceride concentrations were determined using standard enzymatic spectrophotometric methods and high-density lipoprotein-cholesterol was determined after separation with phosphotungstic acid and magnesium chloride, all using established kit methods from Pars Azmoon, Tehran, Iran. Low-density lipoprotein cholesterol was calculated by Friedwald formula. All data were analyzed using SPSS statistical software (version 10.0). The paired t-test was performed when comparing the mean of two groups and the results are given as mean ± standard deviation (SD). P values less than 0.05 were considered as significant.

Results

Mean age, weight, and duration of hemodialysis therapy were 47.9±13.1 years, 58.3±10.7 kg, and 17.9±9.8 months, respectively. Vitamin E supplementation 400 mg per day for 90 days caused a significant decrease in the TBARS level as a marker for lipid peroxidation (P<0.001). Determination of the TAC by FRAP assay shows a significant increase in total antioxidant status of plasma by vitamin E supplementation (P<0.01). Although there was a decrease in the level of all lipid profile components, there were no st-

TABEL 1. Oxidative stress markers and lipid profile changes before and after vitamin E supplementation in hemodialysis patients.

	Before (mean±SD)	After (mean±SD)
Oxidative stress markers		
TBARS (µmol/l)	2.97±0.52	2.55±0.44*
TAC (µmol/l)	1252.1±348.2	1398.3±372.0*
Lipid profile		
TG (mg/dl)	152.2±47.4	135±51.7
Chol. (mg/dl)	188.5±33.1	176±30.9
LDL-C (mg/dl)	130.3±27.9	121.5±26.3
HDL-C (mg/dl)	27.6±11.9	25.9±12.0

TG: Triglyceride
Cho: Cholesterol
LDL-C: Low Density Lipoprotein Cholesterol
HDL-C: High Density Lipoprotein Cholesterol
*Significant P value <0.05

atistically significant differences in means of cholesterol, triglyceride, high-density lipoprotein and low-density lipoprotein, before and after vitamin E supplementation among patients (Table 1).

Discussion

The main results of this study were a significant decrease in the lipid peroxidation levels and an increase in the TAC of plasma after vitamin E supplementation for 90 days in hemodialysis patients. There are similar results from specific interventions introduced to reduce oxidative stress in hemodialysis patients. A study conducted on 36 uremic patients administered oral vitamin E 600 mg/daily for 14 weeks demonstrated a significant increase in glutathione peroxidases (GSHPx) and superoxide dismutase (SOD) activities and a decrease in TBARS concentrations.[16] In a placebo-controlled study that was performed on 34 hemodialysis patients, vitamin E was administered 300 mg/day for 20 weeks. A significant decreasing effect was seen on lipid peroxidation in patients on hemodialysis.[17] Bayes et al. showed that oral administration of vitamin E , 400 mg at the end of each hemodialysis session for 3 months was associated with a significant decrease in malonyl dialdehyde (MDA) concentration.[18] Cristol et al. demonstrated that oral vitamin E, 500mg/d, for 6 months progressively decreased MAD concentration, suggesting diminution in oxidative stress of lipid.[19] Giardini et al. applied vitamin E therapy to 19 hemodialysis patients and observed a decrease in MDA.[20] Inal et al. also reported a significant decrease in MDA level by oral vitamin E therapy (200 mg/d) during 10 months.[21] It was also showed by Miguel A et al. that oral vitamin E supplementation causes a significant decrease in the oxidative susceptibility of low-density lipoprotein.[22] The SPACE trial tested the efficacy of vitamin E (800mg/d) on a combined cardiovascular end-point in 106 hemodialysis patients with preexisting CVD and showed a significant benefit from vitamin E supplementation.[13] Galli et al. showed that oral supplementation of vitamin E, 800mg/d for a period of 3 weeks slightly but not significantly decreased TBARS levels.[23] A significant decrease in TBARS concentration was observed after 14 weeks oral supplementation of vitamin E in a dosage of 600 mg/d by Belma G et al.[24] These results suggest that oral administration of vitamin E can protect against oxidative stress resulting from hemodialysis. This effect seems to be dependent on dose and duration of vitamin supplementation.

Determination of the TAC by FRAP assay in our study showed a significant increase in antioxidant status of plasma by vitamin E supplementation. In a wide variety of studies, it has also been demonstrated that short- and long-term vitamin E administration can reduce the circulating determinants of oxidative stress in chronic renal disease patients.[25-27]

Although there was a decrease in the level of lipid profile including high-density lipoprotein in our study, there was no statistically significant difference for means of cholesterol, triglyceride, high-density lipoprotein and low-density lipoprotein, before and after vitamin E supplementation among patients. Khajehdehi P tested the effect of vitamins on the lipid profile of patients on regular hemodialysis and showed that high-density lipoprotein increased and the ratio of low-density lipoprotein to high-density lipoprotein decreased significantly after vitamin E therapy.[28]

Chapkin RS et al. in one study suggested that short-term high-dose vitamin E ingestion is unlikely to benefit the majority of renal patients on maintenance hemodialysis in regards to their circulating levels of high density lipoprotein.[29] Howard DR et al. was also documented no significant change in serum high-density lipoprotein with vitamin E therapy.[30] The results from recent studies suggest that vitamin E supplementation may be an effective accessory to combat lipid oxidizability in hemodialysis patients.[31]

In conclusion, although there was no lipid-lowering effect of oral vitamin E supplementation in patients with chronic renal failure on maintenance hemodialysis, our results indicated that oral vitamin E supplementation might be able to modify oxidative stress by an increase in TAC, and decrease in lipid peroxidation that could be considered a preventive strategy in hemodialysis patients.

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